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127 Mr Geoffrey Kong
128 Professor Michael Parker

SVI
ST VINCENT'S INSTITUTE
~ continuous discovery

Continuous Discovery

At St Vincent's Institute we believe that medicine is constantly evolving to improve human longevity, health and well–being.

St Vincent's Institute research is focused on exploring both disease cause and prevention, with a commitment to discovering practical and far–reaching solutions to diseases that impact on the everyday life of people around. SVI conducts programs of basic and clinical research into diseases that have a high impact on the community.


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The Institute is a world centre of excellence for medical research in the following areas:

Juvenile diabetes; Metabolism-obesity and cardiovascular disease; Bone diseases such as arthritis and osteoporosis; Cancers (particularly those that spread to bone); Structural biology – 3D study of proteins at the atomic level; Protein Chemistry – studying the end product of the cell's genetic message; Neurological diseases including Alzheimers' disease and epilepsy.

St Vincent's Institute is an independent research body, which is affiliated with St Vincent's Health and the University of Melbourne. Through these links its research programs provide a valuable service to clinical medicine, graduate education and community welfare. St Vincent's Institute hosts the National Serology Reference Laboratory and is a member of Bio 21, the Victorian Breast Cancer Research Consortium, St Vincent's Diabetes Centre of Excellence and the Association of Australian Medical Research Institutes. It is a member institution of Australia-wide health care facilities of the Sisters of Charity.

2005 Pehr Edman Lecture

In June, Sir Peter Morris AC FRS FRCS presented the annual Pehr Edman Lecture, which honours the memory of SVI's founding Director. He presented a fascinating and informative lecture outlining the history of transplantation from the first kidney transplant in 1954. He also talked about pancreatic islet transplantation, groundbreaking work being conducted in specialist centres worldwide to treat patients with type 1 diabetes. During the evening Sir Peter, a graduate of St. Vincent's Hospital and chairman of the British Heart Foundation and Emeritus Nuffield Professor of Surgery at Oxford University, also launched the Tom Mandel Islet Transplant Program. This program is a Melbourne-wide, multi-disciplinary collaboration that will include participants from St Vincent's Institute, St Vincent's Hospital Melbourne, Austin Hospital, and the Centre for Blood Cell Therapies at the Peter MacCallum Cancer Centre. The aim of the program is to bring islet transplantation to people with type 1 diabetes who live in Victoria, Tasmania and South Australia, and investigate ways of improving the survival of transplanted cells. The program is named in honour of Dr Tom Mandel, who was an internationally recognised Australian pioneer in the field of pancreatic islet transplantation.

Major prizes and awards

NHMRC grant success

Project, Special Programs and Fellowship funding starting in 2006 were announced by the NHMRC in October 2005. The Institute was extremely well represented being 12th highest recipient of funds, and the fourth placed independent research Institute with income directed solely to the Institute (behind WEHI, QIMR, and the Baker Institute). If the list were viewed as income per researcher, the Institute would have been at the top of the table.

Grant recipients were:

- Dr Jörg Heierhorst, two 3-year project grants to study DNA damage, chemotherapy and cancer; and sites of cellular DNA repair.
- Professor Bruce Kemp, Dr Belinda Michelle, Dr Greg Steinberg and Dr Bryce van Denderen, 3-year project grant on AMPK in obesity.
- Professor Michael Parker, two 3-year project grants to study bacterial toxins as the basis for design of new antibiotics; and proteins involved in cancer and allergy.
- Professor Bruce Kemp, 5-year Medical Bioinformatics, Genomics and Proteomics Program grant for the study of metabolic and exercise markers for sedentary and trained individuals.

Five-year Fellowships were awarded to:

- Associate Professor Robyn Starr, Senior Research Fellowship
- Associate Professor Duncan Campbell, Senior Research Fellowship
- Dr Natalie Sims, Senior Research Fellowship
- Dr John Price, RD Wright Biomedical Career Development Award

It is also pleasing to note that two individuals (Dr Ora Bernard and Dr David Izon) joining SVI in 2006 were successful in gaining project grants, and Dr Bernard was also successful with her Principal Research Fellowship application.

Sylvia and Charles Viertel Senior Medical Research Fellowship

Dr Robyn Starr was awarded a prestigious Sylvia and Charles Viertel Senior Medical Research Fellowship in 2005.

Charles Viertel was one of eleven children in a poor family in Queensland. He became a lifelong high achiever, believing in helping those who helped themselves. He left an estimated $60m in a discretionary trust upon his death in 1992.

The Viertel Charitable Foundation aims to make a difference to medical research in Australia. It also recognises the need for career research fellowships which bridge the gap between post-doctoral studies and career research positions.

01 A/Prof Robyn Starr
02 Prof Michael Parker in the ACRF Facility

The flagship award of the Sylvia and Charles Viertel Charitable Foundation is the Senior Medical Research Fellowship. These five-year fellowships, totalling $825,000, provide both salary and project grant support for outstanding Australian medical researchers. Only two of these highly prestigious and competitive Fellowships are awarded each year.

Robyn Starr is the head of the Signal Transduction group at SVI. She has been awarded this Fellowship to continue her research into the role of SOCS proteins in the body. SOCS proteins act as 'stop signals' to turn off messages delivered by cellular messengers known as cytokines. Cytokines send signals to cells to change their behaviour in response to changes in their environment, such as the presence of infection. Cytokines are highly potent signals that need to be under tight control, and often they can be overproduced during disease, leading to inflammation.

Australian Cancer Research Foundation support for drug discovery research

On 25 May 2005 St Vincent's Institute and the Australian Cancer Research Foundation (ACRF) signed an agreement awarding a grant of $900,000 for the purpose of funding the establishment of a new cancer research facility to be named "The Australian Cancer Research Foundation Rational Drug Discovery Facility." This completed a process, commenced 2004, of a two-stage submission to the ACRF for a substantial grant under their annual grants program for cancer research in Australia. An official opening will take place in 2006.

The ACRF is a national organisation which provides grants for infrastructure and equipment for the highest quality cancer research in Australia and whose funds are drawn solely from private sources. It deals nationally and exclusively with cancer research funding and is dedicated to helping find a cure for cancer through the continued support of world-class research in Australia.

This generous support will provide SVI cancer researchers and collaborators with state-of-the-art technologies crucial to the next generation of research activity, as well as providing a focus for the consolidation and development of research on the SVH campus and integral to biotechnology development of Victoria.

The Facility, located on the 1st Floor in the Structural Biology Unit, comprises a range of crystallography equipment including new Microfocus X-ray Generator and accompanying equipment which will enable more reliable and rapid data collection on smaller crystals in-house. Additional equipment comprises virtual screening technology in which we dock the structures of millions of commercially available compounds into our crystal structures using specialised computer software. Funds will also be invested in medium throughput technologies to test compounds generated at the virtual screening stage.

The compilation of the grant application was made by the chief investigators: Professor Michael W Parker and Associate Professor Matthew T Gillespie.

Proudly supported by the
Australian Cancer Research Foundation

Research Highlights

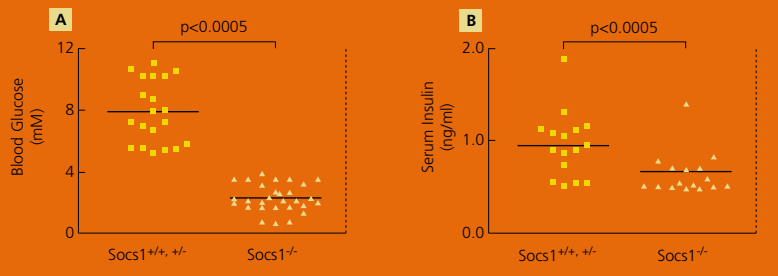
Improving the body's response to insulin

The protein suppressor of cytokine signalling-1, discovered by Robyn Starr and her colleagues, has had implications for many areas of understanding the function of cells in the body. SOCS-1 is a "stop signal" that prevents cells from over-responding to hormones and other proteins in the blood stream. Emma Jamieson and Mark Chong in the Immunology and Diabetes laboratory have studied the implications of this newly-discovered protein in diabetes. They noticed that mice made deficient in SOCS-1 by gene targeting developed low blood glucose readings and how this happens was then studied. One possibility was that the absence of SOCS-1 allowed a greater degree of insulin signalling than is seen in normal mice. Insulin is the main hormone that lowers blood glucose.

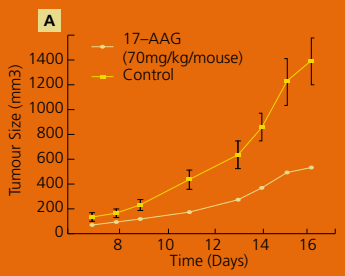
In conjunction with colleagues at The University of Melbourne and the Protein Chemistry and Regulation group at SVI the effect of the absence of SOCS-1 on insulin signalling was studied. It was shown that infusing insulin into SOCS-1-deficient mice (that requires expert mouse surgery and care) resulted in greater insulin action especially in the liver, one of the main insulin-responsive organs, but less so in muscles. This was confirmed by showing biochemically that the signalling proteins that insulin uses in liver cells had increased activity in SOCS-1 deficient mice. This information contributes to detailed understanding of how insulin works - which is particularly important for type 2 diabetes, a problem that has reached alarming proportions all over the world.

Detrimental effects of the cancer drug 17-AAG

Metastasis is a series of steps in which cancer cells leave the original tumor site and migrate to other parts of the body. It is the ability to spread to other tissues and organs that makes cancer a potentially life-threatening disease, so there is great interest in understanding what makes metastasis possible for a cancerous tumor. One gene we have recently identified that may be involved in enhancing the metastasis of cancer cells is Hsp90. We have determined that Hsp90 is increased in cancer cells that have a greater ability to spread to the bone in mouse models of metastasis. Interest in Hsp90 and its role in cancer metastasis has led to development of drugs that block its action.



> Severe hypoglycemia (**A**) and hypoinsulinemia (**B**) in neonatal mice lacking SOCS1

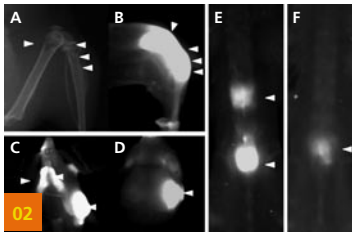


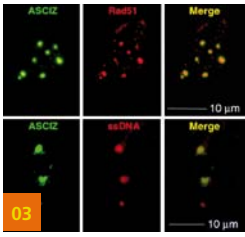
> (**A**) the incidence of bone metastasis to various sites as determined by fluorescent imaging. (**B**) 17-AAG treatment of mice that had been orthotopically inoculated with MDA-MB-231SArfp cells demonstrated a significant decrease in tumour growth compared to the control mice.

01 Model of the ILY pore

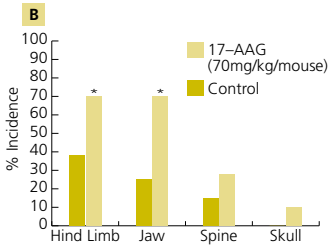
02 (**A**) X-ray analysis of osteolytic lesions (arrows) in the hind limb after 17-AAG treatment. Fluorescent imaging revealed the hind limb osteolytic tumour (**B**); and metastases to the (**C**) jaws, (**D**) skull and (**E**) spine of 17-AGG treated mice. (**F**) less numerous and smaller spine metastases in the control group

03 Colocalization of MMS-induced ASCIZ foci with RAD51 (top) and BrdU-labeled ssDNA (bottom) in single nuclei of GFP-ASCIZ-expressing U2OS cells





These drugs are currently being tested in cancer clinics in the USA and the UK. We have used one of these drugs, 17-AAG, to test whether Hsp90 has a role in cancer metastasis to the bones of cancer patients. We have found that, rather than blocking the spread of cancer cells to the bone, the drug actually enhances the process. It does this by inducing the loss of bone, making it easier for the cancer cells to establish and grow. Our findings will be of great importance in the development of future drugs directed towards Hsp90.



Insights into the action of bacterial toxins

The bacterium *Streptococcus intermedius* is a normal inhabitant of the mouth. However, under certain conditions it can travel to other parts of the body to cause deep-seated infections, particularly in the brain and liver. The bacterium secretes a toxin called intermedilysin, a major virulence factor of the organism. The toxin molecule is a member of a large family of bacterial toxins called cholesterol-dependent cytolysins. The Structural Biology Laboratory has determined the three-dimensional atomic structure of the toxin using the X-ray crystallography facility at SVI. The structure suggests that all cholesterol-dependent cytolysins will look very similar and provides the basis for a detailed understanding of how the toxin contributes to the infective properties of the bacterium. Most importantly, the structure also provides clues as to how drugs could be designed to stop intermedilysin contributing to bacterial disease.

A new way to maintain healthy DNA

Our chromosomes as keepers of our genetic blueprint are constantly damaged. Our cells have a large number of ways to keep the genome intact, but sometimes damage can go unnoticed. It is now clear that the failure to keep the genome intact is the main cause for the development of cancer, and also a main reason why we age. During the last year, researchers in the Molecular Genetics laboratory have discovered a new pathway for prevention of chromosome damage. We found that a new protein called ASCIZ plays important roles in the response to damage to the building blocks of our DNA by regulating the recruitment of the major repair protein RAD51 into tiny (1/1000 of a mm) repair factories in the cell nucleus. This cellular function is reminiscent of the BRCA2 protein that is defective in a large set of patients suffering from inherited breast cancer. However, ASCIZ seems to fulfill its function in a highly specific manner in response to lesions called DNA base methylations. Interestingly, some anti-cancer chemotherapeutics work by causing just such base methylations, indicating that ASCIZ could play a dual role both in prevention of spontaneous cancer development as well as a drug target to improve the effects of chemotherapeutics in cancer cells.

Report from the Director and Chair

The last year has seen the fulfilment of several years of planning and building at SVI. The new building is in its second full year of operation and continues to fulfil expectations of a much improved work environment and better facilities essential to our work. The BioResources Centre was also opened in 2005. Fund-raising efforts have continued to be successful thanks to the SVI Foundation. All of this culminated in one of the best recent years for success in NHMRC funding setting the stage for further substantial growth.

The BioResources Centre is a project that we have partnered with St. Vincent's Hospital and other campus-based groups for holding transgenic mice – one of the main enabling platform technologies of modern biomedical research. Mouse models of disease have been in use for many years but until recently they have played a relatively minor role because of the difficulty of exactly reproducing human diseases. Their importance and power has been transformed by advances in genetics, particularly the human genome project. There is now an enormous opportunity to use them to help identify the role of newly discovered genes in human biology and medicine. It is also possible to use these technologies to very closely reproduce human diseases, providing a powerful resource for drug discovery. The facility at St. Vincent's is special because the mice are housed in groups of 4-5 mice in physically isolated, air-conditioned cages. This not only increases the physical comfort of the mice, it also reduces the risk of infection. The State Government provided funding to link the facility with other similar facilities in Victoria to share knowledge and mouse strains. The facility therefore supports our ability to collaborate closely with the Hospital and with other research centres.

In last year's Annual Report, we described the important work of the SVI Foundation which raises money to support our activities including the careers of young scientists, new initiatives and state-of-the-art equipment. In 2005, the Foundation was especially active in supporting the careers of three new PhD students – Michelle Kouspou, Nirupa Satchithanandan and David Ascher. These are three highly talented post-graduate students who are very deserving of support. We all truly appreciate the Foundation's support and acknowledge the great contribution it makes. We also acknowledge the strong support we continue to receive from Charitable Trusts and Foundations that play such an important role in Australian medical research.

The details of the results of our applications to NHMRC will be highlighted elsewhere, however in 2005, SVI scientists were remarkably successful in this very competitive system. In this last round, Dr Jörg Heierhorst was especially successful being awarded two project grants. Jörg and his group have discovered new proteins that contribute to the repair of DNA – a process that can lead to the development of cancer if it is imperfect. Additionally new staff members coming to the Institute fared well in the system including Dr Ora Bernard who was awarded a Principal Research Fellowship, Dr Natalie Sims who received a Senior Research Fellowship, and Dr David Izon who was awarded a Project Grant.

Overall, medical research in Australia has had a very positive year with the award of the Nobel Prize to Warren and Marshall and the widespread interest in the human papilloma virus vaccine developed by Ian Frazer at the University of Queensland.

We are now at the end of the 5-year doubling in funding from NHMRC – a welcome initiative of the Federal Government that arose from the Wills Report into the NHMRC. SVI increased its funding from NHMRC over this time by about 3-fold. Nevertheless as we look ahead, with no further increases in the total NHMRC support announced as yet, NHMRC grants will become even more competitive, particularly for young scientists starting their careers. Medical research will need to secure future increases in Government support as well as looking as broadly as possible for other sources of funding.

An increase in Federal Government support came through the NHMRC IRIS scheme support for infrastructure. This means that the indirect operating costs associated with a research project, such as administration, are supported so the award itself can be invested directly in research. This form of funding is essential for an Institute like ours. Infrastructure support also comes from the Victorian State Government which has been a leader nationally in recognising the need for it and for its equitable distribution. The support of the Victorian Government, and the more recent Federal support, is very gratefully acknowledged.

Our funding increases and improved facilities are very positive developments that position SVI well for future growth. The perfect size for a research institute to capture creativity and to be resourced optimally remains debatable. There is no doubt, however, that the support of Governments and the community has created a vibrant research environment at SVI that will produce health benefits for the entire community.

Chair
BM Shanahan

Director
TWH Kay

Members of the Board

Ms Brenda Shanahan
BEc BCom Melb
Chair, St Vincent's Institute
Non–Executive Director, JM Financial Group

Mr Douglas A Wright
FAICD
Deputy Chair, St Vincent's Institute
Managing Director, Wrights

Ms Susan M Alberti
AM
Managing Director of DANSU Group and associate Companies

Mr Jeff Clifton
BCE DIPCe
Consultant, Clifton Coney Group

Professor James A Angus BSc PhD FAA
Dean, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne

Mr Charles A Griss
FCPA FCA FAICD
Until 16th May 2005
Mr Griss joined the St Vincent's Institute Board in 1998 and was an extremely valuable member of the Board. He was the Chair of the Institute's Audit & Finance Committee at the time of his resignation in 2005. Mr Griss was also Chair of the Board sub-committee for SVI redevelopment.

Professor James D Best
MD BS FRACP FRCPath
Professor and Head of The University of Melbourne Department of Medicine, St. Vincent's Hospital, Melbourne

Sister Mary Fankhauser
RSC BapplSci (Nursing Admin) GradDipCommunityHealthNursing ClinPastoralCare Cert
Sisters of Charity Community Care Program

Ms Nicole Feely
BCom LLB FAICD
Chief Executive Officer, St. Vincent's Health

Mr Ian D Reid
BE (Chem) ASA FIEAust MAICD
Until 16th May 2005
Mr Reid served on the Institute's Board of Directors and its Audit & Finance Committee. He was Chair of the Board from May 2000 until April 2003. Mr Reid retired from the Board during 2005 but remains on the Audit & Finance Committee. Mr Reid was a member of the Board sub-committee for SVI redevelopment.

Mr Barry J Jackson
Bcom (Hons) MAICD
Director, Paperlinx Ltd, Alesco Corporation Ltd, Equity Trustees Ltd and CSR Ltd.

Professor Thomas WH Kay
MBBS PhD FRACP FRCPA
Director, St Vincent's Institute

Mrs Ruth O'Shannassy
BCom

Mr Michael McGinniss
BCom (Hons) MEc
From 16th November 2005
Mr McGinniss retired from a senior position as a partner with PricewaterhouseCoopers, Chartered Accountants, in 2000. Since then he has taken up a number of Board positions in the not-for-profit and commercial sectors and also serves as a Trustee of the Marian and EH Flack Trust.

Mr G John Pizzey
BE (Chem) Fell Dip Management
Company Director

Mr Gregory J Robinson
BSc (Hons) MBA
Project Director, Corporation Alignment, BHP Billiton Limited

St Vincent's Institute Foundation Board

Ms Susan Alberti AM

Chair, SVI Foundation

Ms Alberti is co-founder and Managing Director of the DANSU Group. She has a strong commitment to fund raising and promotion of juvenile diabetes, and is the National President of the Juvenile Diabetes Research Foundation Australia and International Board Member of JDRF based in New York. She was recently appointed as Inaugural Chair of the St Vincent's Institute Foundation and is a Board Member of St Vincent's Institute.

Mr Robin Berry

Deputy Chair, SVI Foundation

Mr Berry has a background in the apparel and footwear industry. He has experience in marketing, manufacturing and importing of branded sports and leisure products. He is a partner of a business designing and marketing branded surf apparel, footwear and hardware products.

Mr Benni Aroni

Mr Aroni was Managing Partner of his own legal firm between 1982 and 1998, and has been Developers Representative of Eureka Tower from 1998 to date. He was Vice President of JDRF Victoria between 1993 and 1998 and National Vice President from 1995. He is and has been a Board Member on several companies, listed and unlisted.

Mrs Christine Tarascio

Mrs Tarascio's family companies are Salta Properties Ltd/Westgate Logistics. Christine has been a very active fundraiser for various causes over a long period of time. They include the Lady Mayoress' Charitable Fund, the Queen Elizabeth Centre, PMB (raising funds for prostate cancer research), and Pampering Patients. Christine is currently assisting the family company with the redevelopment of the former Mercy Hospital.

Mrs Claire O'Callaghan

A St Vincent's trainee, Mrs O'Callaghan returned to part time nursing once her five children were in full time education. She has chaired a number of fund raising and educational organisations including the original Noah's Ark Toy Library for Handicapped Children. She is currently Chair of the St Vincent's Institute Support Group.

Ms Marcia Griffin

Ms Griffin was CEO of Pola Cosmetics and a former Victorian Telstra Business Woman of the Year. Current roles include Directorships of PMP Limited and National Pharmacies, as well as a position as a TEC Chair. Marcia is an author of a Business Biography "High Heed Success". She is motivational speaker and Marketing Consultant.

Mr Martin Ralston

Mr Ralston was born in Melbourne and is married with two children. Martin graduated in 1968 with a Bachelor of Economics and spent most of his working life involved with Information Technology. He worked for BHP Computer Accounting Services, then Accenture (formerly Anderson Consulting). Martin was a partner with Accenture from 1985 until 2001 when he retired. He is currently the Treasurer of the Moonee Valley Racing Club, non-Executive Chairman of Transol Corporation and Vice-President of the Hawthorn Football Club.

Mr Andrew Wraith

Mr Wraith is a former senior manager of Shell Australia. He has over 25 years experience in manufacturing, supply and trading, logistics and retail operations including six years working overseas in South Africa and the Netherlands.

Ms Connie McKeage

Ms McKeage is a financial services specialist with many of Australia's premium financial services companies as clients. Connie has also held key executive positions with organisations such as Bankers Trust Australia (BT), Rothschild Asset Management and Perpetual Funds Management (Deputy Managing Director). She has also spent considerable time working in Asia, Canada, Europe and the USA, where she held the position of Managing Director Global Operations for NewRiver Communications. In 2003 Connie was awarded a Centenary Medal for her contribution to Australian Society in the area of Business Leadership.

Mrs Karen Plant

Mrs Plant is a qualified Interior Decorator. Together with her husband Barry they established Barry Plant Doherty Real Estate which now boasts over 60 offices throughout Melbourne and country Victoria. In conjunction with her business commitments Karen has been heavily involved in charitable work for many years. Karen is currently a council member of Camberwell Girls' Grammar School, is a member of the 'Invest in Carey' council at Carey Grammar School. Karen is also a Member of the Chancellor's Circle of Deakin University and a board member of the REIV Foundation.

Ms Danielle de Capele

Ms de Capele, lives in Monaco where she is an organiser of international events and is on the board of various charitable organisations. She travels extensively within Europe and the USA and spends 3 months of the year in Australia.

Mr Jonathon Rowe

Mr Rowe is a founding member of The Loop Agency, a leading creative marketing company. Prior to this he was a Director of Clemenger BBDO, Managing Partner of Publicis Mojo, and is a specialist in communications strategy and effectiveness. He holds an Economics degree, and has studied strategy planning and management in New York and London. After graduating, Jonathon studied the German language in Munich at the Goethe Institute.

Mr Sam Tarascio

Mr Tarascio gained experience with Coopers and Lybrand, then with Jones Lang Wootton before moving in 1999 to the family company Salta Properties, with responsibility for management of the property investment portfolio.

Sam is now Managing Director of Salta Property Group and sits on the Executive Management Committee of Westgate Logistics. More recently Sam has become a Director of Pentacle Property Funds Management Ltd.

Ms Brenda M Shanahan

BEc BCom

Chair, St Vincent's Institute

Non-Executive Director, JM Financial Group

Mr Douglas A Wright

FAICD

Deputy Chair, St Vincent's Institute

Managing Director, Wrights

Professor Thomas WH Kay

MBBS PhD FRACP FRCPA

Director, St Vincent's Institute

St Vincent's Institute Foundation

SVI Visits the Harbour City

The first Sydney function of the SVI Foundation was hosted by Connie McKeage, SVI Foundation Member, in June 2005 at the Sydney Park Hyatt. Over 60 guests enjoyed the harbour view whilst listening to Tom Kay, Director, and Associate Professor Robyn Starr outline the important contribution researchers play, not only in disease management but also in the fight for a more enduring quality of life.

The hit of the evening however, was the maiden speech make by Michelle Kouspou, a PhD Student at the Institute and an SVI Foundation Scholarship winner. Her Scholarship sponsors, Connie McKeage and Michael Cole, were in attendance and saw first hand the importance of sponsoring talented students through their PhD program.

As a result of the evening, interest has been generated in both the SVI research programs and the SVI Foundation Student Scholarship Program.

SVI Welcomes New Young Professionals Support Group

The YSVI (Young St Vincent's Institute) Group was formed following a cocktail party at SVI, sponsored by Hall & Wilcox, where 60 young professionals met scientists and toured the Institute.

This enthusiastic young group then organised an Inaugural Cocktail Party on 14th October sponsored by and held at Doncaster BMW. Guest speaker, Dr Rachel Mudge of SVI, introduced many of the guests to the work of the Institute for the first time. The Cocktail Party was a very successful evening generating funds and interest amongst a young vibrant section of the community.

The YSVI Group is planning more events and we extend our thanks to group members for their interest and look forward to working with them in the future.

'Continuous discovery' needs continuous support

YSVI

SVI

SVI Support Group

The SVI Support Group, led by Claire O'Callaghan, has again been actively fundraising and helping to raise the profile of the Institute. The Group held a very successful Black Tie Dinner at The Australian Club in October 2005 at which Brenda Shanahan, Chair and Tom Kay, Director of SVI addressed the gathering.

David Ascher, who is undertaking his postgraduate scholarship at SVI, spoke to the guests about his research. His enthusiasm towards what he hopes to achieve at SVI was evident and encouraged the guests in the room to financially support SVI.

The target for the night was to raise the necessary funds to sponsor a student or students under the SVI Foundation Scholarship Program. The Group was very pleased to have achieved this goal and are now the official sponsors of three talented Honours Students: Angela Tam, Matthew Bird and Sarah Jones.

SVI greatly appreciates the ongoing support received from this hard working Group and looks forward to having their assistance again next year.

SVI Foundation Student Scholarship Program

The SVI Foundation generously supported a new initiative to promote SVI as an excellent research institute for postgraduate training. The Foundation has pledged to secure funding from either corporate or individual sponsorship, for awards of $5,000pa for three years to outstanding students who commence their PhD studies at SVI.

To be eligible for these awards, students are required to have obtained their own PhD scholarship from the Commonwealth Government or Melbourne University, and have committed to commencing a PhD at SVI. The successful applicants are selected on the basis of academic merit and research experience.

The Foundation aims to support at least two new postgraduate students per year, however the response to this initiative was overwhelming and we were delighted to have been able to offer awards to three students beginning their studies in 2005.

The SVI Foundation Award recipients for 2005 are:

- Mr David Ascher, sponsored by Major Engineering and supervised by Professor Michael Parker;
- Ms Michelle Kouspou, Sponsored by Ms Connie McKeage and Mr Michael Cole and supervised by Dr John Price; and
- Dr Nirupa Sachithanandan, sponsored by DANSU Constructions and supervised by Professor Tom Kay.

We congratulate these outstanding students and thank their sponsors for their generous support.

01 Students from Carey Baptist Grammar
02 Barry Plant with Pot Pourri

"An Enchanted Evening"

SVI Foundation held their second Gala Dinner, *"An Enchanted Evening"*, on 2nd April at the Park Hyatt. 400 guests were welcomed by Sue Alberti AM, SVI Foundation Chair, Tom Kay, SVI Director and Benni Aroni, SVI Foundation Board Member.

Special guest speaker, The Hon Julie Bishop MP, Minister for Ageing and Member for Curtain, spoke with passion about the importance of medical research and the significant achievements SVI scientists have made to date.

Mr Steven Skala, Vice Chairman Australia & New Zealand, Deutsche Bank AG, major sponsor of the evening for the second year running, spoke of Deutsche Bank's commitment to SVI and encouraged other guests to become involved with such a prestigious medical research facility.

Barry Plant of Barry Plant Doherty was a fabulous MC and Pot-Pourri entertained the guests in spectacular and elegant style with their repertoires from stage and screen.

The night was a huge success, resulting in over $200,000 net being raised. We are indebted to our sponsors and guests who supported SVI.

Palace Cinemas

Mr Antonio Zeccola, Founder and Managing Director of Palace Cinemas Films, a Trustee Donor of SVI, has committed to donating five Palace Films for promotion as fundraising events. The second promotion event "Harry Potter & The Goblet of Fire" was well attended with net proceeds donated to SVI. We are grateful to Antonio and look forward to working with the team at Palace to ensure the success of this project.

PALACE CINEMAS

Yering Station

Yering Station had another stellar year winning many prestigious wine awards. 2005 was also the fifth year Yering Station has provided a choice of some outstanding wines for our SVI Wine Promotion. SVI supporters took the opportunity to purchase these wonderful wines whilst knowing that their purchase is assisting the Institute to continue its excellent research. We again thank Tom Carson, Nadège Suné and the staff of Yering Station for their continued support.

YERING Station

Director's Dinners

The highly successful Director's Dinners series continued during 2005. These Dinners are a relaxed and informal way of introducing the work of SVI to guests as well as providing an excellent opportunity to hear distinguished speakers, including:

The Hon. Kevin Andrews MP, Minister for Employment and Workplace Relations

Margaret Rohan Kelly – Author

Christine Nixon APM, Police Commissioner

The Hon. Dr Philippa Malmgren, President of Canonbury Group

Andrew Demetriou – Chief Executive Officer, Australian Football League

SVI would like to thank, Peter Crinis, Executive General Manager, at Crown Towers for his continued support of the Director's Dinner series.

CROWN TOWERS

> Sponsors of 'An Enchanted Evening"

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SVI 1000 Club

'Continuous Discovery' through the SVI 1000 Club

Permit me please to remind you that your membership to the SVI 1000 Club directly assists St Vincent's Institute to continue and maintain its international standard of medical research right here in Melbourne. Thanks in no small part to the efforts of the SVI Foundation and our Club the researchers continue to achieve extraordinary results and SVI enhances its stature in the elite research and clinical communities. Every 1000 Club Member is a valued part of the SVI Network focused towards "continuous discovery".

Funds raised by your membership are applied toward the vital research being undertaken by the scientists at SVI who focus on exploring disease causation, prevention, treatment and cure. Their commitment to discovering practical and far-reaching solutions to diseases that impact on the everyday life of people around the world, deserves our emotional and financial support.

We currently have over 260 members many of whom have renewed their membership a second or third time. Events due in the second half of 2006 should significantly increase these numbers but ideally I encourage members to generate further members. There are many good people out there wanting to contribute but not knowing how. Take yourself and them for a tour of our laboratories, have them meet our researchers – all doubts will evaporate.

If you would like to undertake a tour, renew your membership and are not sure of the date you joined, or just have any contribution or thought you would like to share please contact SVI on 9288 2480 and we will assist.

Members of the Club have opportunities for networking whilst at the same time contributing to a charitable organisation. Membership is fully tax deductible.

I would like to thank all the members for their continued support. Some extraordinary events are planned for 2006 and I very much look forward to sharing these with you.

Benni Aroni
Chair of SVI 1000 Club

1000 Club

Abdallah, J & C
Abdallah, T & S
Aitken, B
Alberti AM, S
Alfonso, E
Allen, J
Almslock Pty Ltd
Alpins, N & S
Anderson, D
Aroni, B & Kaldor-Aroni, R
Barberis, J
Barro Group, The
Barro, R
Basser, I & M
Beck, M
Beever, J
Bennett, R
Berry, R
Best, J
Bloom, B
Bloom, N
BNP Paribas Securities Services
Bongiorno, A & A
Bongiorno, J & E
Bovis Lend Lease Sub-contractors
Bowness, WD
Breheny, M
Brown, RV
Brown, SV
Burgess, A
Burkett, D
Bursztyn, P & J
Carew, J
Caro, R
Carson & McLellan PPB
Carson, I
Carson, T & Suné, N
Casper, M & C
Castello, S & N
Caulfield, G
Chappell, J
Chojna, H
Ciconte, A & L
Clancy, W & C
Clarke, B
Clifton, J
Clifton, S
Cole, M
Colman, J
Colorpak Packaging
Commins, C
Commins, H
Conn, WJ
Coote, M
Crinis, P
Curlewis, D
Dale, G & R
Danos, T & E
d'Apice, T & C
de Capele, D
de Gruchy, D
Demediuk, F
Demediuk, N
Deutsche Bank AG
Dougherty, H
Dwyer, M
Dwyer, P & Happell, C
Elliott, M & P
Emergency Care SVH
Emerson, APR
Evans, D
Ezard, T & Stefanou, T
F & J Ryan Foundation
Fanning, M
Fedele, T
Five Oceans Asset Management Pty Limited
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Foti, M
Fowler, M
Fried, T
Fried, E
Frost, R
George Castan Family Charitable Trust
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Gillespie, M
Goh, D
Gold Age Pty Ltd
Goldbloom, L
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Greene, T
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Griss, C & A
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Grogan, D & J
Grogan, M
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Guest, A & E
Gurry, JF
Gutman, J & J & Family
Hale, G
Hall, J & S
Halliday, S
Harcourt, T
Hardy Brothers Jewellers
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Hart, L & C
Heath, WC (Dec)
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Hogarty, E
Holyoake, P & M
Hummerston, EJ & AM
Iacobucci, M
Isaac, JN
Iseli, A & C
Jackson, B
Jelinek, M
Johnstone, A & J
Jolson, C
Jones, WMP
Katsanevakis, C & D
Kay & Burton
Kay, C
Kay, T
Kelly, AP
Kelly, P
Kemp, B
Kerr, L
Kerr, M
Kerr, V
Kirby, R
Kopke, P & L
Kostos, K
Kozica, W
Leigh, P & G
Lempriere, J
Liberman, H
Losa, D
Lowe, D
Lowe, R
Mahemoff AO, J & Mahemoff, H
Mahlab, F & Mahlab AO, E
Marne Development Pty Ltd
Marriner, D & E
Martin AO, J
Martin, S
McGuire AM, E & McGuire, C
McHale, G
McHale, J
McLennan, G
McNamee, B
McNamee, V
McNaught, G
McNulty, M
McPhail, B
McPherson, J
Meadows, P & Cross, P
Meltzer, F & W
Michael & Andrew Buxton Foundation, The
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Michelmore, A
Millen, R
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Molan, M & M
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Mullen, K & J & Family
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Needham, B
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NM Rothschild & Sons (Australia)
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O'Callaghan SC, DJ
O'Callaghan AO, B
O'Callaghan, C
O'Day, J & S
Oliphant, DJ
O'Shannassy, M & R
Otter, G & D
Palace Cinemas
Papas, J
Papházy, J
Pearce, M
Pellicano, N & A
Pinches Consolidated Industries P/L
Pizzey, J & B
Plant, B
Plant, K
Polson, P & R
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Power, T & D
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Ralston, M & J & Family
Red Rock Leisure
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Rodas, M & T
Rowe, J
Rush, B
Rush, G & Menelaus, J
Russel, P & S
Russo, S
Rutman, L
Ryan, F & J
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Salter, W
SapphireOne Pty Ltd
Savas, R & K
Savvides, G
Sax International Pty
Schillier, P & J
Scott, P & O
Shanahan, A
Shanahan, B
Shanahan, C
Signorino, F
Simpson, A
Skala, L
Skala, S
Slatter, M & C
Slattery, P
Smith, C
Smith, P & T
Smorgon OAM, D & Smorgon, R
Smorgon, T
Smorgon, V
Solomon, Q & E
Southwick, G & S
Spry-Bailey AO, P
Spry-Bailey, P
Stapleton, M
Steven, J
Stooke, K
Stops, W
Strategic Advantage Pty Ltd
Strategic Advantage Pty Ltd (2)
Stubbs, C & C
Swaney, S
Tabak, L
Tarascio, L
Tarascio, S & C
Tashi, R
Thomas, C & C
Thurin, D & L
Tuckfield, PC
Turner, J
Turner, R
Verdnik, A
Vermont Cancer Research Fundraising Group
Watson, B & Le Maistre, E
Wellington, C
Westmore-Peyton, C
Whitehead, M & M
Whiting, N & T
Wilkie, R & L
Wilson, P
Wright, D
Xipell, J
Xipell, T
Yencken, T & M
York, G
Young, C
Young, D
Young, D
Young, H
Yu, MK
Zagame Hotels

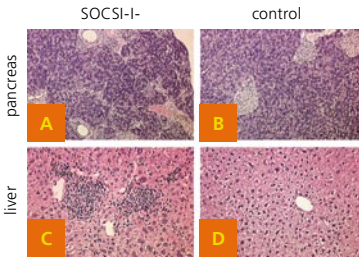
Immunology and Diabetes

Thomas Kay
Helen Thomas
Anne Thorburn
Nadine Dudek
Balasubramanian Krishnamurthy
Thomas Loudovaris
Rochelle Ayala-Perez
Francene Bond
Emma Jamieson
Gaurang Jhala
Lina Mariana
Melanie Rowe
Tara Catterall
Stacey Fynch
Catherine Li
Kylie Gilbert
Eveline Angstetra
Eugene Estella
Mark McKenzie
Nirupa Sachithanandan
Junquan Huang
Cze-Yen Lee
Su Ee Wong

People with type 1 diabetes lack insulin, the hormone that regulates the body's use of glucose. Insulin is produced by cells in the pancreas called beta cells, which are contained within small clumps of cells called islets. In type 1 diabetes, beta cells are mistakenly attacked and destroyed by the immune system. Type 1 diabetes is a major burden because of the lifelong need for several daily insulin injections and finger prick tests to control blood glucose levels, as well as the problems of long-term complications. Approximately one in every 200 Australians has type 1 diabetes. The incidence of type 1 diabetes is increasing, especially in children less than five years of age.

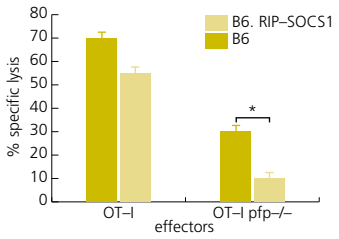
In Immunology and Diabetes we are interested in understanding immune-mediated beta-cell damage. Evidence in mice suggests that "killer" cells of the immune system called CTL have a significant role in killing beta cells. We have studied the molecular mechanisms by which CTL destroy beta cells and we are investigating ways to protect beta cells from the immune system as a potential therapy for treatment of type 1 diabetes. We have recently focused on the role of perforin and granzymes in beta-cell death in transplantation and autoimmunity. We have also extensively studied a molecule called suppressor of cytokine signalling-1 that was discovered by Robyn Starr and colleagues. Increasing the amount of SOCS-1 is a promising approach to limiting the toxic effects of the immune system on individual target cells.

A-D Infiltration in liver and pancreas of mice with SOCS1 deficiency in myeloid and lymphoid cells



Mechanisms of autoimmune CTL-induced death of beta cells

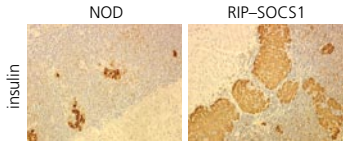
Cytotoxic T cells are the major mediators of autoimmune beta-cell destruction in type 1 diabetes but the molecular mechanisms are not definitively established. We have examined the contribution of perforin and FasL to beta-cell destruction using islet-specific CTL from T-cell receptor transgenic mice. Our results show that CTL use both pathways and that Fas is required for beta-cell killing only in perforin-deficient mice. Islet-specific CTL produced IFNγ and TNF that directly induce islet Fas expression. Overexpression of suppressor of cytokine signalling-1 (SOCS-1) in beta cells provides protection from CTL and we investigated the mechanism of this protection in two different beta-cell-specific models. Using OT-1 CTL, that recognize beta cells expressing ovalbumin, SOCS-1 protection was due to its blockade of cytokine-induced Fas expression on beta cells. NOD8.3 CTL, that recognize the endogenous beta cell antigen IGRP, were unable to kill SOCS-1 beta cells because of reduced target-cell recognition. Therefore CTL use both perforin and Fas pathways to kill beta cells and the prevention of beta-cell death by SOCS-1 overexpression may be due to reduced recognition and lack of cell death machinery on the beta cells.



> CTL-induced lysis of islets is diminished in the absence of perforin (pfp-/-) and further reduced in islets overexpressing SOCS1.

Susceptibility of beta cells to cytotoxic granules of allogeneic CTL

In a collaboration with Prof. Joe Trapani (Peter MacCallum Cancer Institute) we have used mouse CTL raised in strains deficient in cytotoxic effector molecules to assess the importance of the signaling pathways mobilized to kill beta cells. We found that allogeneic CTL require perforin and granzyme B to kill beta cells in short term assays, and a mechanism that requires TNF in a less potent latent phase attack. This study suggests that strategies to protect beta cells from allogeneic CTL attack will need to inhibit the perforin/granzyme and probably also the TNF pathway. As there are currently no known drugs that block perforin, therapeutic approaches based on overexpressing intracellular inhibitors of cytokines such as TNF and granzyme B may hold promise in prolonging beta cell survival in a transplantation setting.



> Islet grafts overexpressing SOCS1 are protected in NOD8.3 recipients.

SOCS-1 in T cells and macrophages is critical for preventing lethal inflammation

The balance between pro- and anti-inflammatory cytokines modulates inflammation. Intracellular inhibitors of signaling contribute to the negative regulation of cytokines. One of these inhibitors is suppressor of cytokine signaling-1 (SOCS-1). Socs1(-/-) mice die by 3 weeks of age with inflammation and necrosis of the liver. Cre/loxP deletion of Socs1 was used to investigate the contribution of specific cells/tissues to inflammatory disease. Mice with SOCS-1 deficiency in myeloid and lymphoid cells, but not lymphoid alone, became ill after 6 weeks of age. These mice developed splenomegaly and T-cell/macrophage infiltration of many organs, including liver, lung, pancreas, and muscle. There were also abnormally high levels of proinflammatory cytokines and activated T cells circulating in these mice. A dysregulated cytokine network between T cells and macrophages was associated with this inflammatory disease. These findings indicate that SOCS-1 is critical in both T cells and macrophages for preventing uncontrolled inflammation.

Signal Transduction

Robyn Starr
Christine Brender
Gillian Tannahill
Joel Fletcher
Ailsa Frew
Sarah Jones
Elena Tucker

Regulation of the immune system by SOCS proteins

Cytokines are important messengers that control the survival, growth, differentiation and function of cells of the immune system. Cytokines are produced in response to changes in the environment (such as infection), and act on cells to change their behaviour in response to these environmental changes. Responses to cytokines are typically transient, and unregulated responses to these potent molecules are generally harmful.

Several years ago, we identified a family of proteins known as SOCS (for suppressor of cytokine signalling). These proteins function as "stop signals" to ensure that cytokine signals are turned off when they are no longer needed. In the absence of SOCS, mice develop immune and inflammatory disease, showing that SOCS proteins are critical for keeping the immune system in check. Drugs that enhance the expression or function of SOCS proteins may be useful in the treatment of diseases in which the immune system is defective, such as autoimmune disease.

Regulation of T cell function by SOCS3

We are investigating the role of SOCS3 in the regulation of T lymphocyte function. Using mice that lack SOCS3 specifically in T cells, we have found that SOCS3 is critical for regulating the activation of T cells in response to antigen. These mice are healthy and thymic development appears normal. Lymph nodes, however, are enlarged and the number of peripheral T cells is increased. In response to an anti-CD3 stimulus, SOCS3-deficient T cells show greater proliferation than wildtype cells. We have analysed the signalling pathways downstream of both the CD3 and CD28 receptors and we find no evidence of amplified or prolonged signalling. Instead, we find that SOCS3-deficient T cells are hypersensitive to cytokines like IL-6 and IL-27 that signal through the gp130 receptor. Our data suggests that SOCS3 functions to regulate T cell behaviour by limiting the action of gp130 cytokines.

Identification of immune regulators using ENU mutagenesis

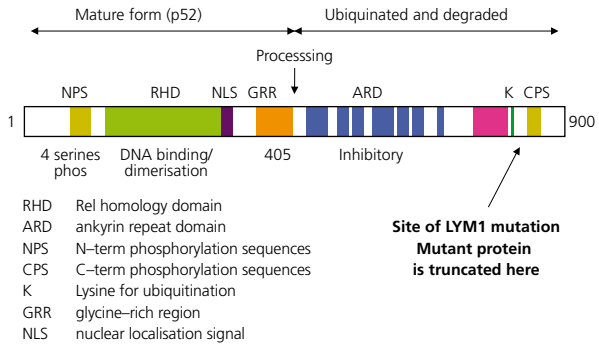
We are using a strategy, known as 'forward genetics', which begins with a biological process of interest to identify genes that contribute to that process. These phenotype-driven gene identification strategies have the advantage that they allow the isolation of genes involved in a biological process without any prior assumptions of their involvement.

We are interested in identifying genes that regulate T cell development and activity. The mutagen ENU is used to induce point mutations throughout the mouse genome, and blood samples from resulting pedigrees of mice are screened for aberrations in T cell development, number and activation state. To date, we are studying several pedigrees in which multiple members exhibit abnormalities in their immune system. We have established that these abnormalities are inherited, and are in the process of identifying the mutated genes.

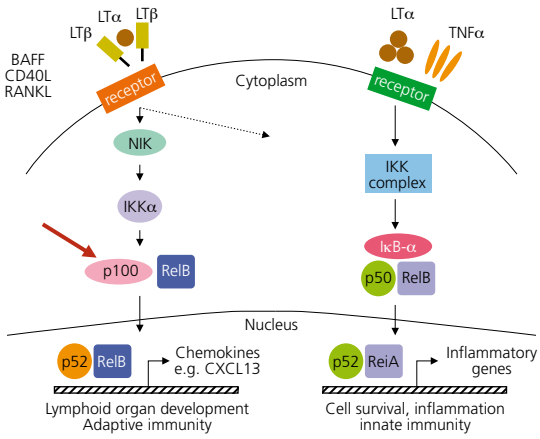
In vivo mutation of the NFκB2 gene using ENU mutagenesis generates an NFκB2 'super repressor'

We have identified a pedigree of mice, termed LYM1, in which affected members lack peripheral lymph nodes and show an expansion in the number of peripheral blood lymphocytes. This phenotype was found to be autosomal dominant and the mutation was mapped to a region on chromosome 19. NFκB2, a candidate gene in this interval, is involved in the "alternative NFκB pathway" which is known to be critical for the genesis of peripheral lymph nodes.

The NFκB2 gene encodes a precursor protein, p100, which sequesters RelB in the cytoplasm. Stimulation of receptors for lymphotoxin α/β, RANKL, BAFF and CD40L triggers a cascade of events that causes p100 to be processed to p52. The p52:RelB complex can then migrate to the nucleus and regulate genes involved in lymph node organogenesis, osteoclastogenesis and B-cell maturation. Sequencing of the NFκB2 gene in LYM1 mice revealed a mutation that introduces a premature stop codon. We have shown that the truncated NFκB2 protein is unable to be processed, and acquires a 'super repressor' function, allowing constitutive inhibition of the alternative NFκB pathway, resulting in defective LN formation, bone homeostasis and B cell maturation.



> **NF-κB2 (p100/p52)**
> The domain structure of the NFκB2 protein, showing the site at which the NFκB2 protein is truncated in LYM1 mice.



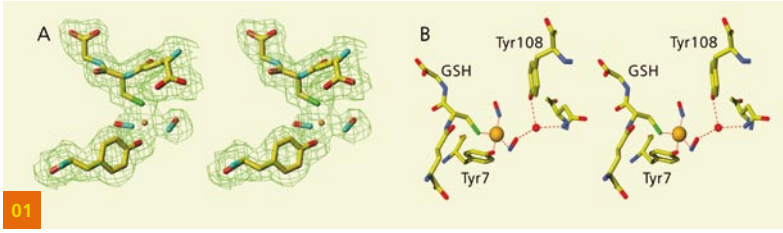
> **Signalling pathways in LN organogenesis**
> Schematic of the "alternative NFκB pathway" (left) and "classical NFκB pathway" (right). The LYM1 mutation occurs in the gene encoding NFκB2 (p100), indicated by the red arrow.

Structural Biology

Michael Parker
Brett Cromer
William McKinstry
Galina Polekhina
Julian Adams
Susanne Feil
Guido Hansen
Luke Miles
Yibin Xu
Brett Bennetts
Nancy Hancock
Hooi-Ling Ng
Belinda Rizzo
Julian Tang
Kwok Soon Wun
David Ascher
Geoffrey Kong
Lorien Parker

Proteins are one of the body's most essential building blocks. In addition to contributing to the structure of the body, proteins are also the "molecules of life", in that they are the molecular engines which control all functions of the body. Essential to understanding the function of proteins, we need to determine their structure. Crystallography offers the means to determine the three-dimensional (3-D) structure of proteins at the atomic level. Knowledge of protein 3-D structure enables the intelligent design of new drugs for the treatment of disease. The major areas of protein crystallography research in the group involve proteins involved in cancer, mental illness and bacterial and viral infection.

01 Model of GST complexed to the dinitroglutathione iron complex
02 Model of the unliganded GHR



Glutathione transferases as nitric oxide carriers

S-nitrosylation of proteins by nitric oxide is accepted as being among the most important posttranslational modifications that occur on proteins bearing reduced thiol groups. Such modification can cause modulation of many different functions with recent examples including proteins involved in signalling cascades, apoptosis, ion channels, redox systems and hemoproteins. It has been suggested that NO may play a role in iron homeostasis and/or metabolism based on observations of Fe nitrosylation of non-heme iron proteins in bacteria as well as in mammals. Iron-free proteins, such as albumin and GSH reductase, can also become targets of nitrosylation in the presence of suitable amounts of iron and thiol ligand (mostly glutathione under physiological conditions). In these cases the formation of Fe-dithiol dinitrosyl complexes are readily detected by EPR spectroscopy. Our collaborators have recently shown that human glutathione transferase P1-1 can interact avidly with dinitrosyl diglutathionyl iron complexes *in vitro* whilst maintaining its well known detoxificating activity towards dangerous compounds.

A similar function has also been proposed for other glutathione S-transferase (GST) classes suggesting a common mechanism by which the more recently evolved GSTs may act as intracellular NO carriers or scavengers. We have determined the crystal structure of GST P1-1 in complex with the dinitrosyl-diglutathionyl iron ligand at high resolution. In this complex the active site Tyr 7 binds covalently to the iron atom through its hydroxyl group by displacing one of the GSH ligands. The crucial importance of this catalytic residue in binding the nitric oxide donor was demonstrated by site-directed mutagenesis of this residue with His, Cys or Phe residues, respectively. The relative binding affinity for the ligand is strongly reduced in all three mutants by about three orders of magnitude with respect to wild-type. Furthermore, electron paramagnetic resonance spectroscopy studies on intact E. *coli* cells which bear the recombinant GST P1-1 enzyme indicated that bacterial cells, in response to NO treatment, are able to form the characteristic dinitrosyl-diglutathionyl iron complex using intracellular iron and GSH. We hypothesise the complex is stabilised *in vivo* through binding to GST P1-1. All together these results suggest an important role for GSTs in intracellular NO metabolism.

Our work on GSTs is a collaboration with Prof Mario Lo Bello, University of Rome 'Tor Vergata", Italy.

Human growth hormone receptor

Growth hormone is believed to activate its receptor by dimerising two identical receptor subunits, leading to activation of Janus Kinase 2 associated with the membrane proximal cytoplasmic domain. For over a decade a hormone-induced receptor dimerisation model has served as a paradigm for cytokine receptor activation. This model was based largely on *in vitro* studies with the purified extracellular domain of the growth hormone receptor (GHR), which forms a 2:1 complex with growth hormone (GH) both in solution and in the crystal structure of the complex. Our collaborators showed by FRET, BRET and co-immunoprecipitation that the receptor exists as a dimer *before* hormone binding as a result of interactions in the transmembrane/juxtamembrane domain. We determined the crystal structure of the unliganded receptor extracellular domain and compared this to the known liganded structures. These structures, together with the finding that the receptor can be made constitutively active by an approximately 40° turn within the transmembrane domain allowed us to propose a new model for growth hormone receptor activation which is based on hormone-induced rotation of receptor subunits within a constitutive dimer.

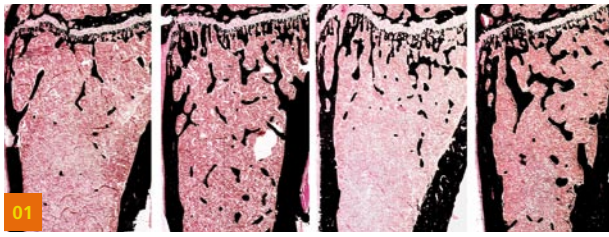
Our work on GHR is a collaboration with Dr Mike Waters, University of Queensland.

Bone, Joint and Cancer

Matthew Gillespie
T John Martin
Julian Quinn
Elizabeth Allen
Steven Bouralexis
Jane Fisher
Karl Häusler
Vicky Kartsogiannis
Rachel Mudge
Akira Nakamura
Melissa Ciccomancini
Chi Ly
Hasnawati Saleh
Emma Walker
Melisa Vasquez
Jan Elliot
Daphne Hards
Patricia Ho
Virginia Leopold
Patricia Smith
Jonathan Gooi
Tali Lang
Frances Milat
Domenic Di Fabio
Sudarshan Rai

A healthy skeleton is important for normal bodily function; it is needed for all physical activity, to protect internal organs and as a source of nutrients for the blood and immune system. Bone diseases such as osteoporosis, arthritis and cancer of bone all result in a reduction in bone mass. Our Unit is seeking new therapeutic targets to treat these common debilitating diseases by studying the cells that build bone (osteoblasts) and the cells that destroy bone (osteoclasts) and the way that these cells interact with each other and with changes to their environment.

01 IL-11R is required for normal bone remodelling. Representative images of proximal tibias showing differences in trabecular bone volume



Coupling factor: communication between the cells of bone

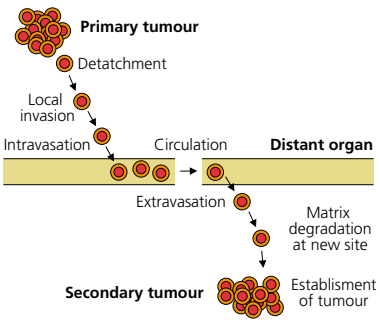
The internal structure of our skeleton is constantly changing; at every moment, small areas of bone are destroyed by osteoclasts and new bone is deposited in the same place by a team of osteoblasts. This constant turnover of bone means that the skeleton is able to respond quickly to dietary stress or changes in physical activity. Yet a mystery remains: how do the osteoblasts know how much bone matrix is needed and how do they know where to deposit it? It appears that osteoclasts release some factor, commonly referred to as "coupling factor", that signals to osteoblasts. When osteoclast activity is increased the release of coupling factor is modified. Recent work in our group has shown that the actions of coupling factor involve the cytokine interleukin-6 (IL-6) and we are investigating this possibility further.

The only known therapy that can reliably increase bone density is daily injection of parathyroid hormone (PTH). Unfortunately, this therapy is expensive to produce and unpleasant to administer to patients. We have evidence now that injections of PTH stimulate osteoclasts to release IL-6-dependent coupling factor, and that in the absence of IL-6, PTH is unable to increase bone mass. By investigating this pathway of PTH action, we are now identifying new targets for osteoporosis therapy.

FGF-2 and Cancer

One of the focus areas of the Bone, Joint and Cancer Unit is the spread of primary cancers to other sites in the body that results in secondary cancer. This process, known as metastasis, is a serious and unfortunately common complication of many cancers including breast cancer, which often spreads to bone. Dr Rachel Mudge is investigating the role of a particular form of the growth factor FGF-2. We have demonstrated that FGF-2 found in the nucleus of a cell, where DNA is made, gives cancer cells a survival advantage. Studies in bladder cancer, which is the fourth most common cancer in the Western world, have revealed that cells that have nuclear FGF-2 are successful at the process of metastasis. These cells form secondary tumors in the lungs of mice that have primary cancers. The work is now directed at understanding how nuclear FGF-2 changes the cells allowing them to spread and to elucidating other factors involved in the process. These studies will provide improved comprehension of the process of metastasis in human cancer and will hopefully lead to therapeutic targets in the future.

> **The Metastatic Cascade**
Schematic of the Metastatic Cascade.



Interleukin-11 receptor signaling is required for normal bone remodeling

Interleukins (IL) -6 and -11 regulate the changing structure of bone and have been implicated in postmenopausal osteoporosis. We found that deletion of IL-11 signaling, but not IL-6, in male and female knockout mice suppressed osteoclast differentiation both in the whole mouse and in cell culture. This caused a lower level of bone formation and increased trabecular bone mass. Surprisingly, IL-11 signaling was not required for the effects of estrogen or estrogen-deficiency on the mouse skeleton. In the absence of IL-11Rα1, the increased trabecular bone mass appeared to result from a cell-autonomous reduction in osteoclast differentiation, suggesting a direct effect of IL-11 on osteoclast precursors. The effects of IL-11Rα1 deletion on the skeleton were not mediated or compensated for by changes in IL-6 signaling. This showed that IL-11 signaling is essential for normal bone turnover and normal trabecular bone mass, yet is not a necessary pathway for postmenopausal bone loss.

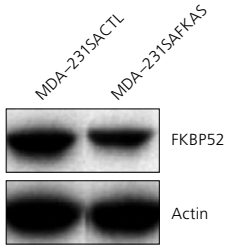
Tumour Cell Migration and Metastasis

John Price
Joseline Ojaimi
Wensheng Deng
Susan Docherty
Jessica Vieusseux
Michelle Kouspou
Matthew Pereira
Kelly Waldeck
Cynthia Soon

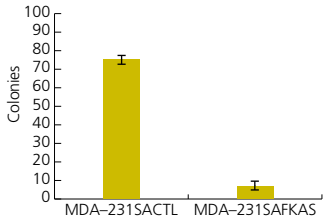
The spread of cancer, rather than the growth of the primary tumour, is ultimately responsible for treatment failure, poor health and death amongst cancer patients. We currently have a limited understanding of the processes and genes that enable tumour cells to leave the primary site of growth, move throughout the body and ultimately establish tumours at other sites, a series of events commonly known as metastasis. Due to our limited understanding few therapies are currently available which directly target these types of aggressive cancer cells. However, our laboratory is attempting to identify the genes within cancer cells that enable them to spread and grow at distant sites. By identifying the genes it will then be possible to isolate and produce new drugs that will be able to block their action resulting in new therapies that will potentially halt the spread and growth of cancer cells. To identify genes involved in metastasis we have isolated cancer cells that either have a high rate or a low rate of metastasis. We have genetically profiled these cells and identified a number of genes that may be involved in enabling the cancer cells to spread and grow.

Novel genes involved in breast cancer growth and metastasis

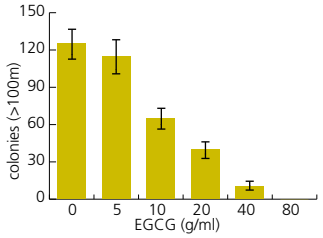
Genetic comparisons of human breast cancer cells with differing metastatic potentials has led to the identification of a number of genes that may play a role in breast cancer growth and metastasis. We are currently characterizing a number of these genes with particular focus upon IFIT1, FKBP52 and HSF-1. Through over-expression and knockdown studies of these target genes in several human breast cancer cell lines we are identifying their importance in breast cancer. For example, we have demonstrated that reduced expression of FKBP52 in the human breast cancer cell line, MDA-MB-231, results in a significant reduction in the ability of the cell to grow. These findings indicate that this gene could be an important regulator of breast cancer growth and may provide a novel drug target in the future. Conversely, we have shown that the interferon-inducible gene, IFIT1, is effective at inhibiting breast cancer cell growth when over-expressed. We are currently examining the mechanism by which IFIT1 achieves this in an attempt to identify novel pathways by which breast cancer cells can be killed. Further characterization of these genes will include their role in cancer cell migration, invasion and cell survival. Through these studies it is hoped that novel drug targets will be identified which will inevitably improve breast cancer treatment.



> Reduced expression of FKBP52 in MDA-231SA cells generated by anti-sense technology.



> Reduced anchorage-independent growth in the human breast cancer cells, MDA-231SA upon reduction of FKBP52.



> The inhibitory effect of EGCG upon anchorage-independenct growth of the human breast cancer cell line, MCF-7.

EGCG, an active anti-cancer component of green tea

Epigallocatechin-3-gallate (EGCG) is the most abundant catechin in green tea with the others being (+)-catechin, (+)-gallocatechin (GC), (-)-epicatechin (EC), (-)-epicatechin-3-gallate (ECG), and (-)-epigallocatechin (EGC). The catechins, especially that of EGCG, have been shown to posses anti-oxidant, anti-carcinogenic and anti-inflammatory properties. Pre-clinical data has supported the initiation of a number of clinical trials to examine the effectiveness of EGCG in cancer patients.

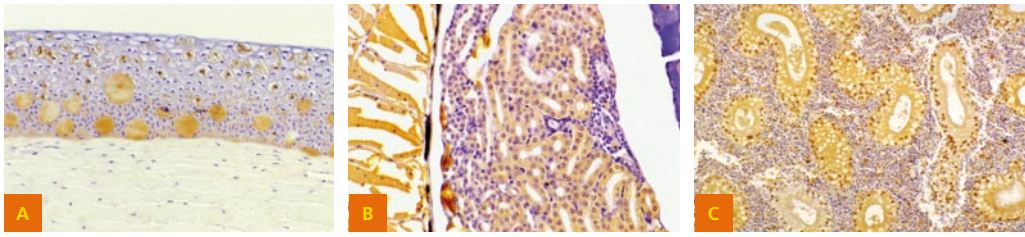
A major project within the laboratory is to investigate whether EGCG could be used as an effective agent to inhibit breast cancer metastasis to the bone and other organs. We have recently demonstrated that EGCG inhibits both anchorage-dependent and -independent cell growth in a variety of human breast cancer cells, including that of MDA-MB-231, MCF-7, MDA-MB-435 and BT-474 cells through the induction of apoptosis. However, we have also demonstrated that EGCG has the ability to prevent the movement or migration of breast cancer cells, indicating that it may not only have the ability to stop tumour growth but also the potential to stop the spread of breast tumours. We are currently identifying the pathways and molecules that are inhibited by EGCG to identify its mechanism of action.

Comparative Endocrinology

Janine Danks
Lisa McCarthy

Our major interest is in the evolution of the parathyroid hormone family, which contain two of the major calcium regulating hormones in vertebrates, parathyroid hormone (PTH) and parathyroid hormone-related protein (PTHrP). Several years ago we isolated PTH from the Japanese pufferfish (*Fugu rubripes*) in collaboration with Prof Jeffrey Zajac from Department of Medicine, University of Melbourne. TeeleOstin Pty Ltd, a company formed by Starfish Ventures, SVI and the University of Melbourne, has funded these animal model studies. It is known that human PTH and certain analogues of human PTH are stimulators of bone growth.

PTHrP staining in the **A)** skin; **B)** tubules of the downstream migrant opisthonephros and nearby skeletal muscle; and **C)** tubules in the upstream migrant kidney



These factors are used clinically in the treatment of osteoporosis, and they are currently the only anabolic bone agents used therapeutically. In contrast, bisphosphonates, which have dominated the osteoporosis field over the last 10 years, can only prevent bone loss. We have demonstrated that *Fugu* PTH can form new bone in rapidly growing young male rats and in 2005 we were awarded a Biotechnology Innovation Fund grant in Round 6 to examine *Fugu* PTH's ability to form new bone in an aged rat model that mimics post-menopausal bone loss in humans.

Developmental and evolutionary perspectives of PTHrP production in the lamprey

Over the last 12 years we have demonstrated the presence of PTHrP in bony and cartilaginous fish, demonstrating it has a long evolutionary history. This year we published a study which explored the distribution of PTHrP and its mRNA in tissues of the lamprey *Geotria australis*, a representative of one of the two surviving groups of an early and jawless stage in vertebrate evolution. The results revealed that antigen and its mRNA were widely distributed among similar sites of tissue localisation to those described for mammalian and avian species. The presence of PTHrP in the lamprey, a representative of a group of vertebrates, that apparently evolved over 540 million years ago, suggests that its functions are fundamental and basic.

Expression of PTH in zebrafish

We are also interested in parathyroid hormone's role in fish and are collaborating with Drs Joan Heath and Graham Lieschke and PhD student, Ben Hogan from the Ludwig Institute in Melbourne to see where and when PTH is expressed in the zebrafish embryo. Fish do not have anatomical structures corresponding to parathyroid glands, and these animals were therefore thought not to produce PTH. The gene and protein were demonstrated in the nervous system and the earliest developing bone and this work was published in the journal *Endocrinology* in 2005. The finding that PTH is expressed in neural tissues suggests it has other biological roles, and may provide hints to some of the many non-classical functions that have been ascribed to PTH in mammals.

Protein Chemistry and Metabolism

Bruce Kemp
Belinda Michell
Kim Branson
Andrew Carey
Zhiping Chen
Frosa Katsis
Gregory Steinberg
Bryce van Denderen
Nicholas Dzamko
Tristan Iseli
Ruby Platt
Mark Walter
Shanna Tam
Matthew Bird

Our team is working on an enzyme known as AMP-activated protein kinase (AMPK). This enzyme – a protein controller of chemical reactions – acts as the body's fuel gauge and monitors its energy level. Our results have relevance for treating obesity, heart disease, diabetes and cancer, for shaping exercise programs, and even for producing higher quality meat. It is well known that exercise is beneficial to health, and that sedentary lifestyles increase the risk of obesity and type 2 diabetes. AMPK has a potential role in mediating the health benefits of exercise. It regulates the burning and storage of fats and sugars, and affects the level of sugars, fats and cholesterol in the blood stream.

Control of the body's energy metabolism by AMPK involves multiple tissues such as the brain, skeletal muscle and liver. In the brain AMPK is involved in the control of appetite through the action of hormones which switch AMPK on or off to stimulate or suppress appetite respectively. AMPK is also required for the insulin sensitizing effects of the type 2 diabetic drug metformin. Therefore, by reducing blood glucose levels and burning fats, AMPK does precisely what's required to offset the effects of obesity and diabetes.

Thus AMPK, an enzyme with powerful and far reaching effects, could play a significant role in treating conditions that cost Australia's health system billions of dollars a year. This has attracted global attention because of the epidemics of obesity and diabetes.

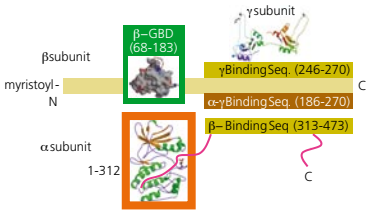
A second upstream regulator of AMPK is discovered

A highlight of the year has been the discovery of a second upstream kinase that regulates AMPK. This work involved a three-way collaboration with Lee Witters' laboratory at Dartmouth College, New Hampshire and Anthony Means at Duke University, North Carolina. It was found that AMPK could be phosphorylated and activated in cells that had little or no LKB1 kinase indicating that there was a second kinase kinase activity. This was shown to be calmodulin dependent kinase kinases' α and β, enzymes we had worked on previously. A decade earlier we had sequenced CaMKKβ in collaboration with Anthony Means and Art Edelman. The CaMKK α and β are most highly expressed in the brain suggesting that they may be important in mediating the activation of AMPK in the brain responsible for the control of appetite. The regulation of AMPK by CaMKK involves calcium and calmodulin and does not require changes in cellular AMP.

The role of AMPK in obesity

Understanding the role of AMPK in obesity is an important focus of our laboratory and this has been spear headed by Gregory Steinberg. During the year we found in collaboration with David Cameron-Smith at Deakin University that obese diabetic patient's are insensitive to adiponectin, which switches on AMPK in skeletal muscle of normal individuals to promote fat oxidation. Importantly it was found that the AMPK levels were normal in these patients and that if you activate AMPK pharmacologically, bypassing the adiponectin resistance fat oxidation could be stimulated in the muscle of these patients. This work explains why obese diabetic patients have such difficulty in losing weight but importantly gives great encouragement to our efforts to develop drugs that can be used to directly activate AMPK in these patients and restore their metabolism and body weight.

> **AMPK Structure**



Using AMPK as a metabolic fitness indicator

We, and others have shown that AMPK is rapidly activated in response to exercise. In collaboration with Glenn McConell at University of Melbourne's Department of Physiology we found that as little as 10 days training caused such an improvement in the metabolism of sedentary individuals that they could tolerate the same level of exertion without activation of AMPK. This indicates that AMPK activation can be used as a metabolic fitness indicator. It is not yet known whether the activation of AMPK during training alone is sufficient to improve metabolism. One of the consequences of training is to increase muscle glycogen levels. It has previously been reported that AMPK activation was suppressed in muscle with high glycogen levels. Since AMPK's β subunit has a glycogen-binding domain it was thought that glycogen may directly inhibit AMPK. In the training study Glenn McConell was able to control glycogen levels in the exercise volunteers and show that the effect of training on suppressing AMPK activation was independent of glycogen levels. This was an important observation in terms of understanding AMPK regulation.

Molecular Cardiology

Duncan Campbell
Barry Dixon
Nicholas Dzamko
Phil Au

Cardiovascular diseases are diseases of the heart and blood vessels. These include heart attacks, strokes, and heart failure, and they are the main causes of death and sickness in our community. Our laboratory is investigating new ways to predict who is likely to experience cardiovascular disease, so that we can better prevent and treat these diseases. We are particularly interested in the role of different hormones in cardiovascular disease, and the effects of drug treatments on these hormones.

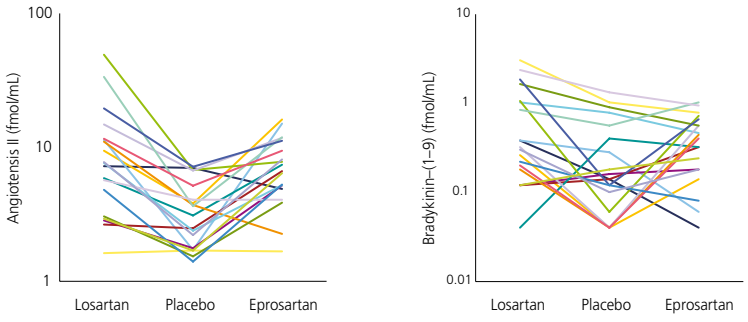
A long term interest in our laboratory is the hormone angiotensin. Angiotensin controls blood pressure by constricting blood vessels, by controlling renal excretion of salt and water, and by controlling adrenal secretion of aldosterone. High levels of angiotensin cause hypertension. Angiotensin has many other actions. High angiotensin levels cause thickening of heart muscle and thickening of the walls of blood vessels. High levels of angiotensin also have toxic effects on tissues, promoting inflammation in tissues and contributing to diseases of the heart and blood vessels. Some of the most valuable drugs we use to treat cardiovascular diseases act by reducing these effects of angiotensin. These drugs include ACE inhibitors, angiotensin receptor blockers, and beta–blockers. ACE inhibitors act by blocking an enzyme which produces angiotensin, called angiotensin converting enzyme (ACE).

Discovery of a new action for an old drug

Losartan is a drug used to treat high blood pressure and heart disease that acts by blocking the action of the hormone angiotensin. When there are high levels of angiotensin in the blood it causes high blood pressure and heart disease. In collaboration with Murray Esler and Henry Krum at the Alfred Hospital, we showed losartan has another action; it increases the amount of a hormone called bradykinin. Bradykinin has many actions that are opposite to those of angiotensin; it causes blood pressure to fall and it helps the heart recover from disease. Our findings provide important new information about how losartan produces benefit in patients.

Study of the role of genes that control angiotensin production

An important question has been whether changes in genes that control angiotensin production can cause high blood pressure and heart disease. In collaboration with our colleagues at the Howard Florey Institute, Melbourne, we addressed this question by measuring angiotensin in mice with different numbers of genes for angiotensinogen (the protein precursor for angiotensin), and ACE. We found no difference in the amount of angiotensin in mice with either one or two genes for angiotensinogen or ACE. These results show that the body can compensate for different levels of gene activity, and point to a likely important role for these compensatory mechanisms in regulating the amount of angiotensin. Abnormalities in these compensatory mechanisms may cause diseases such as high blood pressure and heart disease.



> Increased amount of the hormone bradykinin after treatment with the blood pressure drug losartan.

Cell Cycle and Cancer

Boris Sarcevic
Martin Sadowski
Randy Suryadinata

In humans, controlled cell division and maturation is required for normal growth and development. Incorrect regulation of cell growth pathways leads to unrestrained cell division, and this is a primary characteristic of cancerous cells. Therefore, defining the causes of increased cellular division is pivotal to understanding the development of human cancer.

Two fundamental biochemical processes that control cell division are processes known as protein phosphorylation and protein degradation. Incorrect regulation of these processes is intimately involved in the development of many human cancers due to increased cell division. We are interested in the control of key regulatory molecules in the process of cell division, and how this is altered in human cancer. These studies will increase our understanding of the molecular mechanisms of cell division providing insight into how human cancer begins and progresses.

Identification and characterisation of substrates of cyclin-dependent protein kinases

An important unresolved issue relates to understanding the molecules targeted by cyclin-dependent kinases (CDKs) and how their phosphorylation regulates cell division, since increased CDK activity can contribute to human cancer. The chromatin-remodelling SWI/SNF complexes control cell proliferation by regulating transcription. We have undertaken studies in *Drosophila* in collaboration with Dr. Helena Richardson from the Peter MacCallum Cancer Institute to address if CDKs regulate SWI/SNF and cell cycle progression. Transgenic flies expressing of SWI2 (Brm^{ALA}) which cannot be phosphorylated on CDK sites resulted in the ablation of wing tissue, while a mutant phosphomimic form (Brm^{ASP}) resulted in expansion of the posterior wing region. In addition, expression of Brm^{ASP} in the developing eye resulted in disorganised eyes, consistent with additional cell proliferation. When BrmASP was expressed with cyclin E and with p35 (to prevent cell death), the over-proliferation phenotype was enhanced to lethality. These exciting new data provide the first evidence that the CDK phosphorylation sites on SWI2 (Brm) has important consequences on cell cycle progression *in vivo*. Further studies will involve genetic, cell biological and *in vitro* studies to understand this regulation at a mechanistic level.

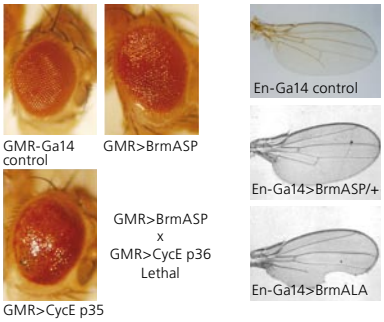
Regulation of cell cycle progression by ubiquitin-conjugating enzymes

Degradation of key cell cycle regulators by the ubiquitin/proteasome system is critical for cell division and deregulation of components of this pathway is also important in human cancers. The ubiquitylation pathway catalyses the covalent binding of the ubiquitin polypeptide to substrate proteins tagging them for proteasome-mediated proteolysis. We are interested in understanding how ubiquitin-conjugating enzymes (UBCs) control proteolysis and cell division. We have focussed on the ubiquitin-conjugating enzyme, Cdc34, which is a critical regulator of cell cycle progression in eukaryotic cells. We have identified the in vivo phosphorylation sites on Cdc34 and demonstrated that these sites are specifically phosphorylated by casein kinase 2. Cell cycle studies indicate that phosphorylation of these sites is important for Cdc34-mediating G1-S phase cell cycle progression.

At a mechanistic level, our data indicate that phosphorylation alters the binding of Cdc34 to other proteins of the ubiquitin pathway. These results indicate that in addition to CDKs, other kinases such as casein kinase 2 play important roles in cell division through phosphorylation and integration with the ubiquitylation machinery.

We have also unveiled a conserved site in UBCs which is critical for their catalytic activity and cell cycle functions. Recent studies have implicated increased expression of UBCs which control cell cycle progression in human cancer development. The conserved site we have identified in UBCs may represent a novel target for the development of new cancer therapeutics. The recent approval of the proteasome inhibitor bortezomib for the treatment of advanced multiple myeloma augurs well for the development of drugs targeting specific abnormalities in the ubiquitylation pathway, such as overactive UBCs.

> Serine 138 is critical for UBC3-mediated cell cycle progression. The *S. cerevisiae cdc34-2* mutant was transformed with empty plasmid or plasmid expressing wild-type or mutant (S138D, S138A, S138T, or S138E) Cdc34s. Only cells expressing wild-type Cdc34 grow at the non-permissive temperature (37°C).



> Left, expression of Brm^{ASP} in the eye and with cyclin E + p35 (disorganised). Right, expression of Brm^{ASP} and Brm^{ALA} in the wing. Arrows indicate over-proliferation and ablation.

Molecular Genetics

Jörg Heierhorst
Brietta Pike
Ana Traven
Andrew Hammet
Carolyn McNees
Nora Tenis
Angela Tam

Damage to DNA can occur spontaneously or in response to the environment. Accumulating DNA damage is one of the key factors that determine the onset and the malignancy of cancer. In addition, the vast majority of clinical cancer therapies act by causing DNA damage. Better understanding of how the cell responds to DNA damage is therefore likely to improve our knowledge of how cancer develops and could reveal new approaches to cancer therapy. It is now clear that different types of agents that can damage DNA cause a range of diverse DNA changes. Human cells contain a number of specific mechanisms to repair these DNA changes. Inappropriate repair of a particular DNA lesion by the wrong repair pathway often leads to escalating genomic changes. Our laboratory is interested in the molecular mechanisms by which cells deal with DNA damage in such a specific manner in order to prevent the onset and progression of human cancer. We have identified a novel family of DNA damage response proteins that is remarkably conserved from yeasts to human. Our hypothesis is that these proteins act by regulating the assembly of other DNA damage response proteins into complexes in the vicinity of damaged chromosomes.

Role of ASCIZ in a novel human DNA repair pathway

The human Rad51 protein is the key enzyme in error-free repair of DNA damage by homologous recombination. Rad51 functions are best understood in response to DNA double-strand breaks, but there is increasing evidence that Rad51 also contributes to the repair of single-stranded DNA lesions, for example when stalled DNA replication forks need to be restarted. In response to DNA damage, Rad51 often relocates into discrete nuclear foci (≤1 µm diameter) that are believed to be sites of recombinational DNA repair. Interestingly, the relocation of Rad51 in response to DNA double-strand breaks is defective in inherited breast cancer resulting from BRCA2 mutation, indicating that the proper sub-nuclear localisation of Rad51 plays critical roles in the prevention of cancer. However, BRCA2-deficient cells can still form normal Rad51 foci in response to DNA lesions other than double-strand breaks, but the mechanisms that regulate Rad51 location under these conditions are largely unknown.

We have recently identified a novel human DNA damage response protein called ASCIZ that forms damage-induced foci specifically in response to DNA base modifications (methylating and oxidative damage). Interestingly, Rad51 is recruited to the same foci with a short delay relative to ASCIZ. And even more importantly, cells that lack ASCIZ are unable to form Rad51 foci in response to methylating DNA damage and then become dramatically hypersensitive to methylating agents.

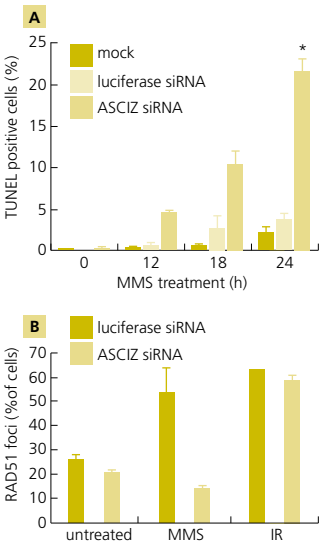
ASCIZ focus formation and hypersensitivity to methylating agents in the absence of ASCIZ depend on components of the mismatch repair machinery. Conversely, ASCIZ focus formation is enhanced when the base-excision repair is inhibited. The simplest explanation for our findings is that ASCIZ foci form when methylated bases are removed from DNA to such an extent that the resulting abasic sites exceed the capacity of the base-excision repair pathway, and are then converted to single-stranded DNA gaps. The accurate repair of these gaps is then regulated by the recruitment of Rad51 into ASCIZ foci.

In truncation analyses we found that over-expression of a core domain of ASCIZ can uncouple Rad51 focus formation from the DNA damage response by redirecting Rad51 into focus-like PML bodies in the absence of DNA damage. Altogether, our findings indicate that ASCIZ may function as a lesion-specific scaffold for Rad51 focus formation.

> Comparison of yeast Mdt1 and human ASCIZ. ZF, Zn^{2+}-finger; NLS, nuclear localisation signal; SCD, SQ/TQ cluster domain; RRM, RNA recognition motif; CC, coiled coil. circles indicate potential ATM/ATR kinase phosphorylation sites.

Identification of a novel family of conserved DNA damage response proteins

Remarkably, ASCIZ is very similar to the yeast protein Mdt1 that we have identified a year earlier. Both proteins contain a potential nucleic acid-binding near the N-terminus (a Zinc-finger domain in ASCIZ or RNA recognition domain in Mdt1), a nuclear localisation signal, and as the main part, a so-called SQ/TQ cluster domain. SQ/TQ cluster domains are a structural hallmark of DNA damage proteins and represent likely sites of phosphorylation by the DNA damage kinases ATM and ATR. Ongoing experiments in yeast indicate that Mdt1 also regulates some aspects of DNA recombination. These similarities will allow us to gain a better understanding of the human protein by taking experimental advantage of the awesomely powerful yeast system.



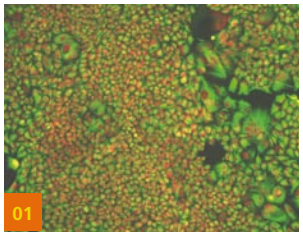
> ASCIZ depletion from cells by siRNA leads to increased apoptosis (**A**) and reduced RAD51 focus formation after MMS-induced DNA damage (**B**) compared to luciferase controls. Note that ASCIZ is not required for spontaneous or ionising radiation (IR) induced Rad51 focus formation.

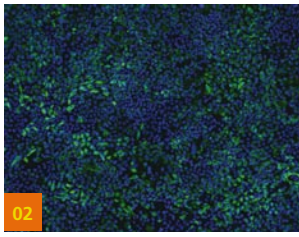
Pharmacogenomics

Mark Waltham
Maria Shache
Angela Arvanitis
Andrea Connor
Sarah Vickery

Pharmacogenomics is the study of how an individual's genetic inheritance affects their response to drugs. It is the cataloguing and processing of information relating to pharmacology (drugs) and genetics. Drugs might one day be tailor-made for individuals and adapted to each person's genetic makeup. The laboratory's primary area of interest is concerned with identifying the molecular processes associated with cancer and diabetes progression. We are particularly interested in identifying genes that cause cancer to spread (metastasis) and identifying/developing drugs that stop that process. We have also recently identified genes associated with onset of diabetic kidney damage and are working closely with the Institute's Structural Biology Laboratory to design inhibitors to one of these key genes.

01 Human breast cancer cells
02 Cancer cells are stimulated to undergo a transformation similar to that which occurs when human tumours first begin to metastasise. The green cells are those which have undergone the transformation





Identifying metastasis genes

During metastatic progression, a small population of cancer cells leave the primary tumour and disseminates to secondary organs. This is a multistep process which involves detachment of cells from the epithelium, their adhesion to the extracellular matrix (ECM), degradation of the ECM and migration. The gain of migratory and invasive properties for these cells is associated with loss of epithelial morphology and acquisition of mesenchymal characteristics; a process referred to as an epithelial-to-mesenchymal transition (EMT). In collaboration with A/Prof Erik Thompson's VBCRC laboratory at SVI, the Pharmacogenomics Laboratory has performed microarray gene expression profiling of human *in vitro* models of EMT to identify molecular mechanisms which regulate and associate with the EMT. Forty differentially expressed genes for this cell system have now been identified. This project is complemented by bioinformatic studies which utilize the ever growing tissue and disease expression databases available through international collaborations. While the established gene-fingerprint of the EMT is being refined for potential application in clinical diagnosis, the identification of functional drivers of the EMT process is being pursued by siRNA technologies to reveal potential drug targets of the metastatic cascade.

New drug targets in diabetic nephropathy

Diabetes often leads to the development of a form of kidney damage known as diabetic nephropathy. Kidney damage in this condition is characterized by an increased accumulation of extracellular matrix (eg collagen) brought about by a high glucose environment, oxidative stress and an associated local over-expression of growth factors. We have used microarray technology to characterise a variety of *in vivo* and *in vitro* models of diabetic nephropathy. The purpose of this work has been to study *en masse* the alterations in genome transcriptional activity and to identify potential new drug targets. One 'up-regulated' gene we identified is known to function in redox signalling and has been recently shown to play a critical role in reactive oxygen species generation and the pathological consequences of oxidative stress. Given that pharmacological modulation of proteins involved in the propagation of oxidative stress may be a be a suitable therapeutic strategy for diabetic nephropathy, we are collaborating with the Institute's Structural Biology Laboratory to elucidate the crystal structure of this protein and design specific inhibitors to block its biological activity.

New drugs that inhibit breast-to-bone metastasis

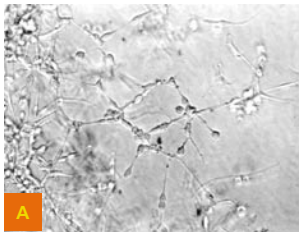
Metastasis represents the most devastating attribute of cancer. A notable feature of this process is the variation in metastatic tissue tropism displayed for different types of cancer. Bone is a particularly frequent site of metastasis in patients with prostate carcinoma, myeloma, and for patients dying from carcinoma of the breast, approximately 85% have demonstrable metastasis to bone. Using mouse models of breast cancer, we have identified two drug molecules that are capable of inhibiting osteolytic bone damage associated with metastasis. While these drugs do not inhibit metastasis to other sites, this bone-specific effect is potentially significant given that bone metastasis represents a distinct and significant clinical problem. One of the drugs is orally active and used for the systemic treatment for a variety of skin disorders clinically (predominantly in Japan & Korea). While its precise mechanism of action is not known it does have a well established safety profile and therefore could be rapidly translated into clinical use. The Pharmacogenomics Laboratory is currently further evaluating the anti-osteolytic activity of both drugs and using a variety of techniques (including gene array technology) to define the molecular basis of action in the cancer/bone environment.

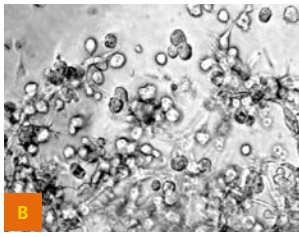
VBCRC Invasion and Metastasis Group

Erik Thompson
Marc Lafleur
Tony Blick

The VBCRC Invasion and Metastasis Group is part of the Victorian Breast Cancer Research Consortium, a series of breast cancer-focussed groups strategically placed amongst Melbourne research institutions (PHIMR, WEHI, PMCC, and the University of Melbourne). Collectively these groups form an "Institute Without Walls" administered by the Cancer Council of Victoria (**www.vbcrc.org.au**). The VBCRC was initiated by state government funding in 1995 for a period of 10 years, and has been highly successful in raising the spectrum of breast cancer research in Victoria, and indeed Australia. Our laboratory studies the process of metastasis, or spread of cancer cells from the primary tumour site to other sites such as the brain, bone or liver. Understanding this activity is crucial to our capacity to combat breast cancer.

Phase contrast images showing the inhibition of BT-549 human breast cancer cells into Matrigel by SPARC. Control (A) and SPARC-treated (B) cultures are depicted.





We have maintained an interest in understanding and targeting a family of molecules capable of breaking down connective tissue structures called matrix metalloproteinases (MMPs). We are examining individual MMPs for their potential role in breast cancer progression by assisting invading cancer cells in cutting through the connective tissue. These MMPs may play important roles not only at the primary tumour site, but also after metastasis to bone, a favoured site for breast cancer spread which causes considerable complications in breast cancer sufferers. We also have an ongoing interest in a protein called SPARC, which controls MMP activity.

MMP inhibition

In collaborative studies with Mark Waltham, we have previously examined the effects of both broad-spectrum (Marimastat or BB2516) and somewhat selective (Prinomastat, AG3340 - selective for MMP-2, MMP-9 and MT1-MMP) MMP-inhibitors in the MDA-MB-231 model. Both Prinomastat and Marimastat significantly inhibited the tumourigenesis of MDA-MB-231 cells inoculated into the mammary fat pad. We also observed a significant delay in the onset and severity of bone metastatic lesions after intracardiac inoculation with AG3340. We propose that specific inhibition of MT1-MMP and/or MMP-13 will cause inhibition more translatable to humans and are working to provide support for this. We have extended our studies into the 4T1 model of syngeneic mouse mammary carcinoma in collaboration with Robin Anderson, PMCC. We have assessed the MMP-13 and MT1-MMP expression in these cell lines *in vivo* and *in vitro*. Analysis of the 4T1.2 syngeneic system showed progressive increase in MMP-13 expression with increased aggressiveness and substantially higher mMMP-13 expression levels in *in vivo* samples tested, the latter consistent with induced stromal MMP-13 expression and/or stimulated tumoural expression.

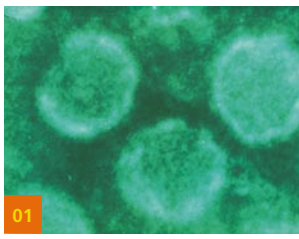
SPARC studies

SPARC (Secreted Protein and Rich in Cysteine), also known as BM-40 and Osteonectin, is highly upregulated around tumours including breast. It has been shown to cause increased aggressiveness in glioma and melanoma models, however, we have found SPARC to suppress the proliferation of breast cancer cells *in vitro* and to suppress xenograft growth *in vivo*. In collaboration with Takako Sasaki, Max Plank Institute, Germany, we have obtained mutated forms of SPARC which lack specific domains, or have specific mutations. These valuable reagents have allowed us to focus on the specific regions of SPARC which cause certain biological effects. We have found that the amino-terminal domain (Domain I) causes reduced levels of a MMP inhibitor (TIMP-2) around the cell, and thus causes increased activation of MMP-2. This confirms and extends previous work with synthetic peptides derived from Domain I, which is the unique component of SPARC compared to other members of the FS-EC family. Furthermore, we have found that determinants in Domain III, the extracellular calcium binding domain which comprises two EF Hands, block inhibition of breast cancer invasion in a calcium-dependent manner.

National Serology Reference Laboratory

Elizabeth Dax
Susan Best
Dale McPhee
Thein Thein Aye
Hayley Croom
Denison Chang
Bradley Dent
Larissa Doughty
Thu-Anh Erickson
Barbara Francis
Rosina Gribben
Darren Jardine
Marina Karakaltsas
Sally Land
Lena Panagiotopoulos
Scott Read
Kim Richards
Joanne Schlegel
Kathy Smeh
Sandy Walker
Kim Wilson
Alicia Arnott
Erin Verity

The National Serology Reference Laboratory, Australia (NRL) is committed to helping curb the spread of blood-borne and other infections by assuring and maintaining quality and confidence in laboratory results in Australia and internationally. Our objectives are achieved by providing multi-faceted quality assurance programmes, acting as an adjudicator on problematic sample results, conducting targeted research and leading training and education endeavours to secure laboratory best practice and quality. Research at the NRL focuses on the development of new and improved diagnostic tests for infectious diseases and better defining the immune responses to infection and disease progression. Commercial imperatives drive the development of diagnostic tests (or assays) and this can leave issues pertinent to less lucrative markets unaddressed. Our research programme tackles such problems.



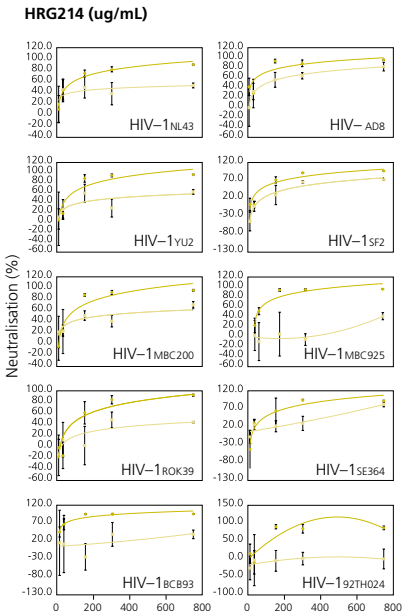
Improved avidity assay for detection of primary humoral immune response to Rubella infection

An assay capable of distinguishing between the immune response generated by recent exposure to rubella and the immune response existing as a result of past exposure or immunization is required for the diagnosis of primary rubella infection, especially in pregnant women. In an effort to accomplish this, avidity assays, based on the premise that chaotrophic agents can be used to dissociate selectively the low avidity antibodies generated early in the course of infection, have become routinely used. We have thoroughly investigated the immunological basis of an avidity assay using a viral-lysate based assay and an ELISA based on a peptide analogue of the putative immunodominant region of the E1 glycoprotein ($E1^{208-239}$). The relative affinity of the antibodies directed against $E1^{208-239}$ were measured by surface plasmon resonance and found to correlate well with the avidity index calculated from the ELISA results. We found that the immune response generated during primary rubella infection consists of an initial low affinity peak of IgM reactivity followed by transient peaks of low avidity IgG_3 and IgA reactivity. The predominant response is an IgG_1 response which increases in concentration and affinity progressively over the course of infection. Incubation with the chaotrophic agent used in the avidity assay abolished the detection of the early low affinity peaks of IgM, IgA and IgG_3 reactivity while leaving the high affinity IgG_1 response relatively unaffected. This study supports the premise that avidity assays, based on appropriate antigens, can be useful to confirm primary rubella infection.

Viral lysis and potent blocking ability – identification of two novel polyclonal neutralising antibodies targeting HIV-1

Individuals infected with HIV-1 mount robust immune responses that are not capable of clearing infection or preventing disease progression. Neutralising antibodies or those capable of killing virus target the envelope glycoproteins on the virus. These are often of poor quality or strain-specific, and drive virus evolution and the emergence of escape mutants. HIV-1 employs a number of strategies to avoid neutralisation including mutation and glycosylation of its envelope proteins which results in virus evading immune responses. We have characterised two novel, potent, polyclonal neutralising antibodies. The first is HRG214, which was raised in goats against purified HIV-1 and HIV-2 particles. It was found to neutralise and lyse all HIV-1 isolates tested. These included viruses encompassing clades A to E, and both CCR5 and CXCR4 phenotypes. The mechanism of action was found to be mediated predominantly by complement dependent virion lysis.

We also investigated neutralising antibody responses in individuals infected with attenuated HIV-1 that had deletions in the *nef* gene. Such deletions are associated with attenuated infection resulting in long-term non-progression. The long-term survival of infected individuals is likely to be dependent upon reduced viral pathogenicity, and it is unclear what role neutralising antibodies play. Plasma (containing neutralising antibodies) from subjects with detectable, but low viral loads (<10,000 RNA copies/ml, i.e. reduced pathogenicity) potently neutralised contemporaneous viruses and diverse heterologous viruses, in contrast to the poor and strain-specific responses normally observed. Thus, *nef*-attenuated HIV-1 infection can potentiate neutralising antibody responses, but depends on the presence of detectable HIV-1 antigen to drive antibody production. Novel antibodies such as those described here may be used to prevent HIV-1 infection or in controlling virus replication in infected individuals.



Potent neutralisation of diverse HIV-1 isolates by HRG214 in the presence ( ) and absence ( ) of complement.

Staff members

Patron

Gustav JV Nossal, AC CBE MBBS BSc(Med) *Syd* PhD *Melb* HonLLD *Mon* HonLLD *Melb* HonMD *Mainz* HonMD *Ncl* HonMD *Leeds* HonMD *UWA* HonDSc *Syd* HonDSc *Qld* HonDSc *ANU* HonDSc *UNSW* HonDSc *LaT* HonDSc *McMaster* HonDSc *Oxon* FRCP FRACP FRCPA FRACOG (Hon) FRCPath FRACGP FRSE FTSE FAA FRS

St Vincent's Institute

Director

Thomas WH Kay, BMedSci MBBS PhD *Melb* FRACP FRCPA; Professor (Medicine), The University of Melbourne

Associate Directors

Matthew T Gillespie, BSc (Hons) PhD *Mon*; NHMRC Principal Research Fellow; Associate Professor (Medicine), The University of Melbourne

Michael W Parker, BSc (Hons) *ANU* DPhil *Oxon*; NHMRC Senior Principal Research Fellow; Professor (Biochemistry and Molecular Biology), The University of Melbourne

John Holt Fellow

T John Martin, AO MD DSc *Melb* HonMD *Sheffield* FRACP FRCPA FAA FRS; Emeritus Professor (Medicine), The University of Melbourne

Pehr Edman Fellow

Bruce E Kemp, BAgSci (Hons) *Adel* PhD *Flinders* FAA FRS; ARC Federation Fellow; Professor (Medicine), The University of Melbourne

Research Faculty

Duncan Campbell, BMedSci MBBS PhD *Melb* FRACP Grad Dip Epid Biostat; Associate Professor (Medicine), The University of Melbourne

Brett Cromer, BSc (Hons) PhD *ANU*

Janine Danks, BSc *LaT* MSc *Melb* PhD *Mon*; NHMRC Research Fellow; Associate Professor (Medicine), The University of Melbourne

Heidi Drummer, BSc(Hons) PhD *Melb*; Fellow (Microbiology and Immunology), The University of Melbourne
(until 1/05)

Jörg Heierhorst, MD *Hamburg*; NHMRC Senior Research Fellow; Senior Fellow (Medicine), The University of Melbourne

William McKinstry, BSc (Hons) *Tas* PhD *Melb*; Senior Fellow (Medicine), The University of Melbourne
(until 8/05)

Belinda Michell, BSc (Hons) MBA *Mon* PhD *Melb*

Galina Polekhina, MSc (Hons) *Moscow State* PhD *Aarhus*; NHMRC RD Wright Fellow

Pantelis Poumbourios, BSc(Hons) PhD *Melb*
(until 1/05)

John Price, BSc (Hons) PhD *Aberdeen*; NHMRC RD Wright Fellow

Julian Quinn, BSc (Hons) MSc DPhil *Oxon*

Boris Sarcevic, BSc (Hons) *LaTrobe* PhD *Melb*

Robyn Starr, BSc (Hons) *Adel* PhD *Maryland*; ARC QEII Fellow; Associate Professor (Medicine), The University of Melbourne

Helen Thomas, BSc (Hons) *UWA* PhD *Melb*; NHMRC RD Wright Fellow; Senior Fellow (Medicine), The University of Melbourne

Erik Thompson, BSc (Hons) PhD *Griffith*, Associate Professor (Surgery), The University of Melbourne

Mark Waltham, BSc (Hons) PhD *Qld*; Senior Fellow (Surgery), The University of Melbourne

Research Scientists

Julian Adams, BSc MSc *Cantab* PhD *Massey*
(until 1/05)

Elizabeth Allen, BSc *Otago* PhD *Melb*; Fellow (Medicine), The University of Melbourne

Steve Bouralexis, BSc *Flinders* BCompSc *Uni SA* BHealthSc (Hons) PhD *Adel*; NHMRC Peter Doherty Fellow

Kim Branson, BSc(Hons) Adel PhD Melb; NHMRC Peter Doherty Fellow

Christine Brender, BSc MSc PhD *Copenhagen*
(until 11/05)

Andrew Carey, BSc(Hons) PhD RMIT; NHMRC Peter Doherty Fellow

Zhiping Chen, BSc *Shanghai* PhD *ULP France*

Nadine Dudek, BSc (Hons) *ANU* PhD *Melb*

Susanne Feil, BSc MSc *Stockholm* PhD *Melb*

Jane Fisher, BSc (Hons) PhD *Mon*
(until 9/05)

Guido Hansen, Dip Biol PhD *Cologne*
(from 10/05)

Karl Häusler, BApplSc *PIT* MAppSc *RMIT* PhD *Melb*

Ian Jennings, BSc PhD *Melb*
(until 7/05)

Vicky Kartsogiannis, BSc (Hons) PhD *Melb*

Frosa Katsis, BAppSc IIC *PIT*

Balasubramanian Krishnamurthy, MBBS *Bangalore* MD *Agra* DM *Lucknow*; JDRF Postdoctoral Fellow

Marc Lafleur, BSc (Hons) *Ottawa* PhD East *Anglia*
(until 2/05)

Thomas Loudovaris, BSc (Hons) PhD *Melb*
(from 5/05)

Nathalie Martinek, BSc(Hons) PhD *Toronto*
(from 8/05 to 11/05)

Luke Miles, BSc (Hons) PhD *LaT*

Rachel Mudge, BSc (Hons) PhD *Melb*; NHMRC CJ Martin Fellow

Akira Nakamura, MD PhD *Keio Univ*
(until 8/05)

Joseline Ojaimi, BSc (Hons) PhD *Melb*
(from 9/05)

Brietta Pike, BSc (Hons) PhD *Melb*

Martin Sadowski, Diploma *Giessen* PhD *Basel*

Maria Schache, BSc (Hons) PhD *Melb*

Gregory Steinberg, BSc PhD *Uni Guelph*; NSERC Postdoctoral Fellow

Gillian Tannahill, BSc (Hons) PhD *Belfast*
(from 10/05)

Ana Traven, BSc (Hons) MSc PhD *Uni Zagreb* NHMRC Peter Doherty Fellow

Bryce Van Denderen, BSc (Hons) PhD *Melb*

Yibin Xu, BSc *Suzhou* MSc *Beijing* PhD *ANU*

Travelling Fellows

Andrew Hammet, BSc (Hons) PhD *Melb*; NHMRC CJ Martin Fellow

Visiting Scientists

Wensheng Deng, BMed MMed *Shandong*

Research Assistants

Angela Arvanitis BSc (Hons)
(from 4/05 to 7/05)

Rochelle Ayala-Perez, BSc *Melb*

Brett Bennetts, BSc (Hons) *Adel*

Tony Blick, BSc (Hons) *Mon*

Francene Bond, BBiomedSc (Hons) *Melb*
(until 5/05)

Irene Boo, BBiomedSc (Hons) *Mon*
(until 1/05)

Melissa Ciccomancini, BSc (Hons) *Mon*

Andrea Connor, BSc
(from 8/05 to 10/05)

Susan Docherty, BSc (Hons) *LaT*
(until 3/05)

Joel Fletcher, BSc (Hons) *Melb*
(until 10/05)

Ailsa Frew, BSc (Hons) *ANU*
(until 2/05)

Nancy Hancock, BA *California State Fresno* MA *San Francisco State*

Emma Jamieson, BSc (Hons) *Curtin*
(until 1/05)

Gaurang Jhala, BSc MSc *Pune*
(from 5/05)

Chi Ly, BSc (Hons) *Melb*

Anne Maerz, BAppSc *RMIT*
(until 1/05)

Lina Mariana, BSc (Hons) *Melb*

Carolyn McNees, BSc (Hons) *Melb*

Hooi-Ling Ng, BSc (Hons) *Melb*

Belinda Rizzo, BSc (Hons) *Melb*
(until 11/05)

Hasnawati Saleh, MSc *Qld*

Julian W Tang, Dip Biotech *Temasek Polytechnic* BSc *Melb*

Nora Tenis, BSc *Mon* Grad Dip Med Lab Sc *Uni SA*

Emma Walker, BSc (Hons) *Deakin*

Kwok Soon Wun, Dip Biotech *Ngee Ann Polytechnic* BSc(Hons) *Melb*

Melisa Vazquez, BAppSc *RMIT*

Jessica Vieusseux, BBtech(Hons) *Flinders*

Chief Technical Officers

Jan Elliot

Daphne Hards, BAppSc *RMIT*

Patricia Ho, BSc *Mon*

Virginia Leopold, BSc (Hons) *LaT*

Patricia Smith, Dip Med Lab Tech *RMIT*

Senior Technical Officers

Melanie Rowe, Dip App Sci Animal Tech *Box Hill*

Technical Officers

Tara Catterall, Dip App Sci Animal Tech *VUT*
(until 4/05)

Kylie Gilbert, Dip App Sci Animal Tech *VUT*

Stacey Fynch, Dip App Sci Animal Tech *NMIT*
(from 10/05)

Catherine Li, Cert Lab Tech *Hong Kong Polytechnic* BAppSc *RMIT*

Laboratory Assistants

Rebecca Cotter

Stacey Deering

Shadie Emini

James Katsis
(until 8/05)

Senior Principal Research Associates

Peter Choong, MBBS MD *Melb* FRACS FAORTHA; Professor of Othopaedics, St Vincent's Hospital and The University of Melbourne

Tony d'Apice, MBBS MD *Syd* MRACP FRACP FRCPA; Professor/ Director of Clinical Immunology and the Immunology Research Centre, St Vincent's Hospital and The University of Melbourne

Jane Moseley, BSc PhD *Lond*; Associate Professor (Medicine), The University of Melbourne

Brendan Murphy, MBBS PhD *Melb* FRACP FAICD; Chief Medical Officer St Vincent's Health, Professor (Medicine), The University of Melbourne

Kong Wah Ng, MBBS (Hons) *Mon* MD *Melb* FRACP FRCP Edin; Associate Professor (Medicine), The University of Melbourne

Principal Research Associates

Michael Henderson, MBBS FRACS, Associate Professor (Surgery), St Vincent's Hospital and The University of Melbourne

John Slavin, MBBS FRACPA; Department of Pathology, St Vincent's Hospital

Senior Associates

Craig Morton, BSc (Hons) PhD *Melb*; Biota Structural Biology Laboratory

Harshal Nandurkar, MBBS *Bombay* PhD *Melb* FRACP FRCPA; Staff Haematologist, St Vincent's Hospital

Evange Romas, MBBS PhD *Melb* FRACP; Senior Lecturer (Medicine), The University of Melbourne; Department of Rheumatology, St Vincent's Hospital

Natalie Sims, BSc (Hons) PhD *Adel*; NHMRC RD Wright Fellow; Department of Medicine, The University of Melbourne

Associates

Julian J Adams, BSc MSc *Cantab* PhD *Massey*
(from 2/05)

Sue Rogers, BSc (Hons) PhD *Lond*; Department of Medicine, The University of Melbourne

Jerome Wielens, BApplSci (Hons) PhD *Mon*

Commercialisation Development Manager

Anthony Mason, PhD *ANU*
(from 7/05)

Business Manager

David Rees, BBus *RMIT* CPA ACIS Grad Dip CSP

Laboratory and Technical Services Manager

David Murfitt, HNC AppBiol *Cambridge CAT*

Development Manager

Clare Lacey

Diabetes Program Manager

Anne Thorburn, BSc (Hons) PhD *Syd*

Executive Officer Policy And Projects

Claire Tanswell, G Cert Bus Admin *Swinburne*

Personnel And Grants Administrator

Gayle McMurray

Assistant Accountants

Froilan Altarez

Lisnawati Wirawan-Liauw, SE *Atmajaya Katolik Uni*

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Steven Boz

Beth Castles

Leonie Loveday

Kathryn O'Connell

Dimitra Samaras

It Manager

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It Support Officer

James Mugg, BA *LaT*

National Serology Reference Laboratory

Director

Elizabeth Dax, AM MBBS *Melb* PhD *Mon* MD *Melb*; Associate Professor (Medicine), The University of Melbourne

Operations Manager

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Research Coordinator

Dale McPhee, BSc (Hons) PhD *Mon*; Associate Professor (Microbiology and Immunology), The University of Melbourne

Quality Manager

Roderick Chappel, BAgrSc PhD *Melb*

Project Manager

Wayne Dimech, BAppSc *RMIT* FAIMS GDipMgt *Deakin*

Scientists

Thein Thein Aye, MBBS *Yangoon* PhD *Japan*

Denison Chang, BSc (Hons) *Mon*

Hayley Croom, BSc *Melb*
(until 11/05)

Bradley Dent, BSc (Hons) *Melb* MPhil *Cantab*

Larissa Doughty, BSc (Hons) *Mon*
(until 10/05)

Thu-Anh Erickson, BAppSc MAppSc *RMIT*

Barbara Francis, BSc *Melb* GdipAppSc (Health Stats) PhD *Swinburne*

Rosina Gribben, BSc *Syd*

Darren Jardine, BSc (Hons) PhD *LaT*

Marina Karakaltsas, BSc *LaT*

Sally Land, BSc (Hons) DipEd *Melb*

Lena Panagiotopoulos, BSc *LaT*

Scott Read, BSc (Hons) *Lond*

Kim Richards, BSc (Hons) *VUT*

Joanne Schlegel, BAppSc *RMIT*

Kathy Smeh, BSc (Hons) BEd MEd *Melb*

Sandy Walker, BSc (Hons) *LaT*

Kim Wilson, BAppSc *QIT* PhD *Melb*

Data Management and Website Officers

Amasy Alkhateeb, BBiomed (Hons) *Deakin*
(from 2/05)

Rosanna Fahmy

Clare Kinnear, BSc *Melb*

Laboratory Assistant

Frank Torzillo

Executive Assistant

Linda Tracey

Communication Officer

Romy Johnson
(until 11/05)

Computer Systems Manager

John Tomasov, BSc(Hons) PhD *LaT* Grad Dip Comp Sc *Mon*

Office Manager

Louie Opasinov, BSc Dip Ed *Melb*

Administration Assistant

Helen Hasler
(from 5/05)

Students and Graduates

Postgraduate education at SVI

St Vincent's Institute offers opportunities for Postgraduate training through the University of Melbourne, Department of Medicine and Department of Biochemistry. Currently, 22 students are studying for their PhD at SVI. In addition, MSc and Honours programs are offered at SVI.

Details of projects on offer can be accessed at:

www.svi.edu.au/education/phdprojects

More information about the Postgraduate programs offered by the Department of Medicine can be accessed at:

www.medstv.unimelb.edu.au/Prospective/index.cfml

St Vincent's Institute Foundation Postgraduate Award

The St Vincent's Institute Foundation offers Postgraduate Student Awards to outstanding students commencing their PhD training at SVI. Successful applicants will receive a $5,000 p.a. top-up stipend for 3 years. More information about the award can be accessed at:

www.svi.edu.au/education/studentaward

or from Dr Robyn Starr, Postgraduate Student Coordinator

Tel: 9288 2480

Email: rstarr@svi.edu.au

Applications are due October 31 of each year.

Successful applicants for the St Vincent's Institute Foundation Postgraduate Award in 2005 were:

David Ascher – sponsored by Major Engineering

Michelle Kouspou – sponsored by Connie McKeage and Michael Cole

Nirupa Sachithanandan – sponsored by Dansu Construction

UROP

St Vincent's Institute participates in the Undergraduate Research Opportunities Program (UROP), administered by Bio21. This Program gives undergraduate students the opportunity to undertake their own project in a research lab, in order to introduce them to a research environment and encourage them to pursue careers in science. Currently there are 6 UROP students at SVI.

More information about UROP can be accessed at:

www.bio21.com.au/urop.asp

or from Dr Robyn Starr, Postgraduate Student Coordinator,

Tel: 9288 2480

Email: rstarr@svi.edu.au

Applications are open in April and September of each year, for mid- and end of year intakes, respectively.

St Vincent's Student Society

This society is run by students and organises both social and career development events throughout the year. An offsite Student Retreat is held annually, which provides a great educational and socialising opportunity for the students.

Students

Postgraduate Scholars – Doctor of Philosophy

Eveline Angstetra, BSc (Hons) *Melb*
'Mechanisms of immune destruction of pancreatic beta cells'

Alicia Arnott, BSc (Hons) *Deakin*
'Control of HIV-1 replication after early HAART: the role of viral phenotype and antibody responses'

David Ascher, BSc (Hons) *Qld*
'Structural characterisation of proteins involved in memory'

Nicholas Dzamko, BSc (Hons) *Flinders*
'Hormonal activation of AMP activated protein kinase'

Eugene Estella, MBBS *Qld* FRACP
'Mechanism of β-cell destruction'

Jonathan Gooi, BBiomedSc (Hons) *Melb*
'Osteoclast-mediated regulation of bone formation'

Abhilasha Gupta, BSc (Hons) *Melb*
'The nuclear localisation of AMP-activated protein kinase'

Tristan Iseli, BSc (Hons) *Melb*
'Structure and function of the glycogen binding AMPK-activated protein kinase β-subunit'

Geoffrey Kong, BSc (Hons) *Melb*
'Structural studies of Alzheimer's disease amyloid precursor protein'

Michelle Kouspou, BBiomedSc (Hons) *Melb*
"The role of Heat Shock Factor 1 in cancer cell biology'

Tali Lang, BSc *LaTrobe* (Hons) *Mon*
'Wnt signalling in breast cancer'

Chan-Sien Lay, BSc (Hons) *RMIT*
'Structural and functional features of retroviral envelope glycoproteins'

Lisa McCarthy, BSc (Hons) *Deakin*
'Investigation of cancer cell inhibition by a novel extract of shark cartilage'

Mark McKenzie, BSc (Hons) *Melb*
'Protection of pancreatic beta cells from perforin-mediated cell death'

Carolyn McNees, BSc (Hons) *Melb*
'ASCIZ is required for lesion-specific Rad51 foci formation and DNA damage survival'

Lorien Parker, BSc Hons *Melb*
'Structural studies of glutathione transferases'

Matthew Pereira, BSc *LaTrobe* (Hons) *Melb*
'The role of IFIT1 in tumor cell growth, progression and metastasis'

Ruby Platt, BSc (Hons) *Virginia*
'Novel application of Tranilast for the treatment of acute myeloid leukaemia'

Nirupa Sachithanandan, MBBS *Mon* FRACP
'Association and predictive power of vascular disease risk factors with insulin resistance and the vascular complications of type 1 diabetes'

Randy Suryadinata, BSc (Hons) *Melb*
'Identification and characterization of novel CDK substrates important in cell cycle progression'

Erin Verity, BSc (Hons) *Swinburne*
'The importance of neutralizing antibodies in any potential vaccine against HIV-1'

Kelly Waldeck, BSc (Hons) *UWA*
'The role of FKBP52 in tumor progression and metastasis'

Mark Walter, BSc Hons *LaTrobe* BEc *Adel*
'Structure and function of the γ-subunit of AMP-activated protein kinases'

Postgraduate Scholar – Doctor of Science

Frances Milat, MBBS *Mon* FRACP
'The PTH and wnt pathway as anabolic targets in bone'

Postgraduate Scholar – Master of Science

Emma Jamieson, BSc (Hons) *Curtin*
'Destruction of beta cells in type 1 and type 2 diabetes'

Undergraduate Scholars – Bachelor of Science (Honours)

Domenic Di Fabio, BSc *Melb*
'Fibroblast growth factor-2 in cancer cell survival and metastasis'

Sudarshan Rai, BSc *Melb*
'Expression of facilitative glucose transporters in collagen-induced arthritis'

Cynthia Soon, BSc *RMIT*
'Effects of green tea catechin, epigallocatechin-3-gallate, on breast tumour cell biology'

Undergraduate Research Opportunity Program

Junquan Huang
'Purification of the diabetes autoantigen IGRP'

Sarah Jones
'SOCS1 and IL-23 signalling'

Cze-Yen Lee
'Analysis of diabetes in NOD mice with defective IL-1 and IFNγ signalling'

Elena Tucker
'Isolation of T cell regulatory genes using ENU mutagenesis'

Angela Tam
'Importance of the location of protein interaction domains in modular signalling proteins'

Shanna Tam
'AMPK expression in AMPK B2 Knock out mice'

Su Ee Wong
'The role of macrophages in CD4-dependent models of type 1 diabetes'

Summer Vacation Research Scholars

Phil Au

Matthew Bird

Wensheng Deng

Junquan Huang

Nadia Sadli

Sarah Vickery

Graduations

The Following Graduated Doctor of Philosophy – The University of Melbourne

Angela Arvanitis, BSc (Hons) *Melb*
'Characterisation of an in vitro model of epithelial to mesenchymal transition'

Barry Dixon, MBBS *Syd* FRACP PhD *Melb*
'Characterisation of systemic inflammation following cardiopulmonary bypass'

Michelle Dunstone, BSc (Hons) *Melb* PhD *Melb*
'Structural studies of plasma pathway proteins'

Joseph Pereira, BSc (Hons) *LaTrobe* PhD *Melb*
'Biology of the αvβ3 integrin in breast cancer'

The Following Graduated Bachelor of Science Honours – The University of Melbourne

Julian W Tang, Dip Biotech *Temasek Polytechnic* BSc *Melb*
'Structural studies of pore forming toxins'

Kwok Soon Wun, Dip Biotech *Ngee Ann Polytechnic* BSc *Melb*
'Structural analysis of the amyloid precursor protein'

Fellowships, prizes and grants

Immunology and Diabetes

Fellowships and prizes

- Dr Bala Krishna Murthy was awarded a JDRF/ipac Young Scientists Travel Grant to attend the Immunology of Diabetes Society in Japan in October
- Dr Helen Thomas was awarded a travel grant from the Immunology of Diabetes Society to attend the society's annual meeting in Japan
- Dr Helen Thomas was awarded a St Vincent's Health Research Week Award for best senior investigator presentation
- Mr Mark McKenzie was awarded a poster prize at St Vincent's Health Research Week
- Mr Mark McKenzie received a St Vincent's Hospital Research Grant-in-aid for his PhD studies
- Dr Nirupa Sachithanandan was awarded a Medical Postgraduate Scholarship from the NHMRC
- Dr Nirupa Sachithanandan was awarded a St Vincent's Institute Foundation Postgraduate Student Award
- Dr Nirupa Sachithanandan awarded a JDRF travel grant to attend the JDRF/EASD Young Scientist's training course in islet biology in England

Grants

- TWH Kay. Islet cell Transplantation Program. Department of Human Services
- TWH Kay, LC Harrison, P Colman and A Purcell. T-cell specificity and function in type 1 diabetes pathogenesis and prevention. JDRF Program Grant (3-year support)
- HE Thomas. Protection of pancreatic beta cells from apoptosis induced by cytotoxic T lymphocytes. JDRF Advanced Postdoctoral Fellowship Transitional Funding
- HE Thomas. Genetic analysis of apoptotic changes in pancreatic beta cells induced by CD4+ T cells in a mouse model of type 1 diabetes. Diabetes Australia Research Trust
- TWH Kay. Xenogen IVIS Biophotonic Imaging Unit. Marian & E.H. Flack Trust

Signal Transduction

Fellowships and prizes

- A/Prof Robyn Starr was awarded a Senior Research Fellowship from the NHMRC (relinquished)
- A/Prof Robyn Starr was awarded a Sylvia and Charles Viertel Senior Medical Research Fellowship
- Dr Christine Brender was awarded a poster prize at St Vincent's Health Research Week

Bone, Joint and Cancer Group

Fellowships and prizes

- A/Prof Matthew Gillespie was elected to the Council of the Australia and New Zealand Bone and Mineral Society
- A/Prof Matthew Gillespie was elected to the Board of Directors of the International Bone and Mineral Society
- Dr Natalie Sims was awarded a Senior Research Fellowship from the NHMRC
- Dr Rachel Mudge was awarded a senior investigator prize at St Vincent's Health Research Week
- Dr Steve Bouralexis was awarded a poster prize at St Vincent's Health Research Week
- Prof T John Martin was appointed Vice-President of the Cancer and Bone Society
- Dr Julian Quinn was the Outstanding Abstract Award Winner at the joint ANZBMS / ESA Symposium.

Grants

- TJ Martin and M Gillespie. Identification of a 1,25 vitamin D3 regulated osteoclast inhibitor. Chugai Pharmaceutical Co. Ltd., Japan
- R Mudge. The study of interactions and mechanisms that allow nuclear fibroblast growth factor-2 to act as a survival factor in cancer metastasis. Clive and Vera Ramaciotti Foundation New Investigator Grant
- R Mudge and D Rees. RNA analysis using nano-spectrophotometer. State Trustees

Comparative Endocrinology

Fellowships and prizes

- A/Prof Janine Danks was awarded a Senior Research Fellowship from the NHMRC

Tumor Cell Migration and Metastasis

Fellowships and prizes

- Dr John Price was awarded an RD Wright Career Development Award from the NHMRC
- Dr John Price received a travel award to attend the Cancer Induced Bone Disease Meeting in Davos, Switzerland
- Ms Kelly Waldeck was awarded a Dora Lush Scholarship from the NHMRC, a RJ Fletcher Scholarship for Research in Cancer, a Randall and Louisa Alcock Award for Research into Human Diseases, the Mable Kent Scholarship, School of Medicine, University of Melbourne and a Predoctoral Traineeship Award from the US Department of Defense Breast Cancer Research Program
- Ms Michelle Kouspou was awarded an Australian Postgraduate Award, Dean's Honours List, University of Melbourne.

Grants

- JT Price. Purchase of a Xenogen imaging system. The Clive and Vera Ramaciotti Foundation's Biomedical Research Awards
- JT Price. The role of HSF1 in the enhancement of osteoclastogenesis and bone metastasis by the Hsp90 inhibitor, 17AAG. The Susan G Komen Breast Cancer Foundation
- JT Price. Heat Shock Factors and Breast Cancer Metastasis. Susan G Komen Breast Cancer Foundation

- JT Price. Xenogen IVIS Biophotonic Imaging System. Janina and Bill Amiet Foundation
- JT Price. Xenogen IVIS Biophotonic Imaging System. Equity Trustees

Pharmacogenomics

Fellowships and Prizes

- Ms Nadia Sadli was awarded a Cancer Council of Victoria Vacation Studentship

Grants

- M Waltham. Novel therapeutic strategies targeting breast cancer metastasis. Komen Breast Cancer Foundation
- M Waltham and J Kennedy. Profiling acoustic neuromas. Pratt Foundation
- M Waltham. The molecular basis of rapid growth vestibular schwannomas. St Vincent's Hospital Grant-in-aid

VBCRC invasion and metastasis

Grants

- EW Thompson. Invasion and metastasis of breast cancer. Victorian Breast Cancer Research Consortium

Protein Chemistry

Fellowships and Prizes

- Mr Nic Dzamko was awarded a St Vincent's Health Research Week Award for best Junior Investigator presentation

Grants

- GR Steinberg. Leptin Resistance and skeletal muscle AMP-kinase signalling in obesity and diabetes. Diabetes Australia Research Trust
- BE Kemp. Metabolic stress signalling in the heart. National Heart Foundation
- BE Kemp, BJ Michell, GR Steinberg and B van Denderen. AMP Activated Protein Kinase in Obesity. NHMRC Project Grant (3-year support)
- BE Kemp and B Kobe. Phosphoproteomics: metabolic and exercise signalling markers for sedentary and trained individuals. NHMRC Medical Bioinformatics, Genomics and Proteomics Program (5-year support)

Molecular Genetics

Fellowships and prizes

- Dr Andrew Hammet was awarded The Clive and Vera Ramaciotti Foundation's 2005 Biomedical Research Award for new investigator establishment
- Dr Brietta Pike received a CJ Martin Fellowship from the NHMRC
- Ms Carolyn McNees received a Cancer Council of Victoria Postdoctoral Fellowship to continue her work on the characterisation of the ASCIZ protein
- Mr Joel Fletcher received a Cancer Council Victoria PhD Scholarship (accepted) and an Australian Postgraduate Award (declined)

Grants

- J Heierhorst. DNA damage, chemotherapy and cancer. NHMRC Project Grant (3-year support)
- J Heierhorst. Sites of cellular DNA repair. NHMRC Project Grant (3-year support)

Cell Cycle and Cancer

Fellowships and Prizes

- Dr Boris Sarcevic has been awarded a Senior Research Award from the Multiple Myeloma Research Foundation, USA

NRL

Grants

- K Wilson. Development of an Assay to Distinguish Between Recent and Established HIV-1 Infection. NHMRC Development Grant

Structural Biology

Fellowships and Prizes

- Mr Geoffrey Kong was awarded an Australian Society for Biochemistry and Molecular Biology Fellowship
- Mr Geoffrey Kong was awarded a Ted Maslen 1987 Scholarship from the Society of Crystallographers in Australia and New Zealand
- Ms Lorien Parker has been awarded a Ludo Frevel Crystallography Scholarship by The International Centre for Diffraction Data (USA)
- Ms Lorien Parker was awarded a Ted Maslen 1987 Scholarship from the Society of Crystallographers in Australia and New Zealand

Grants

- MW Parker. Study of bacterial toxins as the basis for the design of new antibiotics. NHMRC Project Grant (3-year support)
- MW Parker, T Hercus. Studies of proteins involved in cancer and allergic disease. NHMRC Project Grant (3-year support)
- MW Parker and MT Gillespie. ACRF Rational Drug Discovery Facility, Australian Cancer Research Foundation Research Grant
- C Ward, T Garrett, MW Parker, P Ramsland, O El-Kabbani and M Lawrence. Bio21 Nanolitre Protein Crystallisation Facility for Rational Drug Design and Therapeutic Development. Victorian State Government Bio21 STI funding
- PJ Walsh, LA Miles. Liquid Handling Robot. The Eirene Lucas Foundation

Molecular Cardiology

Fellowships and Prizes

- A/Prof Duncan Campbell was awarded a Senior Research Fellowship from the NHMRC

New Groups Starting in 2006

- Dr Ora Bernard was awarded a Principal Research Fellowship from the NHMRC
- O Bernard. LIM kinase regulates the polymerisation of tubulin to microtubules. NHMRC Project Grant (3-year support)
- D Izon. Novel T cell oncogenes derived from a cDNA library screen. NHMRC Project Grant (3-year support)

Service to the scientific and wider community

Service on Scientific Advisory Boards and Committees

Thomas Kay
- Chair, Diabetes Research Consultative Committee
- Member, Scientific Advisory Board, VBCRC
- Member, Research Council, Diabetes Australia
- Member, Scientific Advisory Committee, Bio21
- Member, National Serology Reference Laboratory Management Committee
- Member, Medical and Scientific Advisory Committee, Juvenile Diabetes Research Foundation
- Member, St Vincent's Hospital Research Development Committee
- Member, St Vincent's Hospital Medical Executive Committee
- Member, NHMRC Grant Review Panel

Matthew Gillespie
- Member, Science Policy & Nominations Committee, American Society for Bone and Mineral Research
- Member, National Committee for Medicine for the Australian Academy of Science
- Member, Medical and Scientific Committee, Cancer Council Victoria
- Chair, Scientific Review Committee, Australian Cancer Council
- Member, St. Vincent's Hospital Institutional Biosafety Committee

Michael Parker
- Member, BioCARS Sub-Committee of the Australian Synchrotron Research Program
- Member, Bio21 Medicinal Chemistry Working Group
- Member, Committee to oversee the running of ~$5M worth of crystallisation robotics.
- Member, St Vincent's Hospital Research Grants Committee
- Member, Bio21 Nanolitre Protein Crystallisation Consortium

Jack Martin
- Member, Medical and Scientific Committee, Cancer Council of Victoria
- Chairman, Scientific Advisory Board, Victorian Breast Cancer Research Consortium
- Member, Medical Research Advisory Committee, Australian Cancer Research Foundation
- External Scientific Reviewer, Mater Research Institute, Brisbane
- Member, Scientific Advisory Board Nordic Biosciences, Inc, Copenhagen, Denmark
- Member, Scientific Advisory Board, Botnar Research Centre, Nuffield Department of Orthopaedics, University of Oxford, UK
- Member, Overseas Fellowships' Committee, Royal Society, UK
- Member, Subcommittee 9, Australian Academy of Science
- Vice President, Cancer and Bone Society
- Consultant, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, USA

Bruce Kemp
- Member, Scientific Advisory Board & Management Committee for National Serology Reference Laboratory
- Member, Scientific Advisory Board, Mercury Therapeutics Boston

Jock Campbell
- Member, NHF Heart Failure Guidelines Committee

Janine Danks
- Member-at-large, International Federation of Comparative Endocrinology Societies Council
- Member, Women in Bone and Mineral Research Committee, American Society of Bone and Mineral Research

Jörg Heierhorst
- Member, Human Research Ethics Committee A, St. Vincent's Health Melbourne

John Price
- Member, St Vincent's Hospital Research Week Organizing Committee
- Member, University of Melbourne, Department of Medicine Postgraduate Research
- Scientific Consultant, Avolix Pharmaceuticals Inc., Arizona, USA

Robyn Starr
- Member, PhD Confirmation Committee, SVI/Melbourne University Department of Medicine
- Member, UROP committee (Bio21)
- Member, NHMRC Training Fellowship Assessment Panel

Helen Thomas
- Member, St Vincent's Hospital Animal Ethics Committee

Erik Thompson
- President, Australasian Microarray & Associated Technologies Association
- Treasurer, The EMT International Association
- Member, Translation Research Working Group and Management Committee, Australian Prostate Cancer Collaboration
- Member, NHMRC Grant Review Panel
- Member, NSW Cancer Council Program Grant Review Panel
- Member, Tissue Bank Management Committee, Shared SVH/PeterMac Tissue Bank
- Member, St. Vincent's Hospital Research Development Committee

Francis Milat
- Member, Diabetes Cardiovascular Advisory Clinic, Southern Health Committee

Elizabeth Dax
- President, Australasian Society HIV Medicine
- Secretary, Australasian Society History of Medicine
- Associate Member, Medical Devices Evaluation Committee
- Member, National Coordinating Committee on Therapeutic Goods In Vitro

Service on Boards and Editorial Boards

Thomas Kay
- Editor, Journal of Molecular Endocrinology
- Regional Editor, Autoimmunity
- Associate Editor, Endocrinology

Matthew Gillespie
- Board Member, Research Australia.
- Board member, International Society for Bone and Mineral Research
- Board member, Australian and New Zealand Bone and Mineral Society
- Editor, Journal of Bone and Mineral Research
- Editor, Journal of Molecular Endocrinology

Jack Martin
- Board member, Victorian Breast Cancer Research Consortium
- Associate Editor, Bone
- Associate Editor, Endocrinology
- Associate Editor, Calcified Tissue International
- Editorial Board, Trends in Endocrinology and Metabolism
- Editorial Board, BoneKey

Bruce Kemp
- Editorial Board, Cellular Signalling
- Editorial Board, Journal of Molecular and Genetic Medicine

Janine Danks
- Editorial Board, General and Comparative Endocrinology

John Price
- Editorial Board, Recent Patents on Anti -Cancer Drug Discovery Journal

Erik Thompson
- Board Member, Metastasis Research Society (International)
- Associate Editor, The Breast Journal
- Associate Editor, Clinical and Experimental Metastasis

Service on Conference Organizing Committees

Matthew Gillespie
- Program Committee, 2nd Joint European Calcified Tissue Society and International Bone and Mineral Society, Geneva, 2005
- Program Committee International Bone and Mineral Society, Montreal, 2007
- Member, Scientific Committee, Cancer Induced Bone Disease Meeting, Davos, Switzerland, March 2005
- Member, International Program Committee, 2nd Joint Meeting of the European Calcified Tissue Society and the International Bone and Mineral Society, Geneva, June 2005

Michael Parker
- Chair, Program and Media Sub-Committees of the Lorne Protein Conference Organizing Committee
- Member, Scientific Program Committee, 13th Annual International Conference on Intelligent Systems for Molecular Biology Meeting, June 2005

Jack Martin
- Co-organiser, Symposium on Advances in Molecular Pharmacology and Therapeutics of Bone, University of Oxford, July 2005

Bruce Kemp
- Member, Organizing Committee, Lorne Conference on Protein Structure and Function Committee

Janine Danks
- Chairman, Organizing Committee, Comparative Endocrinology of Calcium Regulation Satellite Symposium of the XVI International Bone and Mineral Society, June 2007
- Member, Meetings Committee, International Bone and Mineral Society
- Chair, Local Organizing Committee, Sydney Satellite Symposium, International Conference on Comparative Endocrinology, Hong Kong, 2009.

Jörg Heierhorst
- Member, Local Organising Committee and Program Committee, XXIII International Conference on Yeast Genetics and Molecular Biology, Melbourne 2007

Robyn Starr
- Program Convenor, ASMR National Scientific Conference, November 2006

Erik Thompson
- Co-Convenor, 5th Discovery Science and Biotechnology Conference, Melbourne, May 2006
- Co-Convenor, 4th Discovery Science and Biotechnology Conference, Melbourne, May 4-6, 2005
- Member, Organizing Committee, 2nd International EMT Conference, Vancouver, October 2005

Mark Waltham
- Member, Conference Program Committee, Discovery Science and Biotechnology, May 2005

Collaborations

Immunology and Diabetes

- Prof L Harrison, Dr S Mannering, Dr A Lew, Dr R Sutherland, Dr S Londrigan, The Walter and Eliza Hall Institute. Immune mechanisms of beta cell life and death
- Prof J Trapani, Peter McCallum Cancer Institute; Dr A Strasser, The Walter and Eliza Hall Institute; Dr J Allison, The University of Melbourne. T-cell mechanisms of beta cell destruction
- Prof R Thomas, The University of Queensland. Clinical trial of Anakinra in type 1 diabetes mellitus
- Dr P Santamaria, The University of Calgary. Mechanisms of pancreatic beta cell death in TCR transgenic mouse models of type 1 diabetes
- Dr M von Herrath, La Jolla Institute for Allergy and Immunology. Mechanisms of beta cell death in the LCMV model of type 1 diabetes
- A/Prof P O'Connell, Westmead Millenium Institute. Clinical islet transplantation
- Dr Sof Andrikopoulos, The University of Melbourne, The role of SOCS proteins in insulin resistance

Signal Transduction

- Prof T Kilpatrick and B Emery, Howard Florey Institute. The role of SOCS3 in immune pathology of EAE
- Dr B Jenkins and Dr M Ernst, Ludwig Institute. The role of SOCS3 in the regulation of gp130 cytokines in T cells
- Dr D Tarlinton, The Walter and Eliza Hall Institute. The effect of the LYM1 NFκB2 mutation on B cell development and function
- Prof D Hilton and Dr B Kile, The Walter and Eliza Hall Institute. ENU mutagenesis and the immune system
- Dr W Alexander, The Walter and Eliza Hall Institute. The role of SOCS proteins in T cell development and function

Structural Biology

- Dr H Drummer and Dr A Poumbouris, Macfarlane Burnet Institute. HCV
- Prof L Tilley, La Trobe University. Malarial proteins
- Dr B Rawlinson, Prince of Wales Hospital. Cytomegalovirus
- Dr D Rhodes, Avexa. HIV
- Dr S Tucker, Biota. Viral respiratory diseases
- Dr P Young, Queensland University. Respiratory syncytial virus
- Dr R Baker, John Curtin School of Medical Research; Prof D Bowtell, Peter MacCallum Cancer Institute. Proteins involved in ubiquitination
- Dr O Bernard, St. Vincent's Institute. LIM kinase
- Prof P Board, John Curtin School of Medical Research. Glutathione transferases
- Prof A Frauman, Austin Health. Prostate cancer proteins
- Dr M Gillespie and Prof J Martin, St. Vincent's Institute. PTHrP
- Prof B Graham, Victor Chang Cardiac Research Institute. Transglutaminase
- Prof B Kemp, St. Vincent's Institute; Dr D Stapleton, Bio21 Institute. Protein kinase regulation
- Prof A Lopez, Hanson Centre for Cancer Research. Cytokine receptor
- Prof E Simpson, Prince Henry's Institute of Medical Research. Steroid receptors
- Dr R Thier, University of Queensland. GSTs
- Prof M Vadas and Dr J Gamble, Hanson Centre for Cancer Research, Protein kinases
- Dr M Waters, University of Queensland, Growth hormone receptor
- Dr F Mendelsohn, Dr A Albiston and Dr S Yeen Chai, Howard Florey Institute. IRAP
- Dr A Christopoulos, Melbourne University. Muscarinic receptors
- Prof C Masters and Dr R Cappai, Melbourne University. Proteins implicated in Alzheimer's disease
- Dr P Curmi, University of New South Wales. CLICs
- Dr J Jamie, Macquarie University; A/Prof R Truscott, University of Wollongong. IDO
- Dr J Lynch, Queensland University. Ligand-gated ion channels
- Dr S Petrou, University of Melbourne. Ion channels
- Dr P Sexton, Howard Florey Institute. GPCRs
- Dr S Bottomley, Monash University. Serpins
- Prof J Goding, Monash Medical School. Ecto-phosphodiesterases
- Dr R Pace, Australian National University. Photosystem II
- Dr P Thompson, Victorian College of Pharmacy. Phosphodiesterase inhibitors
- Dr R Tweten, University of Oklahoma. Pore-forming toxins and receptors
- Dr G van der Goot, University of Geneva. Aerolysin
- Prof A Aceto, Prof C Di Ilio Università "G. D'Annunzio", Chieti; Prof M Lo Bello, Prof G Ricci, University of Rome "Tor Vergata"; Dr S Copley, University of Colorado; Dr L Garcia-Fuentes, University of Almeria; Dr N Labrou, Agricultural University of Athens; Prof B Mannervik, Dr G Stenberg, Uppsala University. Glutathione transferases
- Prof P Dyson, Ecole Polytechnique Federale de Lausanne. Cisplatin drugs
- Prof A Aceto, Università "G. D'Annunzio", Chieti. Prions
- Dr J Cook, University of Wisconsin-Milwaukee. GABA receptors
- Prof S Ferreira, Universidade Federal do Rio de Janeiro. APP
- Dr M Karsdal, Nordic Biosciences, Copenhagen. Chloride channels

Bone, Joint and Cancer

- Dr B Jenkins and Dr M Ernst, Ludwig Institute. IL-11 actions upon bone.
- Dr P Croucher, University of Sheffield. Myeloma effects upon bone cells.
- Dr J Onyia and Dr N Kularni, Eli Lilly and Company. PTH anabolic actions.
- Dr L Suva, University Medical School of Arkansas. IL-8 in breast cancer metastasis.
- Dr P Croucher, University of Sheffield. Myeloma effects upon bone cells.
- Dr A Fosang, Murdoch. Aggrecan effects upon the growth plate.
- Dr E Gardiner, Princess Alexandra Hospital Brisbane. NPY actions on bone.
- Dr D Handelsman, ANZAC Institute. Sex hormones in bone turnover.
- Dr M Henderson, Peter McCallum Cancer Institute. Breast cancer metatasis.
- Dr M Karsdal, Nordic Biosciences, Copenhagen. Bone antiresorptives.
- Dr L Robb, The Walter and Eliza Hall Institute. IL-6 effects upon bone.
- Dr M Smyth, Peter Macallum Cancer Institute. Natural Killer Cell and Dendritic Cell Functions
- Dr N Udagawa, Matsumoto Dental University Japan. Osteoclast inhibition
- Dr I Wicks, The Walter and Eliza Hall Institute. Animal models of arthritis.

Tumour Cell Migration and Metastasis

- Dr D Newgreen, Murdoch Children's Research Institute; Dr L Ackland, Deakin University; Dr Erik W. Thompson, St Vincent's Institute. Epithelial-Mesenchymal Transition and its Role in Cancer Progression.
- Dr J Rossjohn, Monash University; Dr D Thomas, Peter MacCallum cancer Institute; Dr J Marshall, ICRF, St Thomas' Hospital, London. αvβ3 Integrin Biology
- Dr F Burrows, Conforma Therapeutics., San Diego. Hsp90 inhibitors and HSF-1 activation in Metastasis

- Dr T Magliocco, University of Calgary. Novel Molecular Modulators of Metastasis
- Avolix Pharmaceutical Inc., Arizona. Identification of Novel Cell Migration Inhibtors for Metastatic Therapy

Comparative Endocrinology

- Dr T Walker, Marine and Freshwater Resources Institute, Department of Primary Industry.
- Prof J Clement, University of Melbourne.
- Prof J Zajac, University of Melbourne.
- Dr N Suzuki, Kanazawa University. The actions of fish parathyroid hormones on fish osteoclasts
- Dr B Venkatesh, National University of Singapore. Isolation, analysis and physiology of the calcium regulating hormones in the elephant fish

Protein Chemistry and Metabolism

- Dr D Cameron-Smith Deakin University. Obesity and muscle metabolism
- Dr M Febbraio, RMIT University. Skeletal muscle lipid metabolism
- Dr D Fulton, Vascular Biology Center Medical College of Georgia Endothelial nitric oxide synthase
- Dr R Gilbert, University of Melbourne. Flt3 kinase
- Dr L Goodyear, Joslin Diabetes Centre Boston. AMP activated protein kinase
- Dr J Hawley, RMIT University. AMPK skeletal muscle
- Dr D Jans, Monash University. Nuclear Transport
- Dr L Macaulay, CSIRO Molecular & Health Technologies. Obesity and energetics
- Dr A Marette, Laval University Quebec City.
- Dr G McConell, University Melbourne. AMPK skeletal muscle exercise
- Dr A Means, Duke University Medical Centre. CaM kinase kinase
- Dr D Power, Austin Research Institute. AMPK in the kidney
- Prof R Simpson, Ludwig Institute for Cancer Research; Dr J Visvader, Walter & Eliza Hall Institute. Breast cancer protein StarD10
- Dr T Tiganis, Monash University. Signal transduction
- Dr R Venema, Vascular Biology Center Medical College of Georgia, Endothelial nitric oxide synthase
- Dr L Witters, Dartmouth Medical College. AMP activated protein kinase

Molecular Cardiology

- Dr M Woodward, Dr J Chalmers, Dr S Colman, Dr A Patel, Dr B Neal and Dr S MacMahon, The George Institute for International Health. Perindopril Protection Against Recurrent Stroke Study (PROGRESS) collaboration: Study of plasma markers that predict cardiovascular events in subjects with cerebrovascular disease
- Mr. M Yii and Mr J Kenny, St. Vincent's Hospital; Dr M Black, Monash University. The SVHM Cardiac Tissue Bank
- Prof M Esler, Baker Heart Research Institute; Prof H Krum, Alfred Hospital. Study of the inter-relationships between the sympathetic nervous system, the renin angiotensin system and the kallikrein kinin system in hypertension and heart failure, and the therapeutic ramifications of these inter-relationships
- Professor J Horowitz, The Queen Elizabeth Hospital. Study of the effects of ACE inhibitors on platelet function and the role of ACE inhibitor-platelet interactions in mediating the prevention of cardiovascular events by ACE inhibitors
- Dr A Aggarwal, Royal Melbourne Hospital. Study of the effects of ß -blocker therapy on aldosterone levels.
- Prof K Bernstein, Emory University. Study of genetic models of tissue ACE expression.
- Prof B Kemp, St. Vincent's Institute; Dr Xiao-Jun Du, Baker Heart Research Institute. Study of AMPK ß -subunit gene knockout mice.
- Dr B Dixon and Dr J Santamaria, St Vincent's Hospital. Study of the systemic inflammatory response to cardiopulmonary bypass
- Prof Richard Gilbert, St Vincent's Hospital. Study of the effects of renin inhibition on the Ren2 diabetic model of renal disease
- Prof F Alhenc-Gelas and Dr M Azizi, INSERM France. Study of the effects of the R53H mutation of the tissue kallikrein gene on urinary kallidin levels in humans
- A/Prof J Zhuo, Henry Ford Hospital and Wayne State University School of Medicine. Study of angiotensin peptides in the kidney

Molecular Genetics

- Prof Ming-Daw Tsai, Ohio State University. Structural analyses of FHA domain functions
- Prof S Takeda, Kyoto University. Analyses of novel DNA repair pathways
- Prof B Andrews, University of Toronto. Robotic synthetic genetic array analysis of hte yeast MDT1 gene
- Dr B Bhullar, Harvard University. Activation of Rad53 kinase by DNA damage
- A/Prof G McArthur, Peter MacCallum Cancer Institute. Recombinational repair analyses in human cells
- Dr X Du, Baker Medical Research Institute; Prof W Koch and Dr P Most, Thomas Jefferson University; Prof T Parker, University of Toronto; Dr A Remppis, University of Heidelberg; Dr J Baudier, INSERM Grenoble. Collaborative studies on S100A1 functions in mice

Cell Cycle and Cancer

- Dr H Richardson, Peter MacCallum Cancer Institute. Regualtion of cell cycle progression by CDK-mediated phosphorylation of the Brahma chromatin-remodelling complex

Pharmacogenomics

- Dr A Stevenson, CSIRO. Phase-contrast X-ray radiography in biomedical research
- Dr G Brownlee and Dr T Brown, Monash University. Role of hyaluronan synthase in breast cancer progression

VBCRC Invasion and Metastasis

- Dr R Anderson, Peter MacCallum Cancer Institute. MMPs in mouse mammary metastasis model; breast cancer growth and metastasis in MMP-deficient mice
- Dr I Campbell, Peter MacCallum Cancer Institute. Genotyping breast cancer cell variants
- Dr M Henderson, University of Melbourne. Studies in clinical breast cancer specimens
- Dr J Price, St Vincent's Institute. Molecular basis of breast-bone metastasis and cellular migration
- Dr M Waltham, St Vincent's Institute. MMP inhibition studies in breast cancer systems and gene array analysis of epithelio-mesenchymal transition
- Dr N Dean, ISIS Pharmaceuticals. Antisense oligonucleotides in breast cancer
- Dr R Fridman, Wayne State University. MMP-integrin interactions
- Prof A Raz, Karmanos Cancer Center. Role of galectin-3 in breast cancer progression
- Dr H Sato, Kanazawa Medical School. MT-MMP regulation during epithelio-mesenchymal transition
- Dr M Seiki, University of Tokyo. Collagen regulation of MT1-MMP function
- Dr T Sasaki, Max Planck Institute. SPARC / osteonectin / BM40 effects on MMP-2-activation in breast cancer cells
- Prof Z Werb, UCSF. MMP analyses

Publications

Alexiou, T., Boon, W.M., Denton, D.A., Nicolantonio, R.D., Walker, L.L., McKinley, M.J., and Campbell, D.J. 2005. Angiotensinogen and angiotensin-converting enzyme gene copy number and angiotensin and bradykinin peptide levels in mice. *J Hypertens* 23:945-954.

Allison, J., Thomas, H.E., Catterall, T., Kay, T.W., and Strasser, A. 2005. Transgenic expression of dominant-negative Fas-associated death domain protein in beta cells protects against Fas ligand-induced apoptosis and reduces spontaneous diabetes in nonobese diabetic mice. *J Immunol* 175:293-301.

Bennetts, B., Rychkov, G.Y., Ng, H.L., Morton, C.J., Stapleton, D., Parker, M.W., and Cromer, B.A. 2005. Cytoplasmic ATP-sensing domains regulate gating of skeletal muscle ClC-1 chloride channels. *J Biol Chem* 280:32452-32458.

Borie, D.C., Starr, R., Hendry, S., Changelian, P.S., and O'Shea, J. 2005. Janus kinase 3 inhibition for immunosuppression: getting close to the starting line. *Curr Opin Organ Transplant* 10:273-278.

Bouralexis, S., Findlay, D.M., and Evdokiou, A. 2005. Death to the bad guys: targeting cancer via Apo2L/TRAIL. *Apoptosis* 10:35-51.

Brown, R.J., Adams, J.J., Pelekanos, R.A., Wan, Y., McKinstry, W.J., Palethorpe, K., Seeber, R.M., Monks, T.A., Eidne, K.A., Parker, M.W., and Waters, M.J. 2005. Model for growth hormone receptor activation based on subunit rotation within a receptor dimer. *Nat Struct Mol Biol* 12:814-821.

Campbell, D.J., Johnston, C.I., Kelly, D.J., Lumbers, E.R., Menard, J., Ryan, J.W., and Wilkinson-Berka, J.L. 2005. In memoriam. Sandford Lloyd Skinner (1933-2005). *Hypertension* 46:452-453.

Campbell, D.J., Krum, H., and Esler, M.D. 2005. Losartan increases bradykinin levels in hypertensive humans. *Circulation* 111:315-320.

Campbell, D.J., Woodward, M., Chalmers, J.P., Colman, S.A., Jenkins, A.J., Kemp, B.E., Neal, B.C., Patel, A., and Macmahon, S.W. 2005. Soluble Vascular Cell Adhesion Molecule 1 and N-terminal Pro-B-Type Natriuretic Peptide in Predicting Ischemic Stroke in Patients With Cerebrovascular Disease. *Arch Neurol*.

Campbell, D.J., Woodward, M., Chalmers, J.P., Colman, S.A., Jenkins, A.J., Kemp, B.E., Neal, B.C., Patel, A., and MacMahon, S.W. 2005. Prediction of myocardial infarction by N-terminal-pro-B-type natriuretic peptide, C-reactive protein, and renin in subjects with cerebrovascular disease. *Circulation* 112:110-116.

Campbell, D.J., Woodward, M., Chalmers, J.P., Colman, S.A., Jenkins, A.J., Kemp, B.E., Neal, B.C., Patel, A., and MacMahon, S.W. 2005. Prediction of heart failure by amino terminal-pro-B-type natriuretic peptide and C-reactive protein in subjects with cerebrovascular disease. *Hypertension* 45:69-74.

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Seminar Program

Dr Ross Hannan
Peter MacCallum Cancer Institute
"All roads lead to the ribosome"

Professor Kerin O'Dea
Menzies School of Health Research, Darwin
"The Mediterranean diet and chronic disease risk"

Dr Boris Sarcevic
St Vincent's Institute
"Regulation of cell cycle progression by protein phosphorylation and ubiquitylation"

Associate Professor Marc Achen
Ludwig Institute for Cancer Research, Melbourne
"Regulation of angiogenesis and lymphangiogenesis in cancer"

Dr Eugene Estella
Final PhD Presentation – St Vincent's Institute
"Mechanisms of immune destruction of human pancreatic islet cells"

Ms Abhilasha Gupta
Final PhD Presentation – St Vincent's Institute
"The nuclear localisation of AMP-activated protein kinase"

Dr Jane Visvader
The Walter & Eliza Hall Institute of Medical Research
"Transcriptional regulators of mammopoiesis and stem cells"

Professor Michael Parker
St Vincent's Institute
"The life cycle of pore-forming toxins"

Mr Mark Walter
Final PhD Presentation – St Vincent's Institute
"Characterisation of AMPK mutants involved in a novel cardiac glycogen storage disease"

Dr David Dougan
Department of Biochemistry & Molecular Biology, LaTrobe University
"Adapting AAA+ proteins: an extension of the protein quality control network in bacteria"

Dr Sue Forrest
Australian Genome Research Facility
"Get one jump ahead: new genome technologies and their application to the wallaby sequencing project"

Professor Tom Kay
St Vincent's Institute
"Autoimmune diabetes: a mystery"

Dr Kum Kum Khanna
Queensland Institute of Medical Research
"Defective DNA damage response pathways and cancer susceptibility"

Associate Professor Grant McArthur
Peter MacCallum Institute
"Targeting cell growth in the treatment of cancer"

Associate Professor Erik Thompson
St Vincent's Institute
"Matrix metalloproteinase targets in human breast cancer growth and progression"

Dr Rachel Mudge
St Vincent's Institute
"Nuclear FGF-2 promotes cancer cell survival and metastasis"

Associate Professor Mathew Gillespie
St Vincent's Institute
"Actions of PTHrP and OPG upon breast cancer cells"

Associate Professor Chris Nolan
Australian National University
"Islet beta-cell triglyceride/free fatty acid cycling and the amplification pathway of nutrient-induced insulin secretion"

Dr Brendan Jenkins
Ludwig Institute for Cancer Research
"The level of STAT3 signalling by IL-6 family cytokines is a critical determinant for physiological responses"

Professor Richard O'Hair
Bio 21 Institute, University of Melbourne
"Gas phase fragmentation of peptide ions: from fundamentals to new proteomic tools"

Associate Professor Robyn Starr
St Vincent's Institute
"Regulation of T cell function by SOCS3"

Professor Bruce Kemp
St Vincent's Institute
"AMPK 30 years old and still turning heads"

Dr Tony Tiganis
Department of Biochemistry & Molecular Biology, Monash University
"Regulation of Src signalling by the T-cell protein tyrosine phosphatase in inflammation and cancer"

Dr Paula De Bruyn
Davies, Collison & Cave
"IP, IP and IP; Intellectual property in biomedical research"

Mr Geoffrey Kwai-Wai Kong
Final PhD Presentation – St Vincent's Institute
"Untangling the role of copper ion binding to amyloid precursor protein in Alzheimer's disease"

Dr Robert Karlsson
Biochemistry and Chemistry Biacore AB Sweden
"The expanding use of label free protein interaction analysis across the life science spectrum"

Professor David James
Garvan Institute of Medical Research
"Filling the GAPS in insulin action"

Dr Natalie Sims
St Vincent's Institute
"Signalling through gpl30 in bone; one pathway, many functions"

Dr Steve Bottomley
Department of Biochemistry & Molecular Biology, Monash University
"From lab bench to robotics; the development of a semi-automated approach for protein production at Monash"

Dr Balasubramanian Krishnamurthy
St Vincent's Institute
"Hierarchy of autoantigens in autoimmune diabetes"

Dr Martin Lackman
Department of Biochemistry & Molecular Biology, Monash University
"Eph off – Repulsive language in cell signalling"

Dr Amanda Fosang
Murdoch Children's Research Institute
"Which enzyme destroys cartilage in arthritis? Studies with knock-in and knock-out mice"

Professor Susan Gasser
Friedrich Miescher Institute For Biomedical Research, Basel
"Molecular mechanisms of DNA damage responses"

Dr George Fantus
University of Toronto
"Role of the glucosamine pathway in diabetic complications"

Professor Philip S Low
Purdue University, Indiana
"Architecture and regulation of the glycolytic enzyme complex on the human erythrocyte membrane"

Professor Peter Croucher
University of Sheffield Medical School, UK
"TNF family members and bone disease: lessons from myeloma"

Dr Paul Shore
University of Manchester, UK
"Runx2, a master regulator of bone development, has a role in mammary gland gene expression; implications for bone metastasis in breast cancer"

Dr Brendan Boyce
Department of Pathology & Laboratory Medicine, University of Rochester, New York
"c-src kinase and bone"

Professor Nobuyuki Udagawa
Department of Biochemistry, Matsumoto Dental University
"Osteoclast biology 2005"

Dr Susan Allison
Garvan Institute of Medical Research
"Role of central neuropeptide Y2 receptors in the regulation of bone"

Presentations by SVI staff

Eveline Angstetra
- Australian Diabetes Association annual scientific meeting, Perth. Speaker
- 35th Australian Society for Immunology meeting, Melbourne. Speaker

Thomas Kay
- Australian Diabetes Association annual scientific meeting, Perth. Invited speaker and chair
- Apoptosis and Immunity 2005, Cairns. Speaker
- University of Melbourne Department of Pathology and Immunology. Seminar speaker
- The Walter & Eliza Hall Institute Teaching Series. Seminar speaker
- Box Hill Hospital Grand Rounds. Invited speaker
- Alfred Hospital Grand Rounds. Invited speaker

Balasubramanian Krishnamurthy
- Australian Diabetes Association annual scientific meeting, Perth. Speaker
- Postgraduate Forum, St Vincent's Institute. Seminar speaker

Mark McKenzie
- 35th Australian Society for Immunology meeting, Melbourne. Speaker
- Australian Diabetes Association annual scientific meeting, Perth. Speaker

Helen Thomas
- Monash Institute of Medical Research, Melbourne. Seminar speaker
- Centre for Immunology and Cancer Research, University of Queensland, Brisbane. Seminar speaker
- Research Week, St Vincent's Health. Speaker

Robyn Starr
- Gordon Research Conference on Bone and Teeth, Maine, USA. Invited speaker
- 35th Australian Society for Immunology meeting, Melbourne. Speaker and chair
- 3rd World Congress of Nephrology, Singapore. Invited speaker
- Division of Cancer and Haematology, WEHI, Melbourne. Seminar speaker
- Monash Institute of Medical Research, Melbourne. Seminar speaker
- Stem Cell Hub, Peter MacCallum Cancer Institute, Melbourne. Seminar speaker
- Department of Immunology, Ontario Cancer Institute, Toronto, Canada. Seminar speaker

Brett Cromer
- Brandeis University, USA. Seminar speaker
- University of Indiana, USA. Seminar speaker

Luke Miles
- The Australasian Proteomics Society, 10th Annual Proteomics Symposium, Cowes. Speaker
- Better Lab Design Conference, Melbourne. Speaker
- 6th Annual CSIRO Protein Expression Workshop, CSIRO Molecular & Health Technologies, Parkville. Speaker
- ComBio2005 Combined Conference, Adelaide. Speaker
- Membrane Protein Workshop, Plant Genomics Centre, University of Adelaide. Speaker
- The Queensland Protein Expression Symposium, Institute for Molecular Biosciences, University of Queensland. Speaker

Michael Parker
- 6th Protein Expression Workshop, CSIRO Molecular and Health Technologies, Melbourne. Speaker
- Hunter Cellular Biology Meeting 2005, Pokolbin, Australia. Invited speaker
- Institute for Molecular Bioscience, University of Queensland, Brisbane. Invited speaker
- Second Barossa Meeting – Signalling Networks, South Australia. Invited speaker
- 7th World Congress on Inflammation, Melbourne, Australia. Invited speaker
- 20th Congress of the International Union of Crystallography, Florence, Italy. Invited plenery speaker
- Department of Biology, University of Rome "Tor Vergata", Rome, Italy. Invited speaker

Steve Bouralexis
- 10th World Congress on Advances in Oncology and the 8th International Symposium on Molecular Medicine, Hersonissos, Crete, Greece. Invited speaker
- Australian and New Zealand Bone and Mineral Society Annual Scientific Meeting, Perth. Speaker

Matthew Gillespie
- Department of Physiology and Biophysics and The Center for Orthopaedic Research, University of Arkansas for Medical Sciences, Little Rock, USA. Seminar speaker
- Australian Rheumatology Association Annual Scientific Conference, Melbourne. Invited speaker
- Bone Disease Program of Texas, Baylor College of Medicine and MD Anderson Cancer Center, Houston, TX, USA. Invited speaker
- Cancer Induced Bone Disease Meeting, Davos, Switzerland. Plenery speaker
- 2nd Joint Meeting of the European and Calcified Tissue Society and the International Bone and Mineral Society, Geneva, Switzerland. Invited speaker
- Division of Endocrinology, University of Virginia, Charlottesville, VA, USA. Seminar speaker
- 2005 Gordon Conference on Bones and Teeth, New Hampshire, USA. Invited Chairman and Discussion Leader
- Skeletal Complications of Malignancy Workshop, Boston, USA. Invited Speaker
- 27th Annual Meeting of the American Society for Bone and Mineral Research "International Grant Writers Session", Nashville, USA. Invited Speaker
- Era of Hope, Department of Defense Breast Cancer Research Program Meeting, Philadelphia, USA. Speaker

Karl Häusler
- American Society for Bone and Mineral Research, Nashville, USA. Speaker
- Australian and New Zealand Bone and Mineral Society Annual Scientific Meeting, Perth. Speaker

Vicky Kartsogiannis
- Cancer Induced Bone Disease Meeting, Davos, Switzerland. Speaker
- Academic Unit of Bone Biology, University of Sheffield Medical School, UK. Seminar speaker
- Postgraduate Forum, St Vincent's Institute. Seminar speaker

Jack Martin
- Sydney Leach Memorial Lecture, Lorne Protein Conference. Invited speaker
- New York Academy of Science Conference on Skeletal Biology, USA. Invited speaker
- University of Arkansas. USA. Seminar speaker
- 10th Greek-Australian Medicolegal conference, Mykonos, Greece. Invited speaker
- Botnar Research Centre, Nuffield Orthopaedic Centre, Unversity of Oxford, UK. Seminar speaker
- Bone and Arthritis Symposium, Novartis AG, Boston, USA. Invited Speaker
- Symposium on Advances in Molecular Pharmacology and Therapeutics of Bone Disease, University of Oxford, UK. Plenary speaker

- Australian and New Zealand Bone and Mineral Society Annual Scientific Meeting, Perth. Invited speaker
- ANZAC Institute Research Symposium, Sydney. Invited speaker
- University of Melbourne. Seminar speaker
- International Osteoporosis Foundation, Singapore. Seminar speaker
- 2nd Australian Biotherapeutics and Tissue Regeneration Forum, Margaret River, WA. Session chair

Rachel Mudge
- Research Week, St Vincent's Health. Speaker
- Postgraduate Student Retreat, St Vincent's Institute. Speaker
- Department of Clinical and Biomedical Sciences, Geelong Hospital. Seminar speaker
- Postgraduate Forum, St Vincent's Institute. Seminar speaker

Julian Quinn
- Department of Medicine, Royal Melbourne Hospital, Parkville. Seminar speaker
- Australian and New Zealand Bone and Mineral Society Annual Scientific Meeting, Perth. Speaker

Natalie Sims
- Department of Medicine, Royal Melbourne Hospital, Parkville. Seminar speaker
- Department of Anatomy and Cell Biology, University of Melbourne. Seminar speaker
- Parkville Bone Seminar. Speaker
- 27th Annual Meeting of the American Society for Bone and Mineral Research, Nashville, USA. Speaker
- Australian and New Zealand Bone and Mineral Society Annual Scientific Meeting, Perth. Speaker

John Price
- University of Melbourne, Department of Medicine. Melbourne. Seminar speaker
- Western Australian Institute for Medical Research, Perth. Seminar speaker
- Endocrinology Forum, Sir Charles Gairdner Hospital, Perth. Speaker
- Bart's & The London Queen Mary's School of Medicine & Dentistry, The John Vane Science Centre, London, UK. Seminar speaker
- Novartis Institute for Biomedical Research, Basel, Switzerland. Seminar speaker
- 5th International Meeting on Cancer-Induced Bone Diseases, Davos, Switzerland. Speaker
- University of Calgary, Calgary, Canada. Seminar speaker

Janine Danks
- International Congress on Comparative Endocrinology, Boston, USA Speaker

Bruce Kemp
- 2nd Cell Signalling Symposium, Dundee, Scotland. Speaker
- 1st Asia-Pacific Diabetes and Obesity Study Group, Kobe, Japan. Invited poster and chair
- Frontiers in Vascular Medicine Symposium, Monash University, Clayton. Speaker
- National Institute of Environmental Health Safety / NIH, Research Triangle Park, USA. Seminar speaker
- Duke University Medical Center, North Carolina, USA. Seminar speaker
- Medical College of Georgia, Vascular Biology Center, Augusta, USA. Seminar speaker
- Melbourne Obesity and Diabetes Research Interest Group, RMIT University. Seminar speaker

Greg Steinberg
- University of British Columbia, Department of Medicine, Vancouver, Canada. Seminar speaker
- University of Toronto, Department of Physiology, Toronto, Canada. Seminar speaker

Jock Campbell
- Grand Round, St. Vincent's Hospital, Melbourne. Seminar speaker

Jörg Heierhorst
- XXII International Conference on Yeast Genetics & Molecular Biology, Bratislava, Slovak Republic. Speaker
- Garvan Symposium on Molecular and Cellular Mechanisms in Ageing, Sydney. Invited Speaker
- Annual Conference of the Australian Society for Biochemistry and Molecular Biology, Adelaide, South Australia. Invited Speaker
- 8th Australian Cell Cycle Workshop, Stradbroke Island, Queensland. Speaker
- Department of Biochemistry, La Trobe University, Bundoora. Seminar speaker
- Postgraduate Seminar Series, Department of Medicine SVH, The University of Melbourne. Seminar speaker
- Genetics Discipline Seminar, School of Molecular and Biomedical Science, The University of Adelaide. Seminar speaker
- Department of Biochemistry, University of Washington, Seattle, USA. Seminar speaker
- Department of Biochemistry, Ohio State University, Columbus, USA. Seminar speaker
- Queensland Institute of Medical Research, Brisbane. Seminar speaker
- Department of Radiation Genetics, University of Kyoto Medical School, Japan. Seminar speaker

Carolyn McNees
- Centro Nacional de Investigaciones Oncologicas, Madrid, Spain. Seminar speaker
- Erasmus Medical Centre, Rotterdam, The Netherlands. Seminar speaker

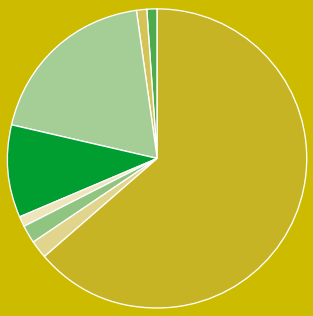
Brietta Pike
- Friedrich-Miescher-Institute Basel, Switzerland. Seminar speaker

Boris Sarcevic
- Peter MacCallum Cancer Institute, East Melbourne. Seminar speaker
- Ludwig Institute for Cancer Research, Parkville. Seminar speaker
- Department of Biochemistry and Molecular Biology, Melbourne University. Seminar speaker

Mark Waltham
- Australian Society of Clinical and Experimental Pharmacologists & Toxicologists Annual Meeting, Melbourne. Speaker
- 5th Australian Microarray Conference (AMATA), Barossa Valley, SA. Invited speaker

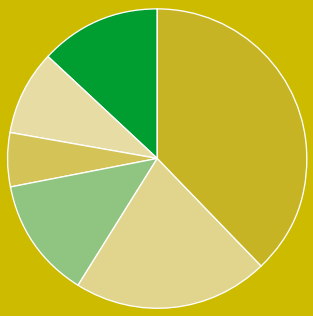
Erik Thompson
- Lorne Cancer Conference, Phillip Island, Victoria. Invited Speaker
- Hunter Cell Biology Conference, Invited chair and speaker
- 2nd Pacific Rim Breast and Prostate Cancer Conference (Think Tank), Palm Springs, USA. Invited speaker
- 6th RGJ-Ph.D. Congress, Pattaya, Thailand. Invited Speaker
- Ludwig Institute Cancer Research, Melbourne. Seminar speaker
- John Curtin School of Medical Research, Canberra. Seminar speaker
- Murdoch Children's Research Institute, Melbourne. Seminar speaker
- IMB, Brisbane. Seminar speaker
- Anatomy and Cell Biology, Monash University, Melbourne. Seminar speaker

Financial Snapshot



Income

Competitive Research Grants	63%
Service Contracts	3%
Industry	2%
Non-operating income	1%
Legacies and Donations	10%
Infrastructure Support	19%
Interest and Dividends	1%
Other operating income	1%



Expenditure

Research/Lab Salaries	38%
Research	21%
Transfer to Collaborators	13%
Infrastructure	6%
Administration Salaries	9%
Depreciation	13%

Directors' Report

Your Directors present their report on the company for the financial year ended 31 December 2005.

1. Directors

The names of Directors in office at any time during or since the end of the year are:

Ms Susan M Alberti
Prof James D Best
Sr Mary Fankhauser
Mr Charles A Griss (resigned 16 May 2005)
Prof Thomas WH Kay
Mr G John Pizzey
Ms Brenda M Shanahan
Mr Michael McGinniss
(appointed 16 November 2005)
Prof James A Angus
Mr Jeffrey N Clifton
Ms Nicole M Feely
Mr Barry J Jackson
Ms Ruth A O'Shannassy
Mr Gregory J Robinson
Mr Douglas A Wright
Mr Ian D Reid (resigned 16 May 05)

Directors have been in office since the start of the financial year to the date of this report unless otherwise stated.

2. Company Secretary

The following person held the position of company secretary at the end of the financial year:

Mr David R Rees – Bachelor of Business, Graduate Diploma Company Secretarial Practice, Certified Practicing Accountant, Chartered Secretary. Mr Rees has worked for St Vincent's Institute of Medical Research for 7 years, performing management roles. Mr Rees was appointed company secretary on 1 January 2004.

3. Principal Activity

The principal activity of the company during the financial year was medical research. There was no significant change in the nature of the company's principal activity during the financial year.

4. Operating Results

The operating surplus of the company amounted to $1,806,523

5. Dividends

In accordance with the company's constitution no dividends are paid either to members of the Board or members of the company.

6. Review of Operations

St Vincent's Institute (SVI) had a very successful 2005, increasing revenue by 20%. The company continues to use leading edge technology to develop new treatments for common diseases including cancer, diabetes, obesity and others, funded primarily by increasing success in peer–reviewed competitive grants. During 2005, researchers were awarded significant national and international research grants. These included a major NHMRC program grant of over $1.1 million per year for 5 years to the cancer research team, a State Government STI grant of $1.78 million to a consortium in which SVI's diabetes team is a member, a $900,000 equipment grant from the Australian Cancer Research Foundation and several overseas grants totalling $US 600,000 over 2 years. In 2005 NHMRC introduced the Independent Research Institute Infrastructure Support Scheme, from which SVI received $975,000. This initiative has enable SVI to expand and provide additional support services to our researchers.

Directors' Report

During the year the SVI Foundation and Institute also raised $1,346,000 from private donors and foundations, which was a 17% increase on 2004. The Foundation was only formed in 2004 and in this short time has proven to be a great asset to SVI in terms of raising funds and also in publicising the work of the institute and recruiting public support.

The company received infrastructure support from the State Government through the Department of Innovation, Industry & Regional Development (DIIRD), totalling $1.655m, which was an increase of 13% on 2004.

SVI continues to grow and with that comes pressure on resources. In 2005 expenditure on equipment was $1,620,000, doubling the 2004 expenditure of $ 791,724. The increase in revenue has also provided a financial base for further equipment purchases in 2006. Staff administration costs increased by 14% as SVI recruited additional staff but the overall direct cost of infrastructure support (administration, building and laboratory support costs) were held steady during 2005 after significant growth (31%) in 2004. The administration and building support services represent 12% of the company's direct expenditure (excluding depreciation and external transfers).

Competitive direct research grants awarded to researchers represent 65% of the total income. Research expenditure remained steady during 2005 but this is expected to increase in 2006. In 2005 the number of staff and students was 117, slightly up from 2004 (115). In addition the company acts as the host institute for the National Serology Reference Laboratory (NSRL), providing administration and research support to the 31 NSRL staff.

7. Significant changes in state of affairs

No significant changes in the state of affairs of the company occurred during the financial year.

8. Adoption of Australian Equivalents to IFRS

As a result of the introduction of Australian equivalents to International Financial Reporting Standards (IFRS), the company's financial report has been prepared in accordance with those standards. A reconciliation of adjustments arising on the transition to IFRS is included in Note 2 to this report.

9. After balance date events

No matters or circumstances have arisen since the end of the financial year which significantly affected or may significantly affect the operations of the company, the results of those operations, or the state of affairs of the company in future financial years.

10. Future developments

Likely developments in the operations of the company and the expected results of the operations in future financial years have not been included in this report. However the company is anticipating further increases in research activity in 2006.

11. Environmental issues

The company operates predominantly within the medical research sector and is committed to conducting its business activities with respect for the environment while continuing to meet expectations of members, employees, customers and suppliers. During the period from 1 January 2005 to the date of this report, this company has complied with the requirements of the *Environmental Protection Act*.

Directors' Report

12. Meetings of directors

During the financial year, 11 meetings of directors (including committees) were held. Attendees were:

	Directors' Meetings		Committee Meetings	
			Audit & Finance	
	Number eligible to attend	Number attended	Number eligible to attend	Number attended
SM Alberti	6	2	–	–
JA Angus	6	3	–	–
JD Best	6	3	–	–
JN Clifton	6	4	–	–
Sr M Fankhauser	6	4	–	–
NM Feely	6	3	–	–
CA Griss	3	3	2	2
BJ Jackson	6	4	–	–
TWH Kay	6	6	5	5
M McGinniss	1	1	1	1
RA O'Shannassy	6	5	5	4
GJ Pizzey	6	5	–	–
ID Reid	2	2	5	3
GJ Robinson	6	6	–	–
BM Shanahan	6	6	–	–
DA Wright	6	5	–	–

13. Directors' and auditors' indemnification

The company has not, during or since the financial year, in respect of any person who is or has been an officer or auditor of the company or a related body corporate:

- indemnified or made any relevant agreement for indemnifying against a liability incurred as an officer, including costs and expenses in successfully defending legal proceedings;
- paid or agreed to pay a premium in respect of a contract insuring against a liability incurred as an officer for the costs or expenses to defend legal proceedings; with the exception of the following matters.

During or since the financial year the company has paid premiums to insure each of the following directors against liabilities for costs and expenses incurred by them in defending any legal proceedings arising out of their conduct while acting in the capacity of director of the company, other than conduct involving a wilful breach of duty in relation to the company: SM Alberti, JA Angus, JD Best, JN Clifton, Sr M Fankhauser, NM Feely, CA Griss, BJ Jackson, TWH Kay, M McGinniss, RA O'Shannassy, GJ Pizzey, ID Reid, GJ Robinson, BM Shanahan, DA Wright.

Directors' Report

14. Proceedings on Behalf of Company

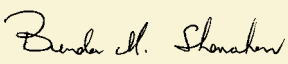
No person has applied for leave of Court to bring proceedings on behalf of the company or intervene in any proceedings to which the company is a party for the purpose of taking responsibility on behalf of the company for all or any part of these proceedings.

The company was not a party to any such proceedings during the year.

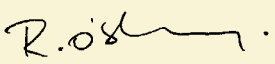
15. Auditor's Independence Declaration

The lead auditor's independence declaration for the year ended 31 December 2005 has been received and can be found on page 60 of the financial statements.

Signed in accordance with a resolution of the Board of Directors.



Director
BM Shanahan



Director
RA O'Shannassy

Dated this 27th day of April 2006, Melbourne, Australia

Webb Callaway Paton
Chartered Accountants

Auditor's Independence Declaration
Under Section 307C of the Corporations Act 2001
To the Directors of St Vincent's Institute of Medical Research

I declare that, to the best of my knowledge and belief, during the year ended 31 December 2005 there have been:

i. no contraventions of the auditor independence requirements as set out in the Corporations Act 2001 in relation to the audit; and

ii. no contraventions of any applicable code of professional conduct in relation to the audit.

Webb Callaway Paton
Chartered Accountants

AP Marks

Melbourne: 27 April 2006

Discussion and Analysis of the Financial Statements

Information on St. Vincent's Institute of Medical Research Concise Financial Report

The financial statements and disclosures in the concise financial report have been derived from the 2005 Financial Report of St. Vincent's Institute of Medical Research. A copy of the full financial report and auditors report will be sent to any member, free of charge, upon request.

The discussion and analysis is provided to assist members in understanding the concise financial report. The discussion and analysis is based on the company's financial statements and the information contained in the concise financial report has been derived from the full 2005 Financial Report of St. Vincent's Institute of Medical Research.

Income Statement

The net surplus from ordinary activities increased by 20% on the previous year. The net surplus can mainly be attributed to new sources of infrastructure funding, significant increase in equipment grants and minimising the increase in expenditure.

In 2005, the key sources of funds for the company were 65% from competitive granting bodies, 19% from Governments for infrastructure support and 10% from donations. Expenditure on research salaries and direct research expenses represents 77% of total expenditure (excluding depreciation and transfers).

Balance Sheet

The total Net Assets increased by $1.80 million, representing an increase of 14.2% on 2004, due to:

- Current assets increased by $2.6 million (81%) to improve the company's liquidity position after the reduction in working capital over the previous 2 years, although part of this is offset by the increase in current liabilities.
- Total current liabilities increased by $1.88 million (74%), which represented an increase in trade creditors and other current liabilities, mainly associated with research funds being received in advance.
- The net value of the property and equipment increased by $0.85 million.

Statement of Changes in Equity

The increase in equity of $1.8million (14%) from 2004 to 2005 is after an IFRS adjustment of $413,692 was made to the 2004 closing balance. The IFRS adjustment related to an increase in unrealised gain on investments of $156,296 and a loss on impairment of plant and equipment of $569,988. The increase in equity in 2005 was due to the $1.8 million net surplus from operating activities.

Cash Flow Statement

The 2005 cash position increased by 75%, from $2.82 million to $4.95 million. Grants Received increased by $3.74 million (39%) and this can be mainly attributed to a new National Health and Medical Research Council (NHMRC) initiative, which provided infrastructure support of $0.97 million and a Victorian State Government, STI grant of $1.78 million. In 2005 payments to suppliers and employees increased by $0.82 million (9%) and this was mainly directed to infrastructure support and coincides with the increased growth of the organisation and availability of additional infrastructure funding from NHMRC.

Financial Statements

Income Statement the year ended 31 December 2005

	Note	2005 ($)	2004 ($)
Revenue	3	14,048,097	11,413,552
Other income		93,623	179,368
Consumables used		(1,884,478)	(1,910,304)
Employee benefits expense		(6,016,734)	(5,878,004)
Depreciation and amortisation expense	4	(1,601,062)	(1,426,911)
Impairment of property plant and equipment		–	(569,988)
Other expenses		(2,832,923)	(1,752,924)
Surplus for the year		**1,806,523**	**54,789**

The accompanying notes form part of these financial statements.

Balance Sheet as at 31 December 2005

	Note	2005 ($)	2004 ($)
ASSETS			
Current Assets			
Cash and cash equivalents		4,956,642	2,823,859
Trade and other receivables		813,243	350,097
Other assets		9,091	10,000
Total Current Assets		**5,778,976**	**3,183,956**
Non–Current Assets			
Trade and other receivables		250,000	250,000
Financial assets		867,595	632,795
Property, plant & equipment		12,142,726	11,285,673
Total Non–Current Assets		**13,260,321**	**12,168,468**
Total Assets		**19,039,297**	**15,352,424**
Current Liabilities			
Trade and other payables		934,506	558,998
Short–term provisions		783,297	737,012
Funds held in trust for NSRL accrued leave		138,280	38,280
Other current liabilities		2,563,578	1,100,365
Total Current Liabilities		**4,419,661**	**2,534,655**
Non–Current Liabilities			
Long–term provisions		154,716	159,372
Total Non–Current Liabilities		**154,716**	**159,372**
Total Liabilities		**4,574,377**	**2,694,027**
Net Assets		**14,464,920**	**12,658,397**
EQUITY			
Retained surplus		14,464,920	12,658,397
Total Equity		**14,464,920**	**12,658,397**

The accompanying notes form part of these financial statements

Financial Statements

Statement of Changes in Equity for year ended 31 December 2005

	Note	Retained Earnings $	Total $
Balance at 1 January 2004		**12,603,608**	**12,603,608**
Retrospective adjustment due to introduction of IFRS	2c	(413,692)	(413,692)
Surplus for the year		468,481	468,481
Balance at 31 December 2004		12,658,397	12,658,397
Surplus for the year		1,806,523	1,806,523
Balance at 31 December 2005		**14,464,920**	**14,464,920**

The accompanying notes form part of these financial statements

Cash Flow Statement for the year ended 31 December 2005

	Note	2005 ($) Inflows (Outflows)	2004 ($) Inflows (Outflows)
Cash Flow from Operating Activities			
Grants received		13,230,351	9,491,400
Payments to suppliers and employees		(10,316,088)	(9,498,694)
Donations, legacies and bequests		1,106,820	1,173,235
Other revenue		557,720	1,237,570
Interest received		150,413	158,951
Dividends		40,462	31,629
Net cash provided by operating activities		4,769,678	2,594,091
Cash Flow from Investing Activities			
Purchase of plant and equipment		(1,632,541)	(885,066)
Leasehold improvements		(825,574)	–
Payments for investments		(178,780)	(61,411)
Net cash (used in) investing activities		(2,636,895)	(946,477)
Net Increase/(decrease) in cash held		2,132,783	1,647,614
Cash at the beginning of the year		2,823,859	1,176,245
Cash at the end of the year		**4,956,642**	**2,823,859**

The accompanying notes form part of these financial statements.

Notes to the Concise Financial Report for the year ended 31 December 2005

Note 1: The concise financial report has been prepared in accordance with Accounting Standard AASB 1039: Concise Financial Reports and the *Corporations Act 2001.*

The financial statements, specific disclosures and other information included in the concise financial report are derived from and are consistent with the full financial report of St Vincent's Institute of Medical Research. The concise financial report cannot be expected to provide as detailed an understanding of the financial performance, financial position and financing and investing activities of St Vincent's Institute of Medical Research as the full financial report.

The accounting policies have been consistently applied by the company and are consistent with those of the previous year unless otherwise stated in Note 1(a) below.

(a) Adoption of Australian Equivalents to International Financial Reporting Standards

The full financial report on which this Concise Financial Report is based is the first annual St Vincent's Institute of Medical Research financial report to be prepared in accordance with Australian equivalents to International Financial Reporting Standards (A–IFRS). AASB 1 *First time Adoption of Australian Equivalents to International Financial Reporting Standards* has been applied in preparing the full financial report.

Financial statements of St Vincent's Institute of Medical Research up until 31 December 2004 have prepared in accordance with previous Australian Generally Accepted Accounting Principles (AGAAP). AGAAP differs in certain respects from A–IFRS. When preparing St Vincent's Institute of Medical Research 2005 financial statements, management has amended certain accounting and valuation methods applied in AFAAP financial statements to comply with A–IFRS. The comparative figures in respect of 2004 were restated to reflect these adjustments.

Reconciliations and descriptions of the effect of transition from previous AGAAP to A–IFRS on the company's equity and its net income are given in Note 2 of the full financial report. A summary of this information is provided in Note 2 to this Concise Report.

Notes to the Concise Financial Report for the year ended 31 December 2005

Note 2: First–time Adoption of Australian Equivalents to International Financial Reporting Standards

Reconciliation of Equity at 31 December 2004

	Note	Previous GAAP at 31 Dec 2004 $	Adjustments on introduction of Australian Equivalent to IFRS $	Australian Equivalents to IFRS at 31 Dec 2004 $
ASSETS				
Current assets				
Cash and cash equivalents		2,823,859	–	2,823,859
Trade and other receivables		350,097	–	350,097
Other assets		10,000	–	10,000
Total Current Assets		**3,183,956**	**–**	**3,183,956**
Non–Current Assets				
Trade and other receivables		250,000	–	250,000
Financial assets	(a)	476,499	156,296	632,795
Property, plant & equipment	(b)	11,855,661	(569,988)	11,285,673
Total Non–Current Assets		**12,582,160**	**(413,692)**	**12,168,468**
Total Assets		**15,766,116**	**(413,692)**	**15,352,424**
Current Liabilities				
Trade and other payables		558,998	–	558,998
Short–term provisions		737,012	–	737,012
Funds held in trust for NSRL		138,280	–	138,280
Other current liabilities		1,100,365	–	1,100,365
Total Current Liabilities		**2,534,655**	**–**	**2,534,655**
Non–Current Liabilities				
Long term provisions		159,372	–	159,372
Total Non–Current Liabilities		**159,372**	**–**	**159,372**
Total Liabilities		**2,694,027**	**–**	**2,694,027**
Net Assets		**13,072,089**	**(413,692)**	**12,658,397**
EQUITY				
Retained surplus	(c)	13,072,089	(413,692)	12,658,397
Total Equity		**13,072,089**	**(413,692)**	**12,658,397**

Notes to the Concise Financial Report for the year ended 31 December 2005

	Note	Previous GAAP $	Effect of Transition to Australian Equivalents To IFRS $	Australian Equivalents to IFRS $

Note 2: First–time Adoption of Australian Equivalents to International Financial Reporting Standards

Reconciliation of Equity at 31 December 2004

Revenue		11,413,552	–	11,413,552
Other income	(d)	23,072	156,296	179,368
		11,436,624	156,296	11,592,920
Consumables used		(1,910,304)	–	(1,910,304)
Employee benefits expense		(5,878,004)	–	(5,878,004)
Depreciation and amortisation expense		(1,426,911)	–	(1,426,911)
Impairment of property plant and equipment	(e)	–	(569,988)	(569,988)
Other expenses		(1,752,924)	–	(1,752,924)
Surplus for the year		**468,481**	**(413,692)**	**54,789**

Notes to the reconciliations of equity and surplus and deficit at 31 December 2004.

(a) Financial assets, in this case shares, are valued to include the unrealised gains arising from changes in the fair value of these assets under the Australian equivalents to IFRS relating to financial instruments.

(b) An impairment loss amounting to $569,988 has been recognised under the Australian equivalents to IFRS relating to fixtures and fittings and equipment, which has been written down to its recoverable amount. Impairment losses are recognised in the income statement.

(c) Adjustments to retained earnings comprise:

	31 Dec 2004 ($)
Unrealised gain of company investments	156,296
Impairment of plant & equipment	(569,988)
Total	**(413,692)**

(d) Realised and unrealised gains and losses arising from changes in the fair value of these assets (shares) are included in the income statement in the period in which they arise.

(e) In the case of research equipment, a prolonged decline in the value of the equipment has arisen. This loss has been recognised in the income statement for the year ended 31 December 2004.

Notes to the Concise Financial Report for the year ended 31 December 2005

Note 3: Revenue

	Note	2005 ($)	2004 ($)
Operating activities			
– government grants	5–6	9,519,559	7,334,336
– other grants		2,352,011	2,243,400
– contract services		342,532	295,853
– legacies, bequests, donations		1,465,821	1,167,235
– dividends	(a)	40,462	31,629
– interest	(b)	153,999	163,933
– royalty		21,324	87,749
– other		152,389	89,417
Total revenue		**14,048,097**	**11,413,552**
(a) Dividends from:			
– other corporations		40,462	31,629
(b) Interest from:			
– other corporations		153,999	163,933
Non–operating activities			
– unrealised gains on shares		56,020	156,296
– realised gain on disposal of shares		37,603	23,072
Other income		**93,623**	**179,368**

Note 4: Surplus from Ordinary Activities

	2005 ($)	2004 ($)
Expenses		
– research	2,355,589	2,342,097
– research salaries and on–costs	4,677,914	4,709,053
– infrastructure	789,029	753,282
– Admin. & Lab. support salaries and on–costs	1,338,820	1,168,951
	9,161,352	**8,973,383**
Transfer of funds to external, joint collaborators	1,572,783	567,849
Depreciation of non–current assets	910,972	761,475
Amortisation of non–current assets	690,090	665,436

Notes to the Concise Financial Report for the year ended 31 December 2005

Note 5: Grants – Commonwealth Government

	2005 ($)	2004 ($)
National Health and Medical Research Council	5,372,218	4,655,067
Australian Research Council	411,530	361,505
Department of Health and Ageing	–	500,000
	5,783,748	5,516,572

Note 6: Grants – Victorian State Government

	2005 ($)	2004 ($)
Department of Innovation, Industry & Regional Development		
– Infrastructure support	1,655,204	1,460,264
– STI grants	1,780,607	–
– Other Direct research grants	300,000	357,500
	3,735,811	1,817,764

Note 7: Segment Reporting

The company operates in the medical research sector where it undertakes basic and clinical research in Australia.

Directors' Declaration

The directors of the company declare that:

1. The financial statements and notes, as set out on pages 62 to 68 are in accordance with the Corporations Act 2001 and:
   a) comply with Accounting Standards and the Corporations Regulations 2001: and
   b) give a true and fair view of the financial position as at 31 December 2005 and of the performance for the year ended on that date of the company:
2. In the directors' opinion there are reasonable grounds to believe that the company will be able to pay its debts as and when they become due and payable.

This declaration is made in accordance with a resolution of the Board of Directors.

Director
BM Shanahan

Director
RA O'Shannassy

Dated this 27th day of April 2006, Melbourne, Australia

Webb Callaway Paton
Chartered Accountants

Independent Audit Report to the Members of St Vincent's Institute of Medical Research

Scope
The concise financial report and directors' responsibility

The concise financial report comprises the income statement, balance sheet, statement of changes in equity, cash flow statement, notes to the financial statements and the directors' declaration for St Vincent's Institute of Medical Research (the company) for the year ended 31 December 2005.

The directors of the company are responsible for the preparation and presentation of the financial report in accordance with Australian Accounting Standard AASB 1039: Concise Financial Reports.

Audit Approach
We conducted an independent audit of the concise financial report in order to express an opinion on it to the members of the company. Our audit was conducted in accordance with Australian Auditing Standards, in order to provide reasonable assurance as to whether the concise financial report is free of material misstatement. The nature of an audit is influenced by factors such as the use of professional judgement, selective testing, the inherent limitations of internal control, and the availability of persuasive rather than conclusive evidence. Therefore, an audit cannot guarantee that all material misstatements have been detected.

We also performed an independent audit of the full financial report of the company for the financial year ended 31 December 2005. Our audit report on the full financial report was signed on 27 April 2006, and was not subject to any qualification.

In conducting our audit of the concise financial report, we performed procedures to assess whether in all material respects the concise financial report is presented fairly in accordance with Australian Accounting Standard AASB 1039: Concise Financial Reports.

We formed our audit opinion on the basis of these procedures, which included:

- testing that the information included in the concise financial report is consistent with the information in the full financial report, and
- examining, on a test basis, information to provide evidence supporting the amounts, and other disclosures in the concise financial report which were not directly derived from the full financial report.

Our procedures include reading the other information in the Annual Report to determine whether it contains any material inconsistencies with the concise financial report.

Independence
In conducting our audit, we followed applicable independence requirements of Australian professional ethical pronouncements and the Corporations Act 2001.

Audit Opinion
In our opinion, the concise financial report of St Vincent's Institute of Medical Research for the year ended 31 December 2005 complies with Australian Accounting Standards AASB 1039: Concise Financial Reports.

Webb Callaway Paton
Chartered Accountants

AP Marks

Melbourne: 27 April 2006

Donations and Bequests

Private Donors, Bequests and Foundations:

$180,000 plus
Anon

$100,000 – $104,999
Alberti AM, S

$50,000 – $54,999
Estate of the Late George Carson
H & L Hecht Trust - administered by Perpetual Trustee
Janina & Bill Arniet Foundation - administered by Equity Trustees
The Jack Brockhoff Foundation
The Marian & EH Flack Trust
The Pratt Foundation

$30,000 – $34,999
Beatrice Harris Estate - administered by Equity Trustees
L & D Investment Pty Ltd
Yu, MK

$25,000 – $29,999
Carson, I
Holyoake, P & M
Shanahan, B
The Eirene Lucas Foundation

$20,000 – $24,999
BNP Paribas Securities Services
Susan Alberti Charitable Foundation

$15,000 – $19,999
George Castan Family Charitable Trust

$10,000 – $14,999
Bell Charitable Fund
Castello, S & N
Iseli, A & C
North, C
Orcadia Foundation Ltd
O'Shannassy, R & M
State Trustees Australia Foundation
The Michael & Andrew Buxton Foundation

$5,000 – $,9999
Anon
Cole, M
Dougherty, H
Lowe, D
Regan, J
Sydney Diocesan Secretariat
The George Hicks Foundation Ltd
Video Cowboys Pty Ltd

$2,000 – $4,999
Dale, G & R
Harris, AW
Jackson, B
Marriner, D & E
McKeage, C
Michelmore AO, J
Michelmore, A
O'Brien, N & C
Power, T & D
Remington Pty Ltd
Spry-Bailey AO, P
Strategic Advantage Pty Ltd
The Dorothy Hill Memorial Trust Fund – administered by Equity Trustees
Xipell, J

$1,000 – $1,999
Aitken, B
Alpins, N & S
Anderson, D
Aroni, B
Barberis, J
Basser, I & M
Bongiorno, J & E
Breheny, M
Brown, RV
Brown, SV
Carson & McLellan PPB
Caulfield, G
Chojna, H
Clarke, B
Commins, C
Coote, M
Demediuk, N & F
Emerson, APR
F & J Ryan Foundation
Fanning, M
Fedele, T
Five Oceans Assets Management
Goh, D
Grady, D
Griss, C & A
Grogan, B
Hale, G
Hall, J & S
Harcourt, T
Hart, L & C
Iacobucci, M
Jones, WMP
Katsanevakis, C & D
Kay, C
Kay, T
Kelly, AP
Kelly, P
Lowe, R
McLennan, G
McNulty, M
McPhail, B
Millen, R
Molan, C & F
Mortensen, PV
Naphtali, M
NEAP
Needham, B & S
NM Rothschild & Sons (Australia) Limited
O'Callaghan SC, D
O'Callaghan, B
O'Day, J & S
Oliphant, DJ
Papas, J
Pearce, M
Pellicano, N & A
Pinches Consolidated P/L
Pizzey, J & B
Polson, P & R
Ralston, M & J
Red Rock Leisure
Rodas, T & M
Salter, W
Savas, R & K
Scott, P & O
Signorino, F
Smith, C & S
Solomon, Q & E
Stooke, K
Stubbs, C & C
Tabak, L
Tarascio, L
Tarascio, S & C
Thomas, C & C
Verdnik, A
William & Evelyn Beveridge Settlement - administered by Equity Trustees
Wilson, P
Yencken, T & M
York, G
Young, C
Young, D

$200 – $999
Bailey, W
Barker, R
Bennett, R
Bloch, F & S
Brizard, C
Brown, IR
Butler, P
Carson, T
Casper, M & C
Dax AM, E
Finley, R
Forrest, LE
Gearing, L
Gehrig, R & H
Hinton & Associates
Lawrence, P B
Little, TF
Masel, L & S
McBreen, R
McNamara, J
Morris AC, Sir Peter
Nicoll, G
Nossal, Sir Gustav & Lady
Parkinson, G
Ralph AC, J
Rees, R
Santamaria, J & S
Sheales, J
Shell, A & R
Stokes, N
Wong, LC

under $199
Beaton, OW
Borden, ML
Burt, C
Douez, T & P
Dowell, N
Dunning, T
Fox, P
Freadman, J
Griffin, J
Grogan, M
Heath, W
Henderson, K
Hurburgh, C
Kempson, P
Loveday, L
McGrath, J
McKay, B & D
McLean, DA
Milledge, J
Mullaly, C
O'Bryan, N
Porter, J
Pot-Pourri
Reeve, F
Robert, JS
Robertson, A
Robertson, B
Robinson, G
Rowe, C
Steadman, R
Steedman, P
Wantirna Hill Club Patrons
Watchorn, R

Trusts and Foundations permanently established for the purpose of allocating funds to the St Vincent's Institute on an ongoing basis.

John Holt Medical Research Endowment – administered by Perpetual Trustee
The Mary Jane Polinelli Foundation – administered by Perpetual Trustee
K & A Bongiorno Research Endowment – administered by Perpetual Trustee
DJ & LM Fox Foundation – administered by a private trustee.

The following permanent funds are included in the company's pool of invested funds with income being directed to the Institute's medical research program:

Albert H Maggs Endowment
Diane B Jones Endowment
George Menzies Carson Bequest
Lorna M Miller Endowment
Mary T Porter Estate
Merna Dorothea Sheahan Estate
The Mary Potter Research Grant

How can you make a difference?

The scientific research of the Institute is aimed at the treatment and cure of diseases that touch the lives of people in our community. Your financial support can have a direct effect on the success of the Institute's research.

There are many ways in which you can help. These include joining the SVI 1000 Club; making single, annual or more frequent gifts; making a donation either personally or from a Prescribed Private Fund (PPF); making bequests via a Will; or making a donation in memory of a loved one or esteemed person. Your business or organisation may also be interested in workplace giving. Information about all these can be obtained from SVI. Enquiries will be welcomed by the Director of the Institute on (03) 9288 2480.

St Vincent's Institute is an endorsed deductible gift recipient and income exempt charity. Contributions are used directly in research, not on administrative or fundraising costs.

However, the Institute will be pleased to use capital or income arising from a bequest for a specific purpose or area of research according to the donor's wishes. It may be advisable to obtain professional assistance in making such a provision.

Suggested wording for bequests:

"I , bequeath unto St Vincent's Institute, 9 Princes Street, Fitzroy, 3065 in the State of Victoria for it's general purposes (indicate the amount and/or item and/or address of property) free of all succession, estate and other death duties and declare that the receipt of the Director or other proper officer of the Institute shall be sufficient discharge to my Executors in respect thereof."

Join us in the voyage of continuous discovery and share in the rewards our research will provide.

SVI 1000 Club Membership

Type of Membership:

- ☐ New
- ☐ Continuing
- ☐ Corporate
- ☐ Individual

SVI 1000 Club Member ($1,000 per annum)

$

- ☐ 1yr ☐ 2yrs
- ☐ 3yrs ☐ 3yrs+

Other Donation

☐ Donation $

All gifts over $1000 will automatically qualify you as a member of the SVI 1000 Club. SVI respects your privacy. If you do not wish to receive some or all of our supporter information, please contact our office on (03) 9288 2480.

Thank you for your support.
All amounts of $2 and over are tax deductible.

SVIMR ABN 52 004 705 640

Postal address:
41 Victoria Parade,
Fitzroy Victoria 3065

☐ Mr ☐ Mrs ☐ Ms ☐ Miss ☐ Other

First Name Surname

Position Company

Address

Suburb P/Code State

Ph Work Fax

Mobile Ph Home

Email

Payment Details

- ☐ Cheque (please make payable to St Vincent's Institute)
- ☐ Credit Card (please tick one of the following cards to complete details.)

☐ Diners ☐ Visa ☐ Mastercard ☐ Bankcard ☐ Amex

☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐

Expiry Date Amount being paid $

Signature

Options

Please email/mail me

☐ All correspondence ☐ Newsletter ☐ Annual Reports
☐ Promotions ☐ SVI 1000 Club events ☐ Forum Invitation
☐ Yes, I would like to take a tour of St Vincent's Institute

Organisation Chart

Sisters of Charity Health Service | **Trustee of Sister's Of Charity Of Australia** | **St Vincent's Health Melbourne**

St Vincent's Institute Board

SVI Foundation Board

Director

Associate Directors

Research
Immunology and Diabetes
Signal Transduction
Bone, Joint and Cancer
Comparative Endocrinology
Tumour Cell Migration and Metastasis
Pharmacogenomics
VBCRC Invasion and Metastasis
Protein Chemistry and Regulation
Cell Cycle and Cancer
Molecular Cardiology
Molecular Genetics
Structural Biology
Virology

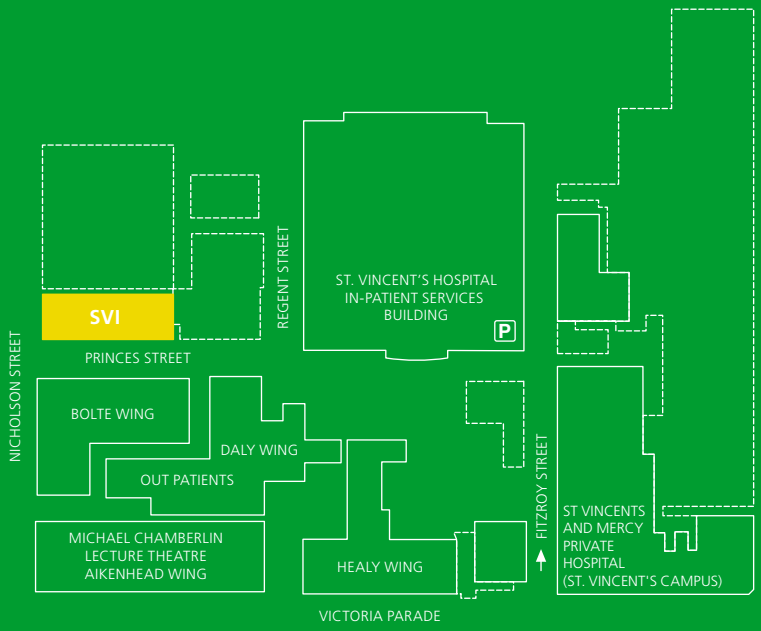
Administration and Services
Development
Finance
Laboratory and Technical Services
Personnel and Administration

National Serology Reference Library

Affiliated with: The University of Melbourne.

Participant in: Bio 21; Victorian Breast Cancer Research Consortium; St Vincent's Diabetes Centre of Excellence.

Disease Focussed Research: Diabetes; Bone Diseases – cancers (breast, lung and prostate) that spread to bone, osteoporosis, arthritis and other joint diseases; Cardiovascular Diseases – including metabolism and obesity; Viral diseases; Neurological diseases.



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ST VINCENT'S INSTITUTE
ABN 52 004 706 640

Postal: 41 Victoria Parade, Fitzroy Victoria 3065
Location: 9 Princes Street, Fitzroy Victoria 3065
Telephone: +61 3 9288 2480
Facsimile: +61 3 9416 2676
Email: enquiries@svi.edu.au
Web: www.svi.edu.au

SVI
ST VINCENT'S INSTITUTE
~ continuous discovery