

DEVELOPMENT REPORT

St Vincent's Institute **2003 Annual Report**

MISSION STATEMENT

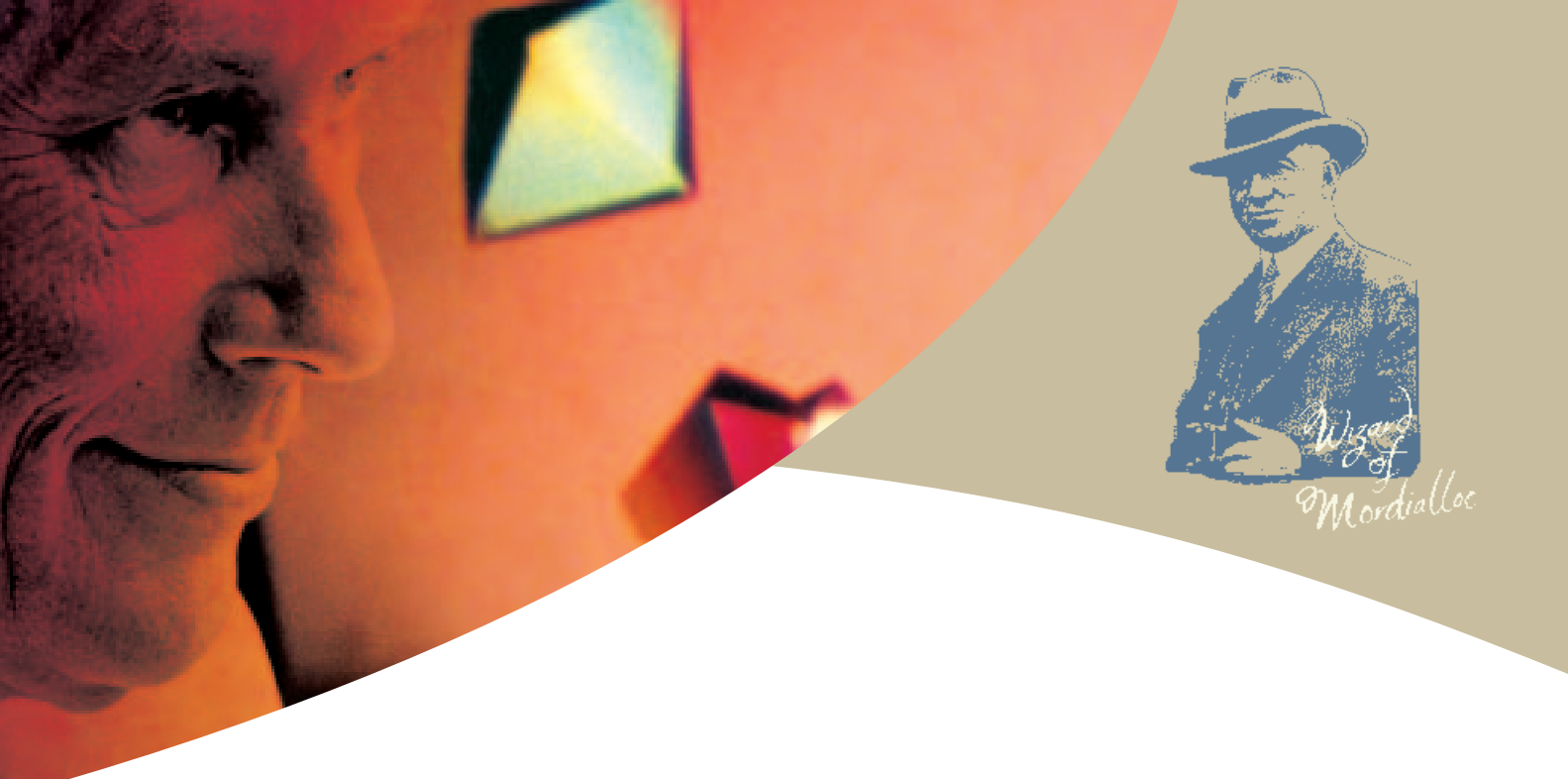
St Vincent's Institute is a centre of excellence in medical research. Its mission is continuous discovery thereby promoting human well-being through the prevention and treatment of diseases. Its programs of basic and clinical research are applied to the study of certain diseases that are of great cost to the Australian and International communities. These include osteoporosis, and other bone diseases, cancers (breast, lung and prostate) that spread to bone, diabetes, virology and also diseases of the heart and blood vessels.

The Institute is an independent one, founded as an initiative of the Congregation of the Sisters of Charity and St. Vincent's Hospital. It is a member institution of Australia-wide health care facilities of the Sisters of Charity, and is sponsored and supported by the Congregation in many ways.

The contribution made by the research of the Institute to the advancement of health care in Australia is an important one, and is conducted in close co-operation with a major teaching hospital, St Vincent's Hospital Melbourne, and with The University of Melbourne. Through these links its research programs provide a valuable service to clinical medicine, graduate education and community welfare.



Image: Functional Proteomics team members.



HISTORY OF SVI

The success of the late Jack Holt, one of Australia's greatest trainers and an inaugural inductee into Australian Racing's Hall of Fame, led to the establishment of the now world-renowned St Vincent's Institute. Jack Holt was a true philanthropist, and stories abound of his quiet generosity to those in need. Following his death in June 1951, the John Holt Medical Research Endowment — a perpetual charitable trust fund — was established with a bequest of £200,000.

Dr Pehr Edman, one of the world's leading biochemists, took up his appointment as the John Holt Director of Research in May 1957 and the St Vincent's School of Medical Research was officially opened on 23 April 1958. To this day Jack Holt's legacy continues to support the internationally recognised work of St Vincent's Institute.

Major discoveries with an impact on clinical medicine

Automating amino-acid sequences

St Vincent's Institute has a long record of breakthrough discoveries, including Edman's development of the world's first automatic protein sequencer allowing the determination of the order of amino acids in proteins. This discovery laid the groundwork for the current understanding of how genes provide the code for protein synthesis, the role of protein abnormalities in causing disease, and the use of proteins like insulin, growth hormone and calcitonin as drugs. The Institute has been described as the birthplace of proteomics, one of the key components of medical research in the 21st century.

Calcium and cancer

Jack Martin and his team discovered parathyroid hormone-related protein (PTHrP), a hormone secreted by cancers that damages the skeleton, causes excessive levels of calcium in the blood and contributes to the spread of cancer to bones. This discovery established the cause of a common complication of cancer and led to its accurate diagnosis. Anti-PTHrP drugs are now in advanced clinical trials based on the Institute's research.

Protein kinases as drug targets

Bruce Kemp has made pivotal discoveries about protein kinases, proteins that carry messages that determine many aspects of the function and behaviour of cells. Most recently Bruce has studied a protein kinase that determines how the body balances food input and use, relevant to obesity, exercise and cardiovascular disease. The pharmaceutical industry has the protein kinases as one of its three top targets for drug development.



THE INSTITUTE TODAY

Today, SVI enjoys an enviable reputation within the global scientific community as one of the world's premier medical research institutes, and is a shining example of Australian intellectual excellence and achievement.

The Institute through its reputation and record has attracted a dedicated and committed team of over 100 staff and students, including some of the best scientists in their chosen fields. SVI 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 the world.

SVI conducts research into diseases that have a high impact on the community. The Institute is a world centre of excellence for medical research in the following areas:

- Juvenile diabetes
- Metabolism — obesity and cardiovascular disease
- Bones, joints and cancer — spread of cancer to the bone, arthritis, osteoporosis
- Structural Biology — 3D study of proteins at the atomic level
- Protein Chemistry — studying the end product of the cell's genetic message
- Virology — infection by AIDS and hepatitis viruses
- Neurological diseases including Alzheimer's disease and epilepsy

SVI is an independent research body, which is affiliated with St Vincent's Health and The University of Melbourne. It 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.

MAJOR PRIZES AND AWARDS

Professor Jack Martin received the prestigious Pieter Gaillard International Bone and Mineral Society Founder's Award in Osaka in June 2003, which is the highest recognition in the bone field. This award recognises outstanding contributions, leadership and dedicated service to the IBMS and the field of bone and mineral research. Professor Martin's close association with the IBMS was evidenced by Melbourne hosting the IBMS meeting in 1995, the only time that this meeting has been held in the southern hemisphere.

Professor Bruce Kemp was awarded a highly prestigious Federation Fellowship from the Australian Research Council, one of the highest awards available in Australian academic life. Professor Kemp's research is focussed on understanding how the body coordinates its energy supply and demand through the key enzyme, AMP-activated protein kinase. This research will have major benefits in biopharmaceutical development, and the livestock, plant and sport/racing industries. The administering institute for the Fellowship is CSIRO and this raises the exciting possibility of establishing close links between SVI and CSIRO groups interested in metabolism and protein chemistry.

An international monitoring agency has identified Professor Jack Martin and Professor Bruce Kemp as being among the top 250 (top half of one percent) of the most highly influential scientists and scholars worldwide in their field during 1981 -1999. There are hundreds of thousands of articles published in research journals every year, and most contain references (or citations) that acknowledge the authors' debt to the published research findings of others. This ranking demonstrates the fundamental contributions Professors Martin and Kemp have made to the advancement of science and technology in the ISI Highly Cited.com Biology and Biochemistry category.

In addition, both Professor Martin and Professor Kemp were awarded the Centenary Medal in recognition of their contribution to Australian society and science in the fields of bone cell biology and biochemistry respectively.

Image: From left
Professor Bruce Kemp and
Professor Jack Martin



RESEARCH HIGHLIGHTS

Prevention of diabetes with SOCS1

We have prevented diabetes in two different mouse models by over-expressing SOCS1 in pancreatic b cells. SOCS1 prevents expression of molecules on the b cell that make it more easily recognised by the immune system.

Characterisation of the role of interleukin-1 in diabetes

It has been known for many years that IL-1 kills b cells in culture. Using mice deficient in receptors for IL-1, we have shown for the first time that IL-1 is unlikely to cause diabetes in the whole animal.

SOCS1 protein regulates T cells

When we deplete SOCS1 protein in mice, their T cells fail to function normally and the mice develop autoimmune diseases. This defect results from unregulated signalling in response to the cytokines IL-2, IL-7 and IL-15.

SOCS3 proteins control T cell activation

The immune system contains safeguards to ensure an effective response to pathogens, while preventing autoimmunity. SOCS3 protein appears to prevent T cells from becoming fully activated until the appropriate signal has been received from the cell. Mice which lack SOCS3 proteins are more susceptible to developing autoimmune diseases.

New inhibitors of bone destruction

We have identified several proteins that stop bone degradation. These are being investigated for their suitability as drug targets, in order to develop new treatments for bone loss in osteoporosis, arthritis and cancer.

Proteins that affect bone growth

We have determined that several types of bone cells produce proteins that reduce bone growth and stimulate the production of bone destroying cells. In contrast, we have found evidence that cells that destroy bone may themselves produce bone growth-promoting proteins.

TeeleOstin

The establishment of a biotech company to develop novel peptides as potential therapeutic agents to treat osteoporosis.

The red fluorescent mouse

We have developed cancer cells that glow red. These cells will allow us to track how tumours spread and grow in animals models of cancer.

Drugs that stop bone metastasis

We recently identified two drugs that stop growth of breast-to-bone metastasis in mice models of the disease. Both drugs are good candidates for the treatment of human bone metastasis and other diseases where bone erosion occurs.

Understanding enzymes involved in cancer metastasis

We have continued our investigations into matrix metallo-proteinases that are critical for the growth and spread of tumours.

Switching on/off proteins

Understanding how the metabolic stress sensing protein kinase AMPK is turned on and off, and what controls endothelial NO synthase a key enzyme in the cardiovascular system.

A new function for AMPK

AMPK glycogen-binding domain has glycogen-independent activity in yeast.

Understanding glycogen storage disease

Mutations in the AMPK c2 gene causes cardiac glycogen storage disease in mice.

ACE inhibitors

We have obtained a new understanding into the effects of drugs called ACE inhibitors on the heart.

Effects of using heart bypass pumps

We have acquired a new insight into how the heart bypass pump causes inflammation following open heart or coronary artery surgery.

Regulation of cancer associated protein kinases

We have identified mechanisms how FHA domains contribute to the regulation of protein kinases in yeast models of the human Li-Fraumeni multi-cancer syndrome.

Functional organization of DNA damage proteins in the cell nucleus

We have found that pro-myelocytic leukaemia protein associated nuclear bodies dissolve in response to specific kinds of DNA damage; this mechanism may facilitate the rapid release of DNA repair proteins stored in these bodies.

Bacterial toxins

We have determined the shape of the bacterial toxin, intermedilysin, a protein that punches holes in cells. This information will allow us to develop new antibiotics to treat bacterial infections.

Growth Hormone receptor

We have determined the three dimensional shape of human growth hormone receptor. This discovery may lead to the design of compounds that could be used for the treatment of a variety of diseases including acromegaly (giantism), diabetes and certain cancers.

Hepatitis C virus glycoproteins

The first description of surface expressed and functional forms of hepatitis C virus glycoproteins E1 and E2. This research allows us to study the role that these molecules play in viral replication.

HIV-1 Incidence assay

We have developed an assay for distinguishing recently acquired HIV infection from established infection.

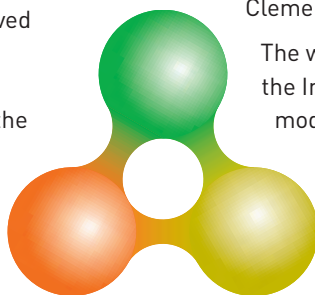
Development of a quality control program

EDCNet, an Internet-based program for the entry, storage and graphical reporting of the quality control sample results was developed by the NRL and is being used by over 150 laboratories throughout Australia and overseas.

NEW LOOK FOR INSTITUTE

St Vincent's Institute has a new look and a new logo. These were developed in consultation with staff and other stakeholders through a process initiated by the Institute Board Marketing sub-committee, which is chaired by Doug Wright.

Initially, the process involved preparing a brief which encapsulated the feeling behind the research that the Institute undertakes. Many members of staff contributed during this early stage, which was overseen by Wrights, a Melbourne public relations and communications consultancy.



The brief was then taken to Clemenger Advertising and their affiliate BBDO Consulting, where under the direction of Jonathon Rowe and Stefan Graefe, a brand trust model was created. From this exercise the brand essence of "Continuous Discovery" was distilled and a further brief devised for Clemenger's creative department.

The work was undertaken pro-bono and the Institute now has a distinctive and modern look which presents the image of "Continuous Discovery" to the world.



Image: Crystallographers at work. From left, Dr Susanne Feil and Dr Galina Polekhina.

PUBLIC RELATIONS AND FUNDRAISING

Philanthropy in Action

The Institute is delighted to welcome Ms Susan Alberti AM as the inaugural Chair of the St Vincent's Institute Foundation. Sue is the co-founder and Managing Director of Dansu Constructions Pty Ltd based at Wheelers Hill in Melbourne, a business she has successfully continued since the tragic death of her husband in 1995.

Complementing Sue's business activities has been a strong personal effort and commitment to fundraising and promotion of juvenile diabetes research. Sue was this year elected Honorary President of JDRF (Juvenile Diabetes Research Foundation) Australia, and as an acknowledgement of her significant contributions was awarded the JDRF International Volunteer of the Year 2003. Since the death of her daughter Danielle from juvenile (type 1) diabetes, Sue's mission in life is to assist those who are researching and seeking a cure for this disease.

Sue's aim is to have St Vincent's Institute, which she describes as Melbourne's hidden treasure, widely known and supported. While her public philanthropic activities are well known, the Institute is also indebted to Sue for the numerous quiet acts of generosity that demonstrate her genuine and practical approach to working closely with a not-for-profit medical research institute. The Institute's researchers are already benefiting in tangible ways from her enthusiasm and high level of personal commitment and involvement.



Image below: Three dimensional model of the intermedilysin toxin pore.





HELFGOTT AT RAHEEN

On March 27 over 100 guests of St Vincent's Institute attended an intimate recital by unique Australian musician David Helfgott, superb pianist, virtuoso and inspiration. Held at the beautiful setting of 'Raheen', home of Mr Richard Pratt AC & Mrs Jeanne Pratt AC, the guests were also treated to a very special welcome, 'The Master of the House' by Richard Pratt.

It was a memorable evening, raising over \$33,000 for medical research at St Vincent's Institute. We are indebted to Richard and Jeanne Pratt, and David and Gillian Helfgott for their outstanding support. Our sincere thanks also to those who attended this special event; your generosity is making a real difference.



2003 DIRECTOR'S DINNERS

The highly successful program of Director's Dinners continued during 2003, with distinguished speakers including:

Andrew Lindberg – Managing Director, Australian Wheat Board

Don Watson – Author

Christine Nixon – Victorian Police Commissioner

Professor Geoffrey Blainey AC – Historian

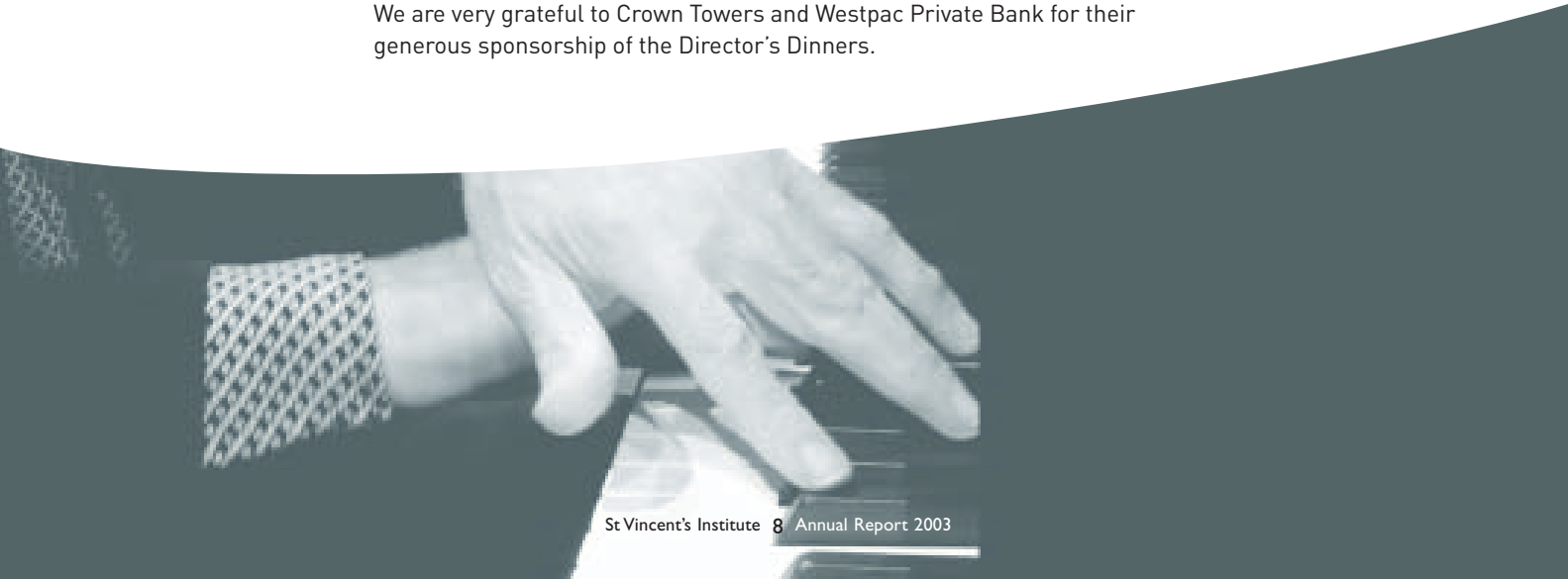
Gerard Vaughan – Director, National Gallery of Victoria (hosted by Carolyn Kay)

In addition, a special lunch was hosted by Sue Alberti, where Mimma and the Three Chianti Chefs entertained supporters of SVI.

The dinners enable SVI to raise its profile in both the business and private sectors and inform guests of the latest developments in medical research. Many of the guests have joined the SVI 1000 Club and several have visited the Institute's research laboratories.

We are very grateful to Crown Towers and Westpac Private Bank for their generous sponsorship of the Director's Dinners.

WESTPAC PRIVATE BANK



SVI SUPPORT GROUP

The SVI Support group led by Claire O'Callaghan and her dedicated committee is a fine example of community support for medical research.

A 'Christmas in June' fundraising dinner was a great success and raised \$16,914 through ticket sales, a raffle and some very special donations. The ongoing support we receive through the work of Claire's committee is very much appreciated. We are pleased that many members of the committee have now visited the Institute to see our scientists at work.

Image: SVI
Support Group



Special thanks to all our community supporters including Vermont Cancer Research Fundraising Group and Wantirna Hill Club patrons.

YERING *Station*

Yering Station – Wine Promotion

This is the third year that Yering Station has most generously offered this wonderful opportunity to not only raise funds for our work but also to increase public awareness of St Vincent's Institute. We would like to sincerely thank everyone at Yering station for their support and thank those who purchased wines as part of this fundraising initiative.

SVI 1000 CLUB

SVI 1000 Club Membership (as at 31 December 2003)

Susan Alberti
Benni & Ros Aroni
Rhonda Barro
Richard Bennett
Robin Berry
James Best
Anthony & Annette Bongiorno
Darrell Burkett
John Carew
Richard Caro
George Carson
Joan Chappell
Jeff Clifton
Julius Colman & Family
Douglas Curlewis
Geoffrey Dale
Denise de Gruchy
Nicholas & Felicity Demediuk
Timothy Greene
Marcia Griffin
Charles Griss
Maureen Grogan
Jack & Judy Gutman & Family
George Hale
Suzanne Halliday
Leo & Carole Hart
William C Heath
Elaine Hogarty

Barry Jackson
Carolyn Kay
Tom Kay
Bruce Kemp
Robert Kirby
Diane Losa
Diana Lowe
Frank & Eve Mahlab
Jack Martin
Gail McHale
JJ McHale
Glenda McNaught
Janet Michelmore
Geraldine Nicoll
Claire O'Callaghan
Justin & Sally O'Day
Maurice & Ruth O'Shannassy
Graham & Dianne Otter
Terry & Dawn Power
Martin & Jill Ralston & Family
John Regan
Ian Reid
Bryan Rush
Paul & Janene Schillier
Peter & Ofelia Scott
Anna Shanahan
Brenda Shanahan
Camille Shanahan

Peter & Cate Slattery
Cliff Smith
Patrick & Tania Smith
Patricia Spry-Bailey
Murray Stapleton
Simon Swaney
Chris & Cheryl Thomas
Paula Campbell Tuckfield
Robert Turner
Christina Westmore-Peyton
Douglas Wright
Jos Xipell
Thecla Xipell
Ted Yencken
Harrison Young

Barro Group
Colorpak Packaging
Crown Towers
Emergency Care SVH – Physicians
George Castan Foundation
Palace Cinemas
Salta Properties Pty Ltd / Westgate
Logistics Pty Ltd
SVI Construction Site Workers



SVI-The 1000 Club

The Aim

The aim of the 1000 Club, established in 2002, is to gather 1000 people to commit \$1000 each to make a million dollar leap in research. The original catch phrase was “your donation can make a 1000% difference”. The initial donation gives you life membership and makes you a part of the SVI network committed to “continuous discovery”.

The funds generated by initial membership fees and then by the continuing involvement and support of 1000 Club members will be utilised to ensure SVI and its scientists can fund ongoing research, and that breakthrough discoveries are not obstructed by fiscal barriers.

There exists a real and tangible relationship between funding and the time taken for the benefits of research to reach the community. The more funds the 1000 Club can raise, which are channelled in a focused and targeted manner by SVI, the sooner cures can be found to alleviate the emotional and physical trauma associated with the diseases SVI researches.

Benefits of 1000 Club membership

There are numerous benefits of membership but the main aim is for members to feel they are part of a collaborative process in a family of scientists, administrators, philanthropists, donors and business people devoted to continuous discovery. Other tangible benefits include:

- All membership joining fees and subsequent donations are tax deductible.
- Members will be invited to participate in activities involving SVI, including guided tours of the research laboratories, information seminars, newsletters, and annual reports.
- Members will be acknowledged and will have opportunities to network with other 1000 club members at SVI events. Functions, guest speakers, artistic experiences are all being scheduled, and members will be canvassed to ensure the events are tailored to members' needs and desires.
- Members will be given the opportunity to have as little or as much continuing involvement in SVI as they choose, and either way rest assured that choice would be respected.

In November 2003 the SVI 1000 Club celebrated its first anniversary with a 'thank you' reception held at the Institute. Following the presentation of membership certificates, SVI 1000 Club members were given the opportunity to take a guided tour of the new research building and meet some of the Institute's scientists.

Image: Histological section of a bone growth plate.



COMBINED REPORT FROM THE CHAIR AND DIRECTOR OF ST VINCENT'S INSTITUTE

The completion of the new research facility is a landmark in the history of the Institute. The cost of the facility, that we occupied in September 2003 after several years of planning and fund-raising was nearly \$10 million. The building period was not without its trials and the staff of the Institute deserves thanks and congratulations for how they coped with multiple laboratory moves, noise and dust. We particularly thank Associate Professor Matthew Gillespie and our laboratory manager David Murfitt for the enormous amount of time and effort they gave to keep the project on track. Thanks also to the Board Building Sub-committee, especially its Chairman, Mr Charles Griss, and to Professor Jack Martin and Dr John McDougall who were so involved in the early phases of the project. Thanks also to the Federal and State Governments and to the Sisters of Charity for their financial contributions and to the many philanthropic organizations and individuals who have helped. The team of Builders (Bovis LendLease) and architects (DesignInc) also deserve our heartfelt thanks for delivering a wonderful new science facility on time and on budget. Throughout the project we had tremendous support from Bovis LendLease, particularly the site team of Trevor Buckland and Scott Decker and the management team of George Tsingos and Geoff Moore.

How will the new facility assist progress in medical research? Improved facilities will accelerate the completion of projects and result in more rapid application of research to important health problems. This is achieved both through first-rate facilities and equipment but also through the outstanding researchers attracted and retained by the facilities. A good example is Dr Robyn Starr who joined the Institute from The Walter and Eliza Hall Institute in October 2003 with her research group. Dr Starr is one of the country's outstanding medical research talents, responsible with her colleague Dr Doug Hilton for discovering a family of important immune system proteins that controls inflammation.

Medical research not only provides hope for the future improvement of medicine and health but is responsible for the treatments we have today.

Advances such as safe anaesthesia or blood transfusion are taken for granted today but are typical of the advances delivered in the past by medical research. SVI scientists have played their part through famous discoveries including the development of the protein sequenator by Pehr Edman and colleagues and the discovery by Jack Martin and colleagues of the role of parathyroid hormone-related protein in the effects of cancer on the skeleton. Making discoveries that contribute to the constant improvement in medicine is the core business of our Institute. For this reason we have adopted "continuous discovery" to describe the essence of the Institute's activities. Continuous discovery reminds us of the boldness and creativity required for success in research and the excitement of the ever-present opportunity to discover new knowledge of potential benefit to health. Discoveries can be very major and have enormous impact – or they can be incremental discoveries that occur more frequently but are still enormously satisfying and significant. Great discoveries are often built on the shoulders of these.

A review of health and medical research was commissioned by the Federal Minister for Health and Ageing in 2003. The review has been chaired by Mr John Grant, affiliated with SVI through his Chairmanship of Biota Holdings Ltd, a close collaborator of our Structural Biology Laboratory. One of the major submissions to the review came from the Australian Society for Medical Research that commissioned a study of the economic returns of medical research carried out by Access Economics. The study highlights the excellent return on investment in medical research with improvements in longevity and well-being bringing highly significant economic benefits estimated at 5-fold the funds invested. The study also shows that Australia ranks at the lower end of OECD countries in most measures of spending on medical research despite the recent doubling in NHMRC funding. We look forward to the outcome of Mr Grant's review.

Collaboration remains a major strategic direction for the Institute. We have become a joining member of the re-structured Bio21 Australia Ltd., the biotechnology cluster



associated with the University of Melbourne. Membership of the Scientific Advisory Committee of Bio21 has been very valuable to the Institute providing opportunities for involvement in collaborative projects and access to funding for infrastructure platform technologies. We also continue to take a leadership role in development of research across the St. Vincent's Health Campus, particularly in relation to shared infrastructure. A new high technology transgenic mouse facility to be shared by Hospital and Institute researchers is in an advanced stage of planning and should be completed by the end of 2004.

The new building is finished but not yet fully paid for. The Institute Board made the brave decision to complete the building with a shortfall of \$4.5 million, covered by a loan facility from the Catholic Development Fund. While good progress has been made with fund-raising particularly through charitable trusts and foundations, it was decided to form the St Vincent's Institute Foundation. We are grateful to Susan Alberti AM, an outstanding Melbourne philanthropist, for taking on the role of Chairman of the Foundation, and John Ralph AC, for becoming the first Patron of the Foundation. Sue has put together a terrific group of Directors who are passionate about building the financial strength of the Institute. The Foundation will complement the role played in recent years by Claire O'Callaghan's fund-raising group. Claire and her team held a highly successful "Christmas in Winter" function last year with over 150 attendees. A very successful night was also held at Raheen when over 100 SVI supporters listened to David Helfgott play the piano.

We are accustomed to the many high honours and awards given to Jack Martin and Bruce Kemp in recent years. This year we congratulate them both on being added to a list of "highly cited scientists" identified by ISI.com, an electronic bibliographic database service. This means that

they are among the top 250 scientists in the world in their field of biology and biochemistry and among only a handful of Australian scientists listed in any of the disciplines. We also congratulate Bruce on receiving a highly prestigious Federation Fellowship from the Australian Research Council that is described in more detail elsewhere in this Report. 2003 also saw the award of a NHMRC Program Grant to Professor Kay's Immunology and Diabetes group in collaboration with researchers elsewhere and several NHMRC Project Grants. It is particularly exciting to see young scientists at the Institute doing well including Dr Heidi Drummer who received a NHMRC grant for studies on Hepatitis C Virus, Dr Stelios Bouralexis who received a Peter Doherty Award to work with the Bone group at the Institute and Dr Andrew Hammet who completed his PhD at the Institute received a CJ Martin Award to work at Cambridge University.

With our new Constitution and Board structure that was adopted last year we have a number of new Directors. Departing Directors were Dr Laurie Clemens who had been representing the Senior Medical Staff of the Hospital, Professor Richard Larkins who moved from his position of Faculty Dean to Vice-Chancellor of Monash University, Mr Graham Rogers, who had given many years of service to the Board, as had Ms Marcia Griffin. New Directors appointed in 2003 are: Ms Sue Alberti, Mr Jeff Clifton, Sr Mary Fankhauser, Professor James Angus and Mrs Ruth O'Shannassy. We thank all of these as well as the continuing Directors for their wonderful support over the past year.

Chair
BM Shanahan

Director
TWH Kay



MEMBERS OF THE BOARD

Image: From left
Mr Ian Reid,
Ms Nicole Feely,
Professor James Best,
Mr Barry Jackson,
Ms Ruth O'Shannassy and
Professor James Angus

Ms Brenda M Shanahan *BEC BCom* **Chair, St Vincent's Institute**

Ms Shanahan has a research background in finance in Australian and overseas economies and sharemarkets. She is Chair of St. Vincent's Health, and is a Board member of Challenger Financial Services Group and JM Financial Group Ltd. She is a former member of the Australian Stock Exchange and former Executive Director of a stockbroking firm, a fund management company and an actuarial company.

Ms Sue M Alberti

AM
From 14th April 2003

Ms Alberti is co-founder and Managing Director of DANSU Constructions Pty Ltd and associated companies. 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. She was recently appointed as Inaugural Chair of the St Vincent's Institute Foundation.

Professor James A Angus

BSc PhD FAA
From 18th August 2003

Professor Angus was recently appointed Dean, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne. Prior to becoming Dean, he was Professor and Head of the Department of Pharmacology and Deputy Dean of the Faculty of Medicine,

Dentistry and Health Sciences, President of the Academic Board, and Pro Vice-Chancellor, The University of Melbourne. He is a member of the Bio21 Institute Management Committee and First Vice-President of the International Union of Pharmacology. He has extensive research experience in preclinical pharmacology in the areas of cardiovascular and antinociceptive drugs.

Professor James D Best

MD BS FRACP FRC Path FRCP Edin

Professor Best is Professor and Head of The University of Melbourne Department of Medicine, St. Vincent's Hospital, Melbourne. He is a Member of the Board of Directors of St. Vincent's Health and Deputy Dean of the Faculty of Medicine, Dentistry and Health Sciences at The University of Melbourne.

Dr Laurence Clemens

MBBS FRACP
Retired 14th April 2003

Dr Clemens is Director of the Department of Rheumatology, St Vincent's Hospital, Melbourne.

Mr Jeff Clifton

BCE DIPCE
From 14th April 2003

Mr Clifton is the Chairman and Managing Director of the Clifton Coney Group. This group provides development and project management services to the building industry in Australia and overseas. He has over 35 years experience in the property industry.

Sr Mary Fankhauser

RSC BAppSci (Nursing Admin)
GradDipCommunityHealthNursing
ClinPastoralCareCert
From 14th April 2003

Sr Fankhauser has a background in health-care, having worked as a nurse in a wide variety of clinical and administrative positions in both the private and public sectors of St. Vincent's Health.

Ms Nicole Feely

BCom LLB

Ms Feely is the Chief Executive Officer, St. Vincent's Health and has a background in business law, politics and administration in both the private and public sectors.

Ms Marcia Griffin

BA DipEd BCom
Retired 14th April 2003

Ms Griffin is a Board Member of PMP Communications Ltd and National Pharmacies.

Mr Charles Griss

F CPA FCA FAICD

Mr Griss is a former Senior Executive of ANZ Banking Group Ltd and former Managing Director of Esanda Finance Corporation Ltd. He is a Director of the SCHS Melbourne Region Board, and Chairman of both the Quality of Safety Committee and Community Advisory Committee for the SCHS Melbourne Region Board.



Mr Barry J Jackson

BCom (Hons) MAICD

Mr Jackson is a Director of Paperlinx Ltd, Alesco Corporation Ltd, Equity Trustees Ltd and CSR Ltd. He was formerly Managing Director of Pacifica Group Ltd (1995-2001) and has over 30 years experience in manufacturing and industrial marketing.

Professor Thomas WH Kay

BMedSci MB BS PhD FRACP FRCPA

From 14th April 2003

Professor Kay is Director of St Vincent's Institute. He holds a Professorial appointment within the Department of Medicine (St. Vincent's Hospital), and The University of Melbourne, and is an Honorary Endocrinologist at SVHM. Professor Kay's research interests are in the areas autoimmunity, particularly of type 1 (childhood) diabetes.

Professor Richard G. Larkins

AO MD BS PhD FRACP FRCP

Retired 31st March 2003

Professor Larkins is Vice Chancellor, Monash University. Past positions have included; Dean of the Faculty of Medicine, Dentistry and Health Sciences and Head of the School of Medicine at the University of Melbourne, Chair of NHMRC, President of the Endocrine Society of Australia, Chair of the

Accreditation Committee of the Australian Medical Council and President of the Royal Australasian College of Physicians.

Ms Ruth O'Shannassy

BComm

From 14th April 2003

Ms O'Shannassy worked in economic research in the finance industry in Melbourne before moving overseas. She spent seven years living and working offshore, primarily as a stockbroker in London and Asia before returning to Australia.

Mr Ian D Reid

BE (Chem) ASA FIEAust MAICD

Mr Reid comes from a manufacturing and industry background. He is a Director of Advanced Riverina Holdings and a Board Member of the Melbourne Anglican Foundation.

Mr Graham EN Rogers

FIA FIAA ASA

Retired 14th April 2003

Mr Rogers is Chairman of SMF Funds Management and serves on the Boards of RACV Financial Services, the Private Health Insurance Administrative Council, and the Atheneum Club. He is President of the Institute of Actuaries of Australia, Chairman of the University of Melbourne Actuarial Foundation and is Principal

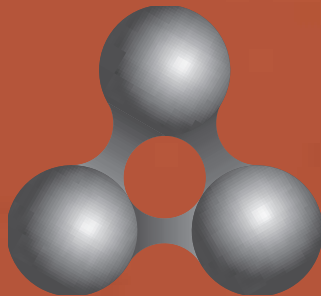
of the Offley House Group. His background includes more than 25 years as a chief executive in the financial services industry including Colonial Investment Management, Jacques Martin Group and Equitable Life.

Mr Douglas A Wright

FAICD

Mr Wright is a Founder and Managing Director of Wrights, an Australian-owned creative communications consultancy. He is a public affairs strategist, and has worked in the media and business in Australia and Europe. He is Chairman of the Victorian Government's Small Business Advisory Council. Mr Wright is a Member of the Public Relations Institute of Australia, the Counsellors' Academy of the Public Relations Society of America, and an Associate Member of the Australian Marketing Institute and Institute of Public Relations (UK).

Image: From left Professor Thomas Kay, Sr Mary Fankhauser, Ms Brenda Shanahan, Mr Jeff Clifton, Ms Sue Alberti, Mr Charles Griss and Mr Douglas Wright



RESEARCH REPORT

St Vincent's Institute **2003 Annual Report**

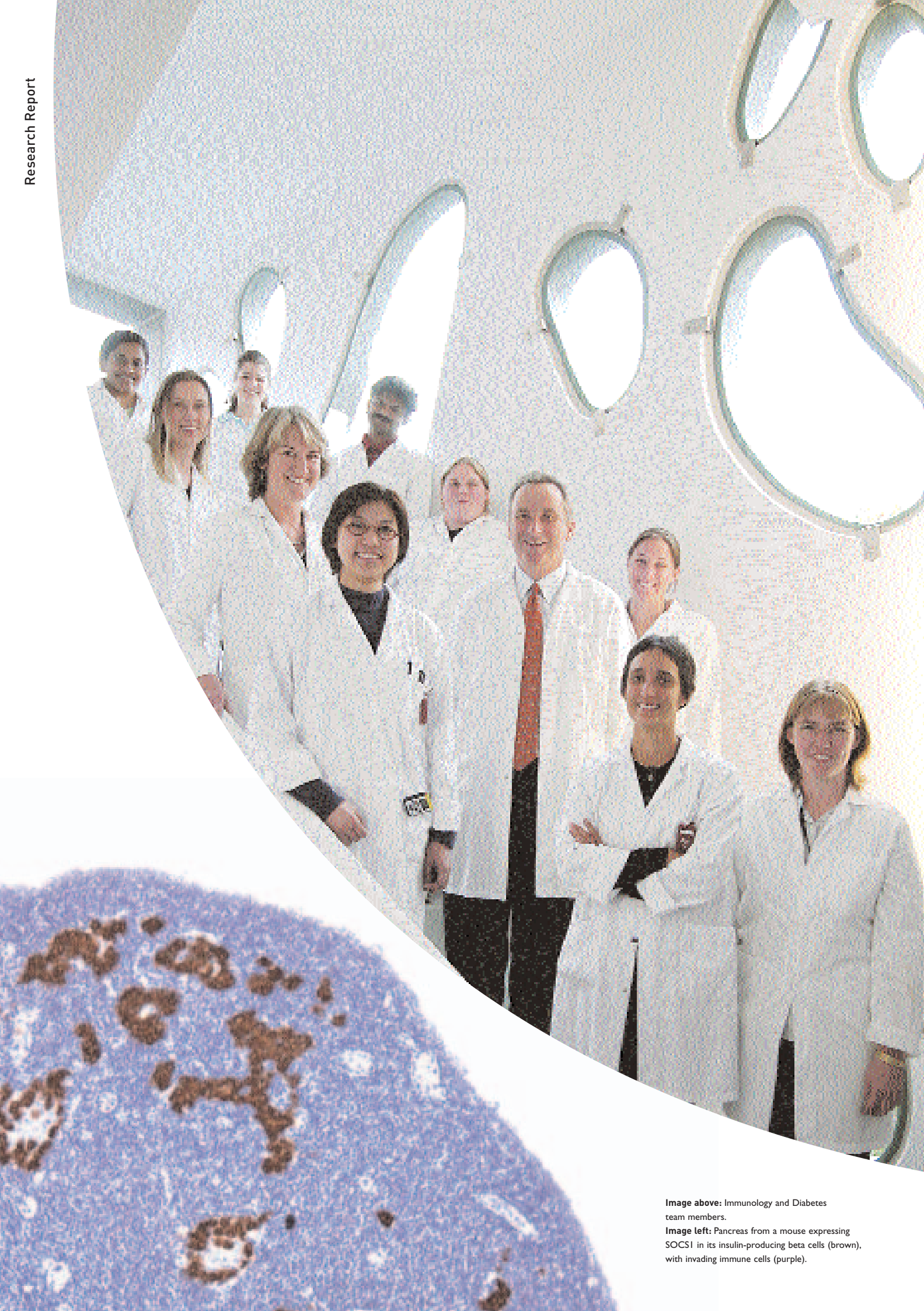


Image above: Immunology and Diabetes team members.

Image left: Pancreas from a mouse expressing SOCS1 in its insulin-producing beta cells (brown), with invading immune cells (purple).

IMMUNOLOGY AND DIABETES UNIT

People with type 1 diabetes lack insulin, the hormone that regulates the metabolism of glucose. Insulin is produced by cells in the pancreas called beta cells (b cells), which are contained within small clumps of cells called islets. In type 1 diabetes, these b 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 the Immunology and Diabetes Unit we are studying how b cells are destroyed, and we are investigating ways to protect b cells from the immune system as a potential therapy for treatment of type 1 diabetes. In particular we have been using genetically-modified mice to block hormones of the immune system called cytokines, which are involved in inflammation and have been shown to damage b cells.

Blocking the action of interleukin-1

One of the cytokines that is toxic to b cells in culture is interleukin-1 (IL-1). This molecule is produced by cells of the immune system within inflamed islets in the pancreas and evidence suggests that it may be involved in the process of b cell death leading to diabetes. To test this, we generated mice deficient in receptors for IL-1 in a strain that is normally susceptible to diabetes. We tested the susceptibility of islets from these mice to different cell death stimuli in the laboratory and found them to be resistant. However, the mice developed diabetes at much the same rate as their normal littermates. It has been known for 15 years that IL-1 kills b cells in culture, however our data shows for the first time that this is unlikely to cause diabetes in the whole animal.

Blocking multiple cytokines using SOCS1

The suppressor of cytokine signalling (SOCS) molecules are a family of proteins that inhibit the action of cytokines on cells. We have expressed one molecule in this family, SOCS1, in b cells of mice genetically susceptible to rapid onset

diabetes (called NOD8.3 mice). These mice develop islet inflammation, however the mice with SOCS1 in their islets never develop diabetes. We have investigated the mechanism by which this protection from diabetes occurs and found that there are very low levels of certain molecules on the b cells which means these b cells are less easily recognized by the immune system. Also, there is absence of the molecule Fas, a cell surface protein that leads to cell death when activated.

We have also used the SOCS1 molecule in a virus induced model of diabetes in collaboration with Dr Matthias von Herrath at La Jolla Institute for Allergy and Immunology in San Diego, USA. As in the NOD8.3 model, SOCS1 expression protects these virus infected mice from diabetes, and b cells have similarly low levels of molecules important in the development of type 1 diabetes. These findings are helping us to understand how SOCS1 protects b cells, and how it may be used as potential therapy.

Human islet transplantation

In recent years, diabetes laboratories in the northern hemisphere have developed successful techniques for the isolation and transplantation of human islets into patients with type 1 diabetes. We have begun the Tom Mandel Islet Transplantation Program as a collaborative effort between SVI, St Vincent's Hospital and other Melbourne hospitals. We have been isolating islets from organ donors, and at this stage we are using the islets for research while we finish developing methods of isolating islets in sufficient quantity and purity for transplantation. We are using the islets to study the mechanisms by which the immune system destroys human b cells, in a similar manner to that which we use for mice. In one particular experiment, we have been using cytotoxic or "killer" T cells isolated from blood to kill the human islets in culture. We are then able to add inhibitors of the toxic molecules produced by the immune system to protect the islets from the killer cells. By the middle of 2004, we hope to transplant islets into patients. Diabetes and transplantation centres in Melbourne will be involved in recruiting and caring for patients before and after the islet transplantation procedure.

Immunology and Diabetes Unit

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SIGNAL TRANSDUCTION LABORATORY

Signal Transduction Laboratory

Robyn Starr, Head
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Ailsa Frew
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Regulation of the immune system by SOCS proteins

Cytokines are important cellular messengers that control the survival, growth, differentiation and effector function of cells of the immune system. Cytokines are produced in response to changes in the environment, and act on specific target cells to induce an appropriate biological response. Responses to cytokines are typically transient, and unregulated responses to these potent molecules are generally harmful. Examples of cytokines include interferons, interleukins and growth factors.

Several years ago, we identified a family of proteins that switches off cytokine signals. These proteins, known as SOCS for suppressor of cytokine signalling, regulate the intensity, duration and quality of responses to cytokine. We are analysing genetically modified mice to understand the physiological roles of SOCS proteins, by observing the consequences of SOCS deletion on immune system function. Our research has shown that disruption of SOCS expression or activity is associated with several immune and inflammatory disorders, suggesting that modification of SOCS expression may be a novel therapeutic strategy for these diseases.

T cells lacking SOCS1 and SOCS3

We are investigating the roles of SOCS1 and SOCS3 in the regulation of T cell function. In order to understand the physiological role of these proteins, we have generated mice that lack functional SOCS genes. SOCS1-deficient mice have abnormalities in T cell development, and T cells lacking SOCS1 appear to be constitutively active and proliferate at a greater rate than normal *in vivo*. These defects appear to be due to uncontrolled signalling in response to a family of related cytokines, including interleukin (IL)-2, IL-7 and IL-15. In the absence of SOCS1, cells are unable to switch off these cytokine signals, and this leads to the development of inflammatory disease as the mice age.

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. The immune system contains a variety of checks and balances to ensure it is sufficiently robust to combat infection, yet not too powerful that the immune cells attack self and induce autoimmunity. One of these safeguards prevents T cells from becoming fully activated unless a safety signal has been received. We find that in the case of T cells lacking SOCS3, there is no longer a requirement for this safety signal to be received before cells become activated. The consequence of this is that T cells are more easily activated and are prone to autoimmunity. This study suggests that SOCS3 expression in T cells functions as a safety net to maintain cells in a resting state until it is clear that infection is present.

Identification of immune regulators using ENU mutagenesis

A method to understand gene function known as 'forward genetics', 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 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. We are studying several pedigrees with abnormalities in their immune system and we are in the process of identifying the mutated genes. In addition to isolating novel genes, this approach is likely to identify known genes that were not previously known to have a role in immune regulation.

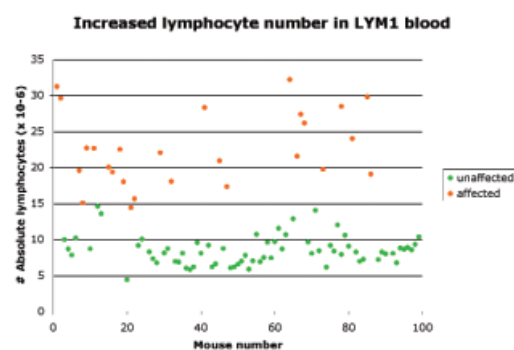


Image: Signal Transduction
Laboratory team members.





BONE, JOINT AND CANCER GROUP

Bone, Joint and Cancer Group

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Our skeleton provides structural support for our body as well as acting as a store of calcium for the body. Our skeleton is continually built up as we grow in childhood and is reshaped or 'remodelled' throughout our life in order to better resist the changing pattern of physical forces that we are exposed to. Bone is also remodelled continuously in order to replace bone that has minor cracks or other damage, and generally to maintain the quality of the bone. However, after attaining a peak bone mass during young adulthood, we gradually lose bone as a normal consequence of ageing, and the rate of bone loss is influenced by our genes, diet and exercise and, in women, by the menopause. If this loss of bone is severe (this is described as osteoporosis) the bone is liable to fracture easily and this is an enormous medical problem in our ageing population. In addition, bone is very prone to invasion by cancer cells that originate in other organs. As they invade, cancer cells destroy and critically weaken the bone, which can be painful and debilitating. Similarly, when rheumatoid arthritis develops in joints the adjoining bone frequently undergoes painful bone destruction. Thus, our group studies not just the functioning of bone itself but also diseases that directly damage bone.

Our Aim

Our integrated research program (involving basic and clinical-related work) aims to improve our understanding of the processes that build up and break down bone both in normal bone and under diseased conditions such as osteoporosis, arthritis and as a result of cancer growth in bone. We

particularly aim to identify new molecules that control these processes that could be developed as targets for the development of new drug treatments that could reduce bone destruction.

Inhibitors of Bone Destruction

The main approach of therapies currently used to maintain the structure of the skeleton is to limit its destruction or breakdown, although there is a new focus on therapies that can actually build up the bone. Agents commonly used in clinical practice to reduce bone destruction include bisphosphonates that kill the cells that are responsible for degrading bone. However, complications that may arise from the long-term usage of bisphosphonates is not known, and the opportunity for new inhibitors of this process remain. We have identified and patented several new agents that stop the formation or activity of the specialized cells that break down bone. We have demonstrated that these agents are effective in laboratory studies and have begun translating this work to appropriate animal models. If this proves effective we can develop this in several ways including developing drugs that mimic the effects of these agents, drugs which ultimately can be used in clinical trials. In addition, we have shown new mechanisms of action of inhibitors, which greatly adds to our understanding of how these agents act in the body.

One particular recent focus of our work has been the link between the immune system and bone. We have previously found new roles for a type of immune cell that is resident in bone but whose influence on bone has been ignored. This cell is the T lymphocyte or T cell, which is critical for



Image: Bone, Joint and Cancer team members.

immune responses to diseases and is required for us to overcome viral and bacterial infections. Our studies have identified agents that act upon these T cells and cause them to produce a vast array of very potent molecules that can either inhibit or enhance bone destruction. These protein molecules are important in diseases where an immune response is evident, particularly in states of pathologically increased bone resorption, such as inflammatory (rheumatoid arthritis) and malignant bone disease. We have extended our previous discovery of IL-18 as an inhibitor of osteoclast formation through the mediation of T-cell-derived GM-CSF, to identify that IL-12, like IL-18, is a potent inhibitor of osteoclast formation. Our work has produced strong evidence for the existence of a novel, T-cell-derived inhibitor of osteoclast formation, and identifying this inhibitor is a focus of our work. Similarly, we have identified that IL-4 acts through T cells to inhibit osteoclast formation.

One particular achievement of our group over the last few years has been the identification of a protein we called OCIL as well as a group of proteins similar to OCIL. These proteins prevent the formation of bone-destroying cells, and we are currently testing their effects in mice. More recently we have begun to uncover other roles for OCIL, mostly relating to bone but also suggesting possible roles in the immune system. This was highlighted by the discovery that OCIL plays an important role in the function of immune cells called the 'natural killer' or NK cell (which can attack cancer cells that evade other immune defences). This furthers the links between bone cells and the immune system, but also suggests that certain proteins important to

NK cells may also play a role in bone. Much of our laboratory work on osteoclast regulation by the immune system is done with a view to applying it to improving understanding of the bone loss associated with inflammatory bone diseases, such as rheumatoid arthritis.

Towards Treatments for Rheumatoid Arthritis

The destruction bone loss around the rheumatoid arthritic joint is a major cause of pain in this disease, and can also further degrade or destabilise. This results in painful joint deformities, progressive functional disability, an increased risk of bone fractures and increased mortality rates. Its cause is a major unsolved problem in rheumatoid arthritis. Until recently, the focal bone erosions found in rheumatoid arthritis were thought to be due to direct invasion by the inflamed membranes of the joint. We have recognized that osteoclasts (cells that break down bone in normal bone remodelling) are the main cause of bone damage in rheumatoid arthritis, and we have investigated agents that stop the activity of these cells as potential treatments for arthritis sufferers. The treatments that stop the development of the bone destroying osteoclast cells cured bone damage, but did not alleviate the joint inflammation or cartilage damage. This suggests that although joint inflammation causes that bone damage, this bone damage does not itself cause or make worse the joint inflammation. Future studies will use combination of an anti-inflammatory agent with an agent that blocks bone destruction.

What Influences Breast Cancer Growth?

We have previously identified a protein we called parathyroid hormone-related protein (PTHrP) due to its close relationship to parathyroid hormone. We determined that PTHrP was produced by a number of tumours, but those principally of the head and neck, lung, breast and kidney. We have provided experimental evidence with tumours that express high levels of PTHrP and have the ability to grow in bone result in enhanced bone destruction. However, we have also found that patients whose tumours make PTHrP survived longer (and their cancer spread less) than those that did not. This suggests that production of

PTHrP by the breast cancer cells makes them less aggressive and lethal. There is no explanation for this at present, but we are actively investigating these two apparently contradictory actions of PTHrP.

We have identified a number of bone related proteins that increase tumour growth in bone, largely by stimulating the production of cells that destroy bone and we are currently examining the mechanisms by which they do this. We are also examining whether the blockers of bone destruction that we have discovered are able to prevent cancers from invading and degrading bone.

COMPARATIVE ENDOCRINOLOGY

Comparative Endocrinology

Janine Danks, Head
Patricia Ho
Lisa McCarthy

In 2002 we identified a parathyroid hormone (PTH) protein and gene from the fish, *Fugu rubripes*. It is known that human PTH and certain analogues of human PTH are stimulators of bone growth. These factors are beginning to be 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.

All the PTHs sequenced so far from mammals and birds are highly homologous and this makes fish PTH

interesting as a potential therapeutic in humans. The venture capital company, Starfish Ventures Pty Ltd formed a company (TeeleOstin), using pre-seed funds, with SVI, The University of Melbourne and the technology developers Janine Danks and Prof Jeffrey Zajac from Department of Medicine, University of Melbourne, Austin Medical Centre. A series of experiments were carried out to expand the initial *in vitro* work and full patent applied for September 2003.



Image left: Histological section of a bone tumour.

Image right: Comparative Endocrinology team members.

Bone Metastasis and Migration Laboratory

John Price, Head
Susan Docherty
Jessica Moore
Joe Pereira

TUMOUR CELL MIGRATION AND METASTASIS LABORATORY

The spread of cancer, rather than the growth of the primary tumour, is ultimately responsible for treatment failure, morbidity and death amongst cancer patients. The process is highly complex and multi-step in nature and involves extracellular matrix degradation, tumour cell migration, altered tumour cell adhesion and proliferation as well as the establishment of new blood vessels (angiogenesis). Modulation of each of these processes enables the tumour cell to escape from the primary tumour microenvironment and spread locally/distally establishing a proliferative focus at a secondary site.

Central to the process of metastasis is the cancer cells' ability to actively move through the tissues of the body, crossing tissue boundaries and gaining access to new sites in which to establish growth. The major goal of the laboratory is to identify novel genes that either promote or inhibit cancer cell movement and metastasis. In doing so, we will identify new therapeutic targets to which new drugs can be designed that will inhibit cell migration and metastasis.

The 'red fluorescent mouse'

To determine whether the genes that we identify, or the new therapeutic drugs that we generate, are effective in altering the ability of tumour cells to metastasize, we use a number of mouse models in the laboratory. To improve these models, we have recently created tumour cells that are labelled with a red fluorescent tag (red fluorescent protein). This allows us to image the growth and the spread of tumours in 'real-time' due to the red fluorescence that is emitted from the tumour in the mice. The use of this technology makes our investigations more sensitive and efficient, allowing the screening of a higher number of genes and drugs than would be normally possible.

The role of avb3 in the metastatic process

In addition to the identification of novel genes in the metastatic process, we have also been examining the effects of one molecule, namely avb3, previously shown to enhance the spread of a number of cancers including prostate, brain and melanoma. This molecule is normally expressed at low levels on the surface of normal cells but is increased in cancer, allowing the cancer cell to adhere, proliferate and move more efficiently. We have generated a soluble form of avb3 by recombinant DNA technology allowing us to identify other molecules that interact with avb3. We believe that this will enable us to better understand how this molecule functions in metastasis. This year, we have identified for the first time, the direct interaction of the avb3 molecule with the IGFBP-2 molecule.

Interestingly, IGFBP-2 has also been shown to enhance the progression of prostate and brain cancers. We are currently investigating whether the interaction between these two molecules represents a novel pathway by which cancers of the prostate and brain can enhance their ability to spread. It is hoped that these investigations will lead to the generation of novel therapeutics targeting towards inhibiting the interaction of IGFBP-2 with avb3 that may prove effective in combating the growth and metastasis of a number of tumour types.

Compounds that inhibit tumour cell migration

In collaboration with Avolix Pharmaceuticals Inc. we are also working to identify novel compounds that effectively inhibit tumour cell migration. Identification of active compounds has already been achieved through the use of a novel high throughput migration screen. Moreover, one of the compounds not only inhibits migration but also enhances the sensitivity of tumour cells to conventional cancer therapies, such as chemotherapy. Therefore, it is hoped that these compounds would not only inhibit tumour metastasis but could also be used in combination with chemotherapeutics to enhance their efficacy in treating cancer.

Image: Red fluorescent cancer cells.

Image: Pharmacogenomics team members.



PHARMACOGENOMICS

The human genome project has provided an extremely valuable resource for the identification of genes that cause disease. As a parallel to this, the development of new drugs and the concept of tailoring patient-specific therapies are benefiting from this new information and the associated technological advances. The focus of the pharmacogenomics group is to apply these new technologies, principally gene expression profiling and proteomics, to define important molecular events underpinning disease progression and drug response.

One of the methods we use to identify genes that cause disease is called gene array. This method allows us to study thousands of different genes in a tissue to identify those genes that are expressed differentially in disease and that may contribute to the disease.

The responses of breast cancers to drug agents

During the year, we have extended our analysis of gene expression patterns to breast tumour cell lines that are stimulated to metastasize, and to map the response patterns for several drug

agents which are in development for treating breast cancer. These profiles help us understand the essential nature of breast cell malignancy and the molecular basis of drug-action in humans. In addition, these studies have enabled us to identify two compounds that are capable of inhibiting breast-to-bone metastasis and we are now characterizing gene expression patterns for the breast tumours growing specifically in the bone environment. These discoveries are potentially of considerable clinical significance.

Genes involved in diabetic kidney disease

In another line of work we have started to use an established model of Type 1 diabetes and identify genes that are associated with diabetic kidney damage. The activity level of nine thousand genes for different groups of rats have been monitored, and from this first phase of analysis our attention has focused on twenty of these which are altered for animals progressing to disease. The next phase of this work will be to examine if these same genes are altered for biopsy samples taken from patients with Type I diabetes. In an associated study using cells taken from both rat and human kidneys and inducing diabetic conditions, one novel finding has been the identification of a dramatically altered level of a specific protease not previously associated with diabetic kidney damage. We are perusing this gene as a potential new therapeutic target.

Pharmacogenomics
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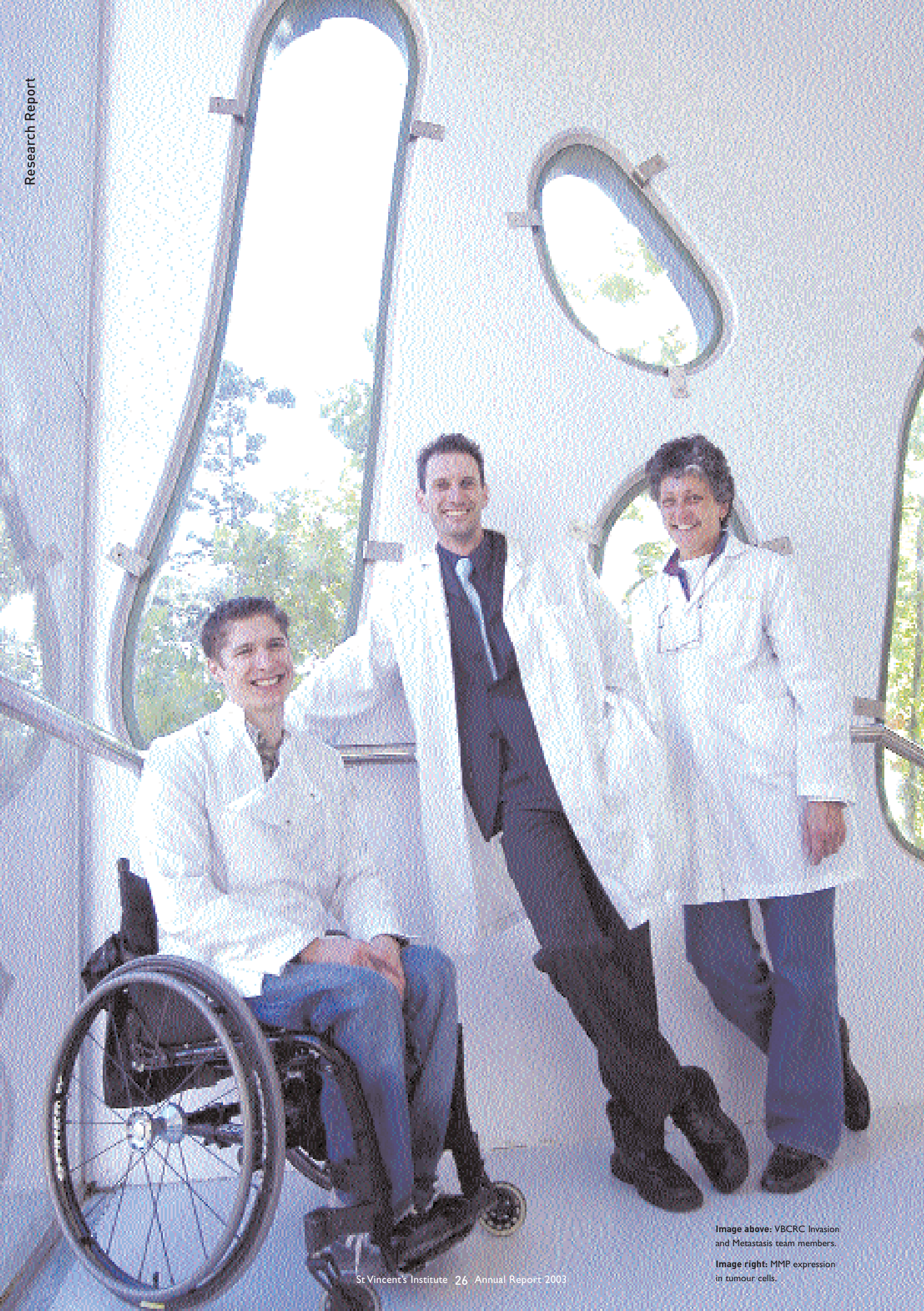


Image above: VBCRC Invasion and Metastasis team members.

Image right: MMP expression in tumour cells.

VBCRC INVASION AND METASTASIS GROUP

The VBCRC Invasion and Metastasis Group is one of five such Groups strategically placed amongst Melbourne Research Institutes, including Hormonal Regulation of Breast Cancer (Prof Evan Simpson, PHIMR), Mammary Development (Drs Jane Visvader and Geoff Lindemann, WEHI), Breast Cancer Genetics (A/Prof Ian Campbell, PMCC), and Molecular Pathology of Breast Cancer (University of Melbourne Department of Pathology). Collectively these groups form an "Institute Without Walls" administered by the Cancer Council of Victoria, with a scientific management committee comprising the directors of most of Melbourne's premier institutions (<http://www.cancervic.org.au/cancer1/research/br eastconsort.htm>). 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.

The SVI Invasion and Metastasis group was initiated in 1997 with the recruitment of A/Prof Thompson from Georgetown, USA, and has maintained two core streams of research: Elucidation of the molecular basis of breast cancer metastasis to bone, and targeting of matrix metalloproteinases (MMPs) - enzymes capable of degrading connective tissue structures, thus allowing the cancer cells to physically move and grow. They also activate many different regulatory pathways. The SVI VBCRC group has been an incubator for other new breast cancer groups at SVI, having recruited and graduated Dr Mark Waltham (Pharmacogenomics) and Dr John Price (breast-bone metastasis and migration) as new SVI group leaders.

MMP expression in tumour cells

Considerable effort has been invested during 2003 in furthering our observation that inhibitors of matrix metalloproteinases (MMPs) block the growth of experimental breast cancers in mice. We have surveyed an increasing number of

individual MMPs in both the mouse compartment and tumour cells, and found very high levels of induction of some. Also, certain MMPs are seen in the tumour component. These studies are paralleled by others where we have introduced specific MMPs into the cancer cells using laboratory procedures, and then seen that they also can grow better in the mice, and also spread better to other sites (metastasize). Thus, we continue to hone in on the MMPs which are present in the growing tumours, and which may be critical for the growth and spread of the tumour. This is important because broad-spectrum MMP inhibitors, such as the one used by us in the past, have not been successful in clinical trials in humans, and it is well accepted that we need to develop inhibitors which are more specific for a given MMP. We need to identify which MMPs should be specifically targeted, and our laboratory is contributing to this world-wide effort to elucidate these key MMPs.

Genes expressed in bone metastasis

We also continue with the bone metastasis experiments initiated by Dr John Price, in collaboration with his group. We have specifically chosen three of the targets which arose from his gene array for further study; Cadherin-11, Galectin-3, and Gravin. Cadherin-11 studies are being developed in collaboration with Prof Steven Byers, Lombardi Cancer Center, Georgetown University Medical Center, whilst those directed to Galectin-3 are collaborative with Prof Avi Raz, Karmanos Cancer Center, Detroit, Michigan, USA. We are employing transfection strategies and specific interventional approaches, where possible, to test these proteins.

VBCRC Invasion and Metastasis Unit
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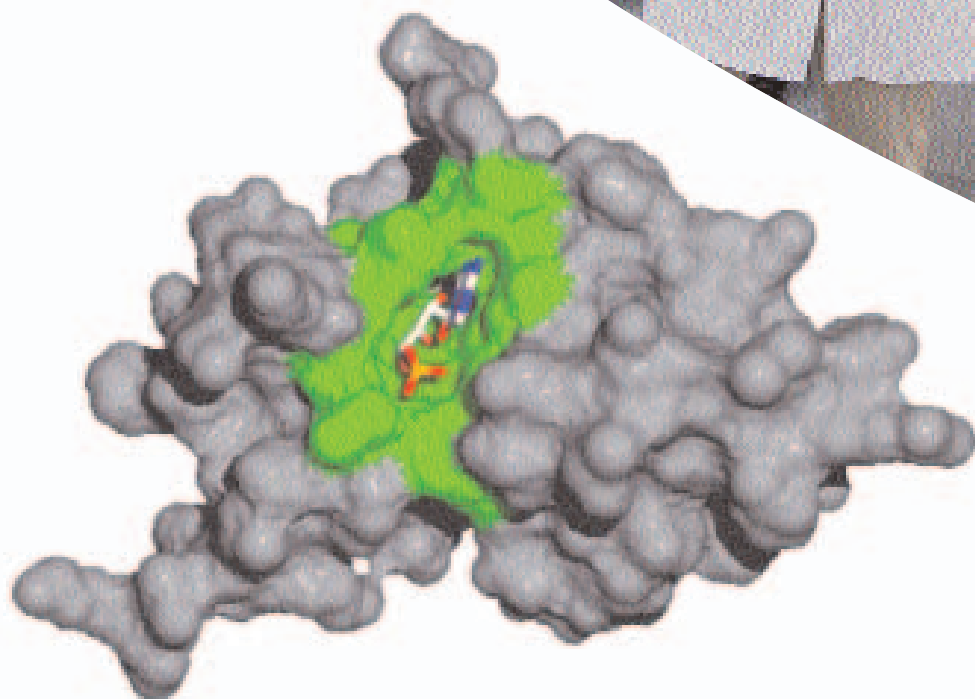


Image above: Protein Chemistry and Regulation team members.

Image left: Molecular model of the AMPK glycogen binding domain.

PROTEIN CHEMISTRY AND REGULATION

METABOLIC HEALTH & CARDIOVASCULAR PROGRAM

The AMP-activated protein kinase (AMPK) is a metabolic-stress-sensing protein kinase that regulates metabolism in response to energy demand and supply by directly phosphorylating rate-limiting enzymes in metabolic pathways as well as controlling gene expression. In 1994 we were the first to identify the AMPK. We now know that AMPK is activated in response to metabolic stress such as exercise or reduced caloric intake. Because of this role in coordinating energy metabolism with supply and demand we expect that the AMPK will have many substrates.

AMPK has become an important target for research aimed at controlling diabetes and obesity since the discovery that drugs used to treat type II diabetes such as metformin activate AMPK. Previously we had purified and cloned the AMPK and showed it was a $\alpha\beta\gamma$ heterotrimer related to the yeast protein kinase Snf1p. We have shown that all three subunits are required for enzyme activity and there are multiple isoforms of the subunits. We have identified an alternate transcript of the $\alpha 1$ gene and are investigating its significance. Studies in several laboratories have recently shown that mutations in the AMPK $\gamma 2$ subunit that is expressed in the heart can give rise to functional defects analogous to the Wolf-Parkinson-White conductance syndrome. We have found that the corresponding mutation in $\gamma 1$ R70Q mutation causes a marked increase in AMPK activity and renders it largely AMP-independent. This activation is associated with increased phosphorylation of the α subunit activation loop T172. These *in vitro* characteristics of AMPK are also reflected in increased intracellular phosphorylation of one of its major substrates, acetyl-CoA carboxylase. Our most important discovery was the binding site for AMP on the γ subunit. Several lines of evidence suggested that the allosteric activation of AMP is mediated by the γ subunits and we modelled its CBS repeat sequences on the bacterial inosine monophosphate dehydrogenase that has a pair of CBS sequences. This allowed us to recognize the binding pocket for AMP. Mutation of the critical contact residues caused loss of AMP regulation and activation of the enzyme. The AMP binding

site comprises three arginines and a histidine and mutation of any of these to glutamine results in loss of AMP allosteric control and generation of a constitutively active form of the enzyme. This structural insight into the allosteric site may greatly facilitate our drug design program.

Physiological effects of manipulating AMP-activated protein kinase genes

AMPK subunits are encoded by a multi-gene family with at least 2 genes for every subunit ($\alpha 1$, $\alpha 2$, $\beta 1$, $\beta 2$, $\gamma 1$, $\gamma 2$ and $\gamma 3$) and tissue specific expression. The aim of this project is to understand the physiological importance of the AMPK subunits by preparing mutant mice (knockout) that lack AMPK $\beta 1$ and $\beta 2$ genes. Thus far we have generated viable $\beta 2$ null mice and expect to have the corresponding $\beta 1$ null by mid May 2004, which will allow us to test whether the double null is viable. Given the important role of the β subunit in AMPK targeting and subunit interactions as well as the aging phenotype in yeast for *sip2* mutants we anticipate that the β null mice will contribute to our understanding of the physiological functions of AMPK.

Endothelial nitric oxide

Endothelial nitric oxide plays an important regulatory role in the cardiovascular system, affecting heart function as well as the vasculature and platelets. Previously we identified two major phosphorylation sites in eNOS, Thr495 (inhibitory) and Ser1177 (activating). In a series of studies we have identified the signalling pathways that control the phosphorylation and dephosphorylation of these sites plus two further sites, Ser617 and Ser635. There is a very highly coordinated reciprocal control with phosphorylation of either site being accompanied by dephosphorylation of the other site. Our work on eNOS regulation is of particular relevance to understanding the molecular basis of cardiovascular disease.

Protein Chemistry and Regulation

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Tristan Iseli
Ian Jennings
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Charles Kemp
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James Nicholson
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Bryce van Denderen

FUNCTIONAL PROTEOMICS

Functional Proteomics

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Matthew Bird
Abhilasha Gupta
Mark Walter

The glycogen-binding domain of AMPK

Work from the functional proteomics laboratory previously identified a specific region in AMPK that we called a glycogen-binding domain that enables AMPK to associate with glycogen. Glycogen is a cellular store of energy that is important for whole body glucose metabolism. The presence of the glycogen-binding domain was an important discovery because several lines of evidence had linked AMPK to glycogen metabolism. For example, in human muscle glycogen levels are high and AMPK is switched off. However following exercise glycogen levels rapidly decrease whilst AMPK is switched on. More recently humans with an unusual heart disease characterized by irregular heart beats and very high glycogen levels, has been found to be due to mutations in AMPK. To further our understanding of this disease our collaborators at Harvard Medical School used genetic engineering to create a mouse model with the same mutation as that found in humans. We have found that the mutation causes that AMPK to be switched on more than normal, and this somehow leads to increased glycogen levels that in turn leads to enlarged hearts and irregular heart beats. In the near future we hope to identify why this happens.

Functional studies of the glycogen-binding domain

The identification of a glycogen-binding domain in AMPK β is important given the close relationship between AMPK and glycogen. In collaboration with Prof Marian Carlson (Columbia University, NY, USA) we investigated the function of the AMPK glycogen-binding domain in yeast where AMPK β

is conserved in the Snf1 kinase β subunits Gal83 and Sip2. Here we used genetic analysis to assess the role of this domain *in vivo*. Alteration of Gal83 at residues that we previously showed were important for the association between AMPK β and glycogen, abolished Gal83 glycogen-binding *in vitro* and various Snf1/Gal83-dependent processes were upregulated *in vivo*.

Unexpectedly, the transcriptional regulatory phenotypes tested were not dependent on the presence of glycogen in the cell. Thus, mutation of the glycogen-binding domain affects Snf1/Gal83 kinase function by a mechanism that is independent of glycogen binding.

We have developed a non-denaturing method to purify intact glycogen particles from different tissues like liver and muscle so that all glycogen-associated proteins can be visualized at once. In the initial stages of this project, using proteomics and electron microscopy, we have identified a new pathway in hepatic glycogen synthesis. In the coming year the lab will focus on differences between glycogen particles isolated from healthy mice and mice carrying the AMPK β 2 (N488I) mutation that causes glycogen storage disease. We have shown that this mutation causes activation of AMPK both *in vitro* and *in vivo*. To date every known enzyme involved in glucose uptake and glycogen metabolism has been measured to determine how activated AMPK leads to this disease, but so far no differences have been identified.

Image right: Molecular Cardiology and Laboratory Services members.

Image below: Electron micrograph of glycogen particles.



MOLECULAR CARDIOLOGY

Despite major advances in treatment and prevention, diseases of the heart and blood vessels remain the most common causes of death and illness in our community. These diseases include heart attack, stroke, and heart failure. Our research aims to improve understanding why these diseases occur, and how we can better prevent and treat them.

Understanding the actions of ACE inhibitors on the heart

ACE inhibitors are drugs that are very valuable for the treatment of heart disease. However, despite their widespread use, there are still many uncertainties about how these drugs produce their benefits. In a study performed in collaboration with Dr Chris Zeitz and Prof John Horowitz at the Queen Elizabeth Hospital, South Australia, we studied the effects of drugs called ACE inhibitors on the heart. This study was performed in patients having coronary angiography, and the drugs were injected intravenously. We studied the uptake of the drugs by the heart and the effects of the drugs on the performance of the heart. In addition, we studied the effects of these drugs on angiotensin and bradykinin peptides in blood from the heart. This investigation gave us valuable new information about the effects of these drugs on the heart, and how they produce benefit for patients.

Understanding the effects of the heart bypass pump

When patients have open-heart surgery and operations on their coronary arteries, a heart bypass pump is used to pump blood around the body during the operation. This bypass pump works very well, except that it can produce inflammation from which the patient may take several days to recover. In collaboration with Drs Barry Dixon and John Santamaria at the Intensive Care Centre, St. Vincent's Hospital, we investigated how this inflammation occurs. We previously found that the heart bypass pump causes the formation of inflammatory peptides called kinin peptides. Our more recent studies show that a substance in blood called plasminogen activator inhibitor (PAI) is present in increased amounts in patients who have more severe inflammation after their operation. Most importantly, we found that PAI levels are increased before surgery in patients with more severe inflammation after surgery. PAI acts to prevent clots from being dissolved, which means that higher levels may result in more clots in blood vessels. This new information gave us an improved understanding of how the heart bypass pump causes inflammation, and we are currently investigating ways to reduce or prevent it.

Molecular Cardiology
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Theodora Alexiou
Phil Au
Barry Dixon
Gareth Symons
Jade Woon

MOLECULAR GENETICS

Molecular Genetics

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 Lindus Conlan
 Krystal Lambrou
 Carolyn McNeese
 Brietta Pike
 Nora Tenis
 Ana Traven
 Kate Warren

As molecular geneticists we use gene manipulations to understand the function and regulation of cellular processes under normal and pathological conditions. Our main research interests are how cells repair DNA damage and how this prevents the onset of cancer.

The role of FHA domains in sensitivity to DNA damage

Chromosome instability as a consequence of inadequate DNA damage repair is now established as a major contributing factor to the onset of cancer. As a consequence of their fundamental importance, cellular mechanisms of maintaining genomic integrity are highly conserved throughout evolution. This allows us to study simple organisms such as brewer's or baker's yeast to gain insight into molecular mechanisms that govern the cellular response to DNA damage as a model for cancer development in humans. We have characterised the role of so-called FHA domains in the regulation of yeast kinases corresponding to the human CHK2 kinase mutated in the Li-Fraumeni syndrome that gives rise to multiple independent cancers in affected patients. We have found that one of these FHA domains is absolutely required to slow down cell growth in response to DNA damage during DNA replication as well as during cell division, in order to give the cell extra time for repair. Surprisingly,

despite these severe cellular defects, mutations in this FHA domain by themselves only result in a moderately increased DNA damage sensitivity of affected cells. However, when these defects are coupled with other minor defects in alternative signalling pathways, cells become dramatically (>100-fold) hypersensitive to DNA damaging agents. The yeast results are similar to the human system where it has been a paradox as to why CHK2 mutations result in a significant cancer predisposition with only minor cellular defects. Our data support the notion that the presence of multiple backup systems protects cells against DNA damage-induced cancer, such that simultaneous failure of multiple systems leads to dramatically increased cancer risk.

DNA repair proteins are found in PML bodies

In addition to the conserved fundamental DNA damage systems, more complex organisms such as humans have acquired additional specialised cancer prevention pathways. An important evolutionary "youngster" is the promyelocytic leukaemia protein PML whose mutation leads to cancer of white blood cells. PML forms dot-like structures in the cell nucleus. These PML bodies serve as storage depots for other proteins including a large number of DNA damage response proteins. We have found that PML bodies dissolve in response to DNA methylating agents. Our data indicate that certain DNA repair proteins are usually segregated into PML bodies in order to not interfere with normal DNA metabolism, and that PML bodies disperse in response to widespread DNA damage to rapidly release repair proteins from this storage depot.



NATIONAL SEROLOGY REFERENCE LABORATORY AUSTRALIA™

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. Commercial imperatives drive the development of diagnostic tests and this can leave important issues unaddressed. Our research programme tackles such problems.

We have developed a new assay for distinguishing recent from established HIV-1 infection. This was achieved by performing a detailed analysis of the specific interactions between antibodies and individual HIV-1 proteins during maturation of the immune response to HIV-1 infection. This assay will provide valuable information for estimating the incidence of HIV-1 infection for epidemiological surveys as well as monitoring new infections during vaccine trials and managing treatment programmes. We also continue to collaborate with HIV vaccine researchers in Australia by investigating the immune response generated by these vaccines.

The group has expanded work on incidence testing to include other viral infections where knowledge of the time of infection is clinically

relevant but cannot always be accurately determined using existing assays. One of these projects is to distinguish primary rubella infection from individuals who are seropositive as a result of past infection or vaccination since rubella acquired during the first trimester of pregnancy is associated with a 90% risk of congenital malformations.

The adverse side effects of medication for HIV-1 make it desirable to minimize the period of time individuals remain on therapy. The serological response to selected HIV-1 proteins is being characterized in individuals prior to and during the interruption of anti-retroviral treatment. The aim of this study is to identify a marker that can predict which participants undergoing treatment interruption will experience viral load rebound and those that will continue to suppress viral replication.

We have developed and validated an assay for Hepatitis C based on dried blood spots. Preparing samples as dried blood spots from a finger prick simplifies sample collection and eliminates the need for refrigeration on storage and transport of the sample.

National Serology Reference Laboratory™
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Susan Best, Senior Scientist
Elizabeth Johnson,
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Rod Chappel
Hayley Croom
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Larissa Doughty
Stacey-Lee Edwards
Darren Jardine
Sally Land
Kim Richards
Anita Sands
Kim Willson

Image left: Molecular Genetics team members.

Image right: Tubes and tips, a scientist's tools.

VIROLOGY

Virology

Andy Pombourios, Head

Heidi Drummer

Chan-Sien Lay

Anne Maerz

Victor Sam

Chris Vassos

Understanding the membrane fusion and replication of HIV

The AIDS pandemic continues unchecked with 5 million new HIV infections and 3 million deaths due to AIDS in 2003. In developed countries, highly active antiretroviral therapy (HAART) can suppress viral replication and extend the life expectancy of HIV-infected people. However, HAART is often associated with severe, sometimes fatal side effects and with the emergence and transmission of drug-resistant variants. Further elucidation of the molecular processes underlying viral replication is essential if we are to uncover new drug targets to extend the therapeutic armoury against HIV.

Membrane fusion, which is mediated by the gp120-gp41 viral glycoprotein complex, is an early and obligate stage of the HIV replication cycle that remains incompletely understood. The gp120 glycoprotein mediates viral attachment to helper T cells, macrophages, microglia and dendritic cells by binding to the CD4 receptor. gp120 then binds to a chemokine receptor, triggering the membrane fusion activity of gp41. The membrane fusion function of gp41 involves its transformation into a stable hairpin-like structure that draws the viral and cellular membranes together such that they fuse. These events deliver the viral nucleocapsid into the interior of the cell where replication occurs.

A major objective of the Virology Unit is to understand how gp120 triggers the membrane fusion activity of gp41 and to determine how the various structural regions of gp41 contribute to its fusion function. We have found that conserved residues in the disulfide-bonded region of gp41 mediate association with gp120. Our data suggests that this gp41 region acts as a sensor of conformational signals that are generated when gp120 binds to CD4 and chemokine receptor, triggering the activation of gp41 fusion function. In addition, we have uncovered a functional interaction between N- and C-terminal regions of gp41 that stabilise the fusogenic hairpin conformation and drive the final, pore expansion phase of fusion. Further characterization of these poorly understood stages of the fusion process is essential for a more complete understanding of HIV-1 entry and for the discovery of new fusion inhibitors.

Structural and functional studies of the Hepatitis C Virus glycoproteins.

Hepatitis C virus (HCV) infects ~ 200 million people world-wide causing recurrent, progressively worsening liver inflammation, cirrhosis and hepatocellular carcinoma. Hepatitis C is the leading indication for liver transplantation in developed countries. Currently, no vaccines exist to prevent infection and treatment of infected people with anti-viral agents has limited success in clearing viral infection.

The HCV glycoproteins, E1 and E2, are generated by signalase action from the HCV polyprotein during viral replication. Until 2003, it was believed that E1 and E2 were retained in the endoplasmic reticulum after signal peptide cleavage and did not become surface expressed. The localization of E1 and E2 to the ER resulted in a pool of glycoproteins that were extremely heterogeneous, forming both non-covalent and covalent heterodimers, and containing large amounts of high mannose carbohydrate. Studies to examine the function of these glycoproteins in cell binding and entry were therefore restricted to studying truncated secreted forms of the glycoproteins rather than native heterodimeric forms. In 2002 we began to re-examine the localization of these glycoproteins within the cell using subcellular fractionation and immunofluorescence. Our studies revealed that contrary to established dogma, E1 and E2 became surface expressed as non-covalent heterodimers. Confirmation that these glycoproteins had exited the ER and entered the secretory pathway was provided by carbohydrate analysis. In addition we showed that cell surface expressed E1E2 heterodimers were functional by pseudotyping the glycoproteins on an HIV-1 virus. The E1E2 pseudotypes were capable of mediating entry into Huh7 cells suggesting that they bound cellular receptors and underwent fusion with cellular membranes. These studies were presented at the 11th International Symposium on Viral Hepatitis and Liver Disease, Sydney Australia, 2003 and published in FEBS letters. We are the only group world-wide to have biochemically characterized the functional form of the HCV glycoproteins.

The development of *in vitro* assays to examine the function of the glycoproteins has also enabled an examination of neutralizing antibody responses in HCV infected people. These studies are underway and we have received funding from the Australian Centre for HIV and Hepatitis Virology to examine antibody responses to HCV in 2004. In addition we are examining the role of E1 and E2 in viral fusion and entry and were awarded an NHMRC grant to continue these studies through 2004-2006.

Image: Virology team members.



Images: Three dimensional structure based drug design.

BIOTA STRUCTURAL BIOLOGY LABORATORY

Biota Structural Biology Laboratory

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Knowledge of protein 3-D structure enables the intelligent design of new drugs

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 mental disease, bacterial toxins that attack cell walls, and proteins that detoxify poisons.

Bacterial toxins

The cells of the body are coated in a lipid membrane that acts as a skin to protect the cell. Some bacteria attack the body by producing toxins that kill cells by punching holes in cell membranes.

In order to understand how these toxins punch holes in cell membranes, we have been determining the 3-D structure of several toxins.

Streptococcus intermedius, a resident of normal human oral flora, is an opportunist pathogen associated with infections leading to abscesses in the oral cavity and at deep-seated sites, such as the brain, liver and lungs. The bacterium secretes a toxin named intermedilysin (ILY) which has been shown to form pores in human cells. Intermedilysin belongs to the cholesterol-dependent cytolysin family of toxins that have been identified in several different bacteria including the serious human pathogens *Streptococcus pneumoniae* and *Clostridium perfringens*. Intermedilysin, however, is the only member showing exclusive specificity for human cells. We have determined the three-dimensional shape of the toxin which reveals unique structural features that help explain how it attacks human cells. The structure provides an important starting point for the discovery of compounds that could be developed into novel antibiotics.

Our work on protein toxins is performed in collaboration with Prof Rod Tweten, Department of Microbiology and Immunology, University of Oklahoma, USA.



Image: Biota Structural Biology Laboratory team members.

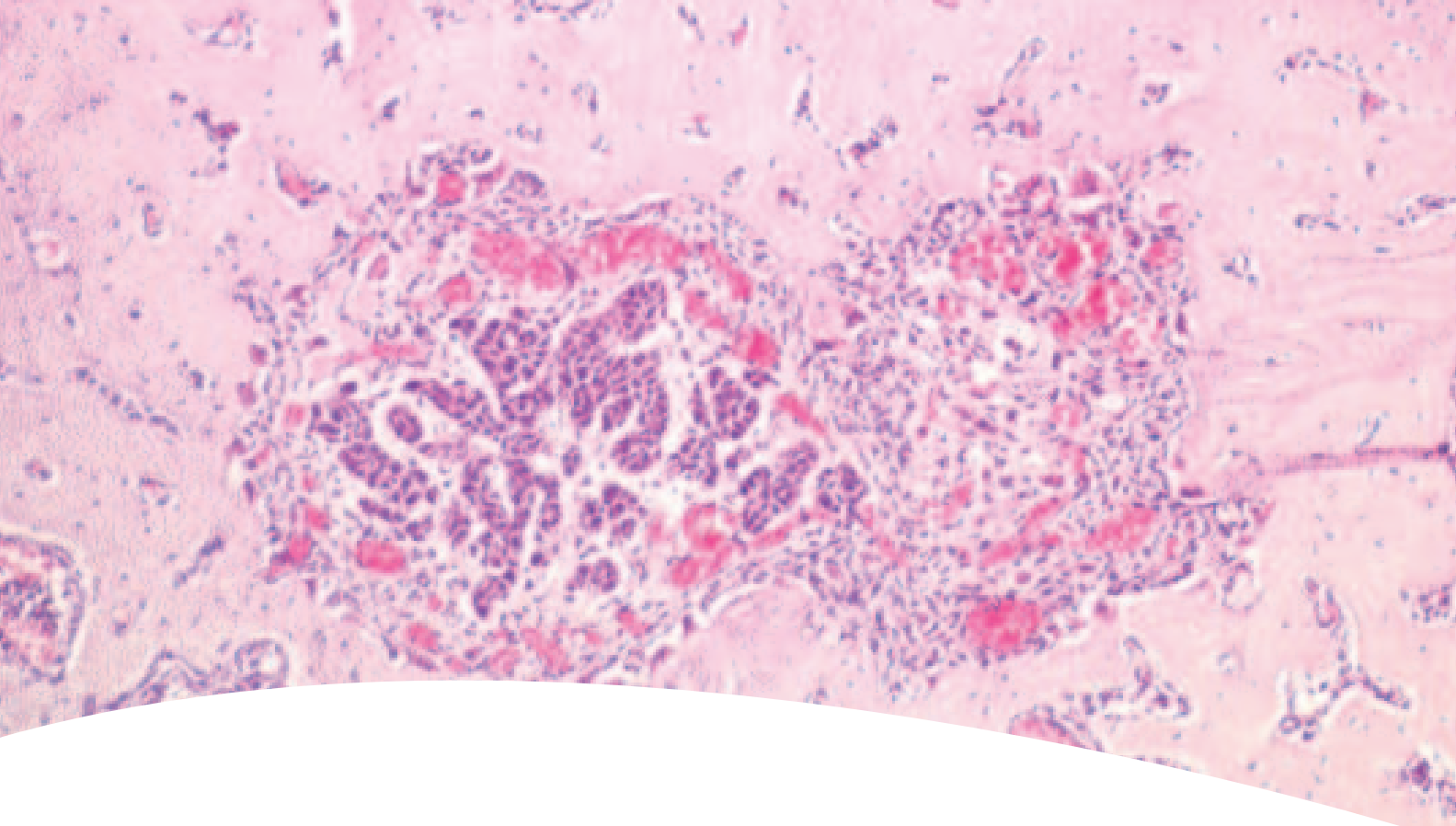
Human growth hormone receptor

Human growth hormone causes a diverse range of biological activities including bone growth, lactation, insulin-like and diabetogenic effects and actions on the reproductive and immune systems. In order to accomplish these effects, growth hormone must bind to its specific cell surface receptor which eventually leads to activation of intracellular signal transduction pathways. Discovery of compounds that stop the receptor signalling are likely to find a role in a variety of diseases such as acromegaly (giantism), diabetes and certain cancers (particularly colon, breast and prostate cancers).

Although the structure of the receptor bound to its hormone has been known since 1992, researchers around the world have been

unable to visualise how the receptor looks in the absence of its hormone. A knowledge of the so-called "apo" receptor structure would be a great help in the design of novel compounds to treat the above mentioned diseases. We have now determined the apo structure and found a number of subtle changes in its structure compared to when it binds hormone. We are hoping to exploit these differences in the design of compounds that might stop the receptor signalling inside cells.

Our work on human growth hormone receptor is a collaboration with Prof Mike Waters, Institute for Molecular Bioscience and School of Biomedical Sciences, University of Queensland.



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Image left: Histological section of a bone cell tumour.

Image: SVI Administration team members.

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Louie Opasinov, BSc Dip Ed Melb

STUDENTS & GRADUATES

STUDENTS

POSTGRADUATE SCHOLARS- DOCTOR OF PHILOSOPHY

Theodora Alexiou, BSc Grad Dip Mon
'Generation and function of brain angiotensin'
Angela Arvanitis, BSc (Hons) Melb
'Characterisation of an in vitro model of epithelial to mesenchymal transition'
Barry Dixon, MBBS Syd FRACP
'Characterisation of systemic inflammation following cardiopulmonary bypass'
Eugene Estella, MBBS Qld FRACP
'Mechanism of b-cell destruction'
Abhilasha Gupta, BSc (Hons) Melb
'The nuclear localisation of AMP-activated protein kinase'
Karl Häusler, BAppSc Phillip MAppSc RMIT
'Stromal and immune factors in osteoclast formation'
Natasha Ilievska, BSc (Hons) VUT
'Role of PTHrP in DNA repair'
Tristan Iseli, BSc (Hons) Melb
'Structure and function of the glycogen binding AMP-activated protein kinase b-subunit'
Geoffrey Kong, BSc (Hons) Melb
'Structural studies of Alzheimer's disease amyloid precursor protein'
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'
Carolyn McNees, BSc (Hons) Melb
'ASCIZ is required for lesion-specific Rad51 foci formation and DNA damage survival'
Sid Murthy, BSc (Hons) Melb
'Regulation of AMP-activated protein kinase'
Danijela Miroslavljevic, BSc (Hons) LaTrobe
'Lymphocyte-derived factors affecting osteoclastogenesis'
Joseph Pereira, BSc (Hons) LaTrobe
'Biology of the avb3 integrin in breast cancer'
Mark Walter, BSc (Hons) LaTrobe BEc Adel
'Structure and function of the C-subunit of AMP-activated protein kinases'

UNDERGRADUATE SCHOLAR - BACHELOR OF SCIENCE (HONOURS)

Francene Bond, BBioMedSc Melb
'Characterisation of cytokine-induced NFj B activation in pancreatic islets during diabetes progression'
Carlie DiCamillo, BSc Melb
'Development of an incidence assay for Rubella infection'
Lina Mariana, BSc Melb
'Characterisation of perforin and granzyme expression in CD8+ T-cells in NOD mice'
Lorien Parker, BSc Melb
'Structural studies of ligand binding and the nitric oxide transport function of the glutathione S-transferase enzyme'

Victor Sam, BBioMedSc Melb
'Evaluation of small molecular inhibitors to hepatitis C virus (HCV) E2 glycoprotein and CD81 interactions'

ADVANCED MEDICAL SCIENCE PROGRAM (Administered through the Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne)

Michael Chen
'The effect of adiponectin on AMPK activation in human skeletal muscle'
James Nicholson
'Expression and purification of Ark5 in insect cells'
Gareth Symons
'Effects of high and low dose fentanyl on extraction ratio following coronary artery graft surgery with cardiopulmonary bypass'

UNDERGRADUATE RESEARCH OPPORTUNITY PROGRAM (Administered through the Cooperative Research Centre for Cellular Growth Factors)

Joel Fletcher
'Expression profiling of SOCS-3 in T-cells'
Elena Tucker
'Isolation of T-cell regulatory genes using ENU mutagenesis'
Kate Warren
'Identification of ASCIZ interacting proteins'

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Eveline Angstetra
Philip Au
Matthew Bird
Justin Chan
Edward Cummings
Stephen Hu
Charles Kemp
Krystal Lambrou
Kwok Soon Wun

GRADUATIONS

THE FOLLOWING GRADUATED DOCTOR OF PHILOSOPHY - THE UNIVERSITY OF MELBOURNE:

Susanne Feil
'Crystallographic studies of pore-forming protein toxins'
Karl Häusler
'Stromal and immune factors in osteoclast formation'
Brietta Pike
'FHA domains in the regulation of cell cycle checkpoint kinases'

THE FOLLOWING GRADUATED DOCTOR OF MEDICINE - THE UNIVERSITY OF MELBOURNE:

P Scott Mackie
'The role of bisphosphonates as an adjunct treatment for osteosarcoma'

THE FOLLOWING GRADUATED BACHELOR OF SCIENCE HONOURS - THE UNIVERSITY OF MELBOURNE:

Jade Woon
'Post-translational modification of haemoglobin in type 1 diabetes mellitus'

SEMINAR PROGRAM 2003

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Austin Medical Centre/The University
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'Racial and Gender Differences in
Bone Fragility'
Mr Mark Chong
The Walter & Eliza Hall Institute
of Medical Research.
'Dissecting the physiological functions
of suppressor of cytokine signalling-1
(SOCS-1) through conditional
knockout mice.'
Dr Matthias Ernst
Ludwig Institute for Cancer Research.
'Lessons learnt from the genetic
manipulation of the gp130 signalling
cascades in knock-in mice.'
Professor Olaf Drummer
Victorian Institute of Forensic Medicine.
'The role of forensic medicine in
public health'
Mr James Godwin
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of Melbourne.
'Pig ICAM-2: its role in xenograft
rejection and its use as a gene
delivery tool.'

Dr Robyn Langham
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Hospital/The University of Melbourne.
'Novel peptides in human diabetic
nephropathy'
Dr Steven Stackler
Ludwig Institute for Cancer Research.
'Lymphangiogenic growth factors play
a key role in metastatic cancer'
Dr Harshal Nandurkar
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'Myotubular myopathy &
phosphoinositide metabolism: delineating
the biochemical link'
Dr Damian Purcell
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Immunology, The University of
Melbourne.
'Inhibition of HIV replication by dsRNA
activated cellular pathways'
Professor Martin Stone
Department of Chemistry, Indiana
University, Indiana, USA.
'Chemokine-receptor specificity: the
molecular basis of leukocyte trafficking
in inflammation'
Professor Carol Pollock
Department of Medicine, University
of Sydney.
'Why diabetic nephropathy occurs?'

Dr Kim Branson
CSIRO Division of Molecular Science.
'Development and application of
computer aided drug design methods'
Dr Patrick Humbert
Peter MacCallum Cancer Institute.
'Cell cycle control by the pRB/E2F
transcriptional pathway: new insights
from mouse models'
Associate Professor Alok Mitra
School of Biological Sciences, University
of Auckland, New Zealand.
'Membrane protein channels and
macromolecular complexes at the
membrane interface studied by electron
cryo-microscopy - what can structure
tell us about function'
Dr Greg Steinberg
St Vincent's Institute of Medical
Research.
'Skeletal muscle fatty acid metabolism
in obesity: the role of leptin'
Ms Natasha Ilievska
St Vincent's Institute of Medical
Research.
'The role of PTHrP in DNA repair'
Associate Professor
Eric Morand
Department of Medicine, Monash
University.
'MIF: A Most Interesting Factor'

Dr Steven Brown
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St. Vincent's Hospital.
'Altered T cell glycosylation leads
to impaired maturation and colitis
in FUT1 transgenic mice'
Dr Helen Maclean
Department of Medicine, ARMC,
The University of Melbourne.
'PTHrP actions during chondrocyte
development: a model for hormonal
regulation of proliferation'
Dr Brett Bennetts
St Vincent's Institute of Medical
Research.
'Permeation and gating of the Torpedo
ClC-0 chloride channel by foreign anions'
Dr Susan McLennan
Department of Medicine, University
of Sydney.
'Matrix metalloproteinases: possible
role in diabetic complications'
Dr Gordon Lynch
Department of Physiology,
The University of Melbourne.
'Developing strategies to combat
sarcopenia - age-related muscle
wasting and weakness'



Image: SVI students.

Dr Bill Heath
Immunology Division, The Walter & Eliza Hall Institute of Medical Research.
"Cross-presentation, dendritic cells and viral immunity"

Professor Henry Krum
Department of Epidemiology & Preventative Medicine and Department of Medicine, Monash University, Alfred Hospital.
"Novel targets in the treatment of heart failure"

Dr Ashley Buckle
Department of Biochemistry & Molecular Biology, Monash University.
"FKBP12: from protein folding to cardiology"

Professor George King
Director of Research & Section Head, Joslin Diabetes Center, Boston, USA.
"The anti-atherogenic actions of insulin"

Dr Pierre Savager
INSERM Bat Recherche Cancerologie, Montpellier, France.

"Cutaneous wound healing, a model for coherent migration and metastable phenotype"

Dr Stella Clark
Bio21 Australia Ltd.
"Bio21 Australia Ltd: What actually is it and what can it do for me?"

Professor Dietmar Richter
Institute for Cell Biochemistry and Clinical Neurobiology, University of Hamburg, Germany.
"Structure and function of synaptic scaffold proteins in the brain"

Dr Sharon Ricardo
Department of Anatomy and Cell Biology, Monash University.
"Macrophages as potential stem cells in renal regeneration and repair"

Dr Alex Dobrovic
Molecular Pathology, Peter MacCallum Cancer Institute.
"Therapeutic implications of profiling DNA methylation in cancer"

Associate Professor Malcolm McConville
Department of Biochemistry and Molecular Biology, The University of Melbourne.

"Identification of new virulence factors in protozoan parasites"

Associate Professor Henrik Dahl
Murdoch Children's Research Institute.
"Genetic aspects of hearing loss"

Mr Joseph Pereira
St Vincent's Institute of Medical Research.
"Investigation of the biology of avb3 integrin in breast cancer - new perspectives"

Dr Boris Sarcevic
Garvan Institute of Medical Research, Sydney.
"Regulation of cell cycle progression by protein phosphorylation and ubiquitylation"

Dr Rajesh Thakker
Oxford University Institute of Musculoskeletal Sciences, The Botnar Research Centre, Oxford UK.
"Hereditary endocrine tumours"

Ms Danijela Miroslavljevic
St Vincent's Institute of Medical Research.
"T cells, cytokines and the regulation of osteoclast formation: novel insights"

Dr Nick Hoogenraad
Department of Biochemistry, La Trobe University.
"Molecular Chaperones, proteins with multiple functions"

Dr Izhak Haviv
Ian Potter Centre for Cancer Genomics & Predictive Medicine, Peter MacCallum Cancer Institute.
"Microarray analysis of intercellular communication: computational tools aimed at samples comparison and extendibility of discriminatory genes"

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Image: Three dimensional structure based drug design.

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Image left: Three dimensional structure of growth hormone receptor.

Image right: Isolated human pancreatic beta cells.

PRIZES, AWARDS AND GRANTS

IMMUNOLOGY AND DIABETES UNIT

FELLOWSHIPS AND PRIZES

Rima Darwiche received a Juvenile Diabetes Research Foundation Travel Award to undertake experimental research at La Jolla Institute for Allergy and Immunology with Dr Matthias von Herrath.

Dr Mark Chong received travel bursaries from AMRAD Corporation Pty Ltd and the Juvenile Diabetes Research Foundation to attend the Joslin Symposium on "Evading beta cell death in diabetes" in Boston, USA, and a travel grant from the Federation of Clinical Immunology Societies to attend the 2003 International Diabetes Congress in Paris, France.

Dr Mark Chong was awarded a Postdoctoral Fellowship from the Cancer Research Institute, USA. This will support his research training in the Laboratory of Dr Dan Littman, Howard Hughes Medical Institute, Skirball Institute of Biomolecular

Medicine, New York University School of Medicine, New York, USA.

GRANTS

LC Harrison, A Lew, T Kay, and G Morahan. Prevention and cure of type 1 diabetes. NHMRC Program Grant. (5-year support)

T Kay. Role of perforin in beta cell destruction. Diabetes Australia Millennium Research Grant. (2-year support)

T Kay. Ian Potter Foundation Establishment Grant for the fit-out of the Diabetes Research laboratories.

T Kay. The Jack Brockhoff Foundation Grant for the purchase of equipment for human islet cell transplantation and research.

T Kay. The H & L Hecht Trust Grant for the purchase of equipment for human islet cell transplantation and research.

SIGNAL TRANSDUCTION LABORATORY

FELLOWSHIPS AND PRIZES

Dr Robyn Starr was awarded the Burnet Prize from The Walter and Eliza Hall Institute of Medical Research in recognition of her work on the discovery of SOCS proteins.

Dr Robyn Starr was awarded a prestigious 5-year Queen Elizabeth II Fellowship from the Australian Research Council to continue her research on SOCS proteins.

GRANTS

NA Nicola, D Metcalf, DJ Hilton, WS Alexander, L Robb, M Baca, R Starr, AW Roberts and R Norton. Molecular control of haemopoietic cells. NHMRC Program Grant (5-year grant support)

BONE, JOINT AND CANCER GROUP

FELLOWSHIPS AND PRIZES

A Freischrift for Jack Martin. With the retirement of Professor Martin as Director of the Institute in 2002, a meeting of the Australian and New

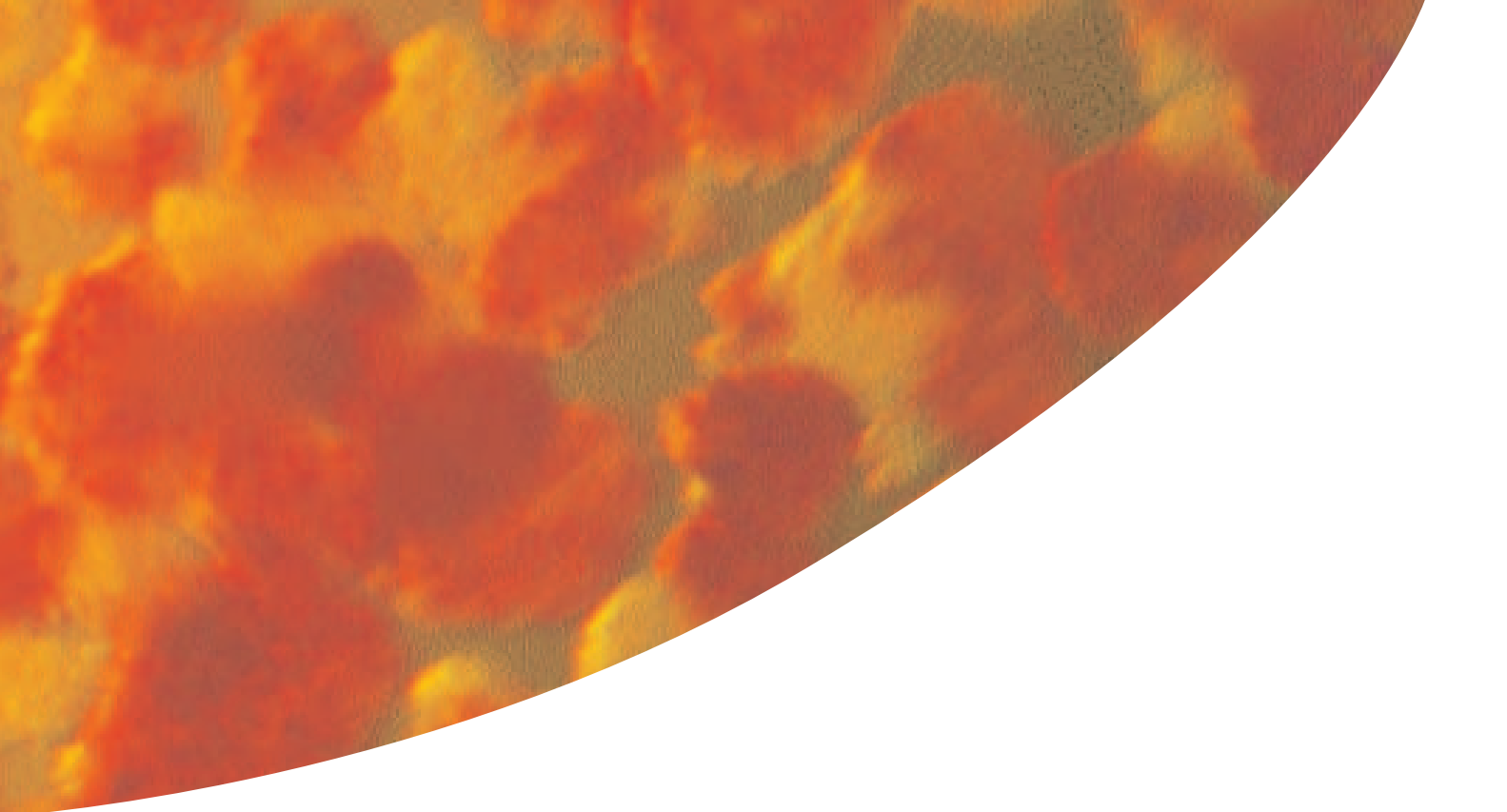
Zealand Bone and Mineral Society, in association with the International Bone and Mineral Society (IBMS), was held at Coolum, Queensland, in June 2003.

This meeting was a celebration of Jack Martin's career, with many international associates of Jack attending the meeting.

Dr Natalie Sims received the International Bone and Mineral Society's best basic research publication award for articles published in the Society's journal - Bone.

Dr Vicky Kartsogiannis received the inaugural Christine and TJ Martin Travel Award from the Australian and New Zealand Bone and Mineral Society, to attend and present at the Davos Bone Meeting 2004 and for sabbatical studies in Oxford and Sheffield in 2004.

Dr Steve Bouralexis was awarded a Peter Doherty Research Fellowship from the NHMRC for post-doctoral studies within the Bone Cell group.



Dr Natalie Sims won the Senior Investigator Award and Best Poster Award during St. Vincent's Hospital Research Week.

GRANTS

TJ Martin, MT Gillespie and MW Parker. Small molecule inhibitors of parathyroid hormone-related protein action: treatment for hypercalcemia and bone metastases. NHMRC Development Grant. (1-year support)

MT Gillespie and MW Parker. Equipment grant to purchase a fluorescent microscope. Clive and Vera Rammaciotti Foundation.

BONE METASTASIS AND MIGRATION LABORATORY

GRANTS

J Price. Mechanism of breast cancer spread to bone. National Institutes of Health (USA) grant. These grants are highly competitive and are difficult to obtain outside of the USA.

PHARMACOGENOMICS

Fellowships and Prizes

Angela Arvanitis received a St. Vincent's Hospital Stipend Award.

FUNCTIONAL PROTEOMICS FELLOWSHIPS AND PRIZES

Both Mark Walter and Abhilasha Gupta were awarded NHMRC Dora Lush (Biomedical) Research Scholarships.

GRANTS

D Stapleton. Career Advancement Award. J. & M.C. Foundation, Indiana, USA.

D Stapleton. Special Research Award, St. Vincent's Health (Melbourne).

MOLECULAR GENETICS

FELLOWSHIPS AND PRIZES

Dr Andrew Hammet, received a prestigious NHMRC CJ Martin Fellowship to undertake post-doctoral training in the laboratory of Professor Steve Jackson at the The Wellcome Trust/ Cancer Research UK Gurdon Institute.

Carolyn McNees, was awarded the Best Student Poster Award during St. Vincent's Hospital's Research Week.

BIOTA STRUCTURAL BIOLOGY LABORATORY

FELLOWSHIPS AND PRIZES

Geoffrey Kong was awarded a Maslen 1987 Scholarship from the Society of Crystallographers of Australia and New Zealand.

GRANTS

MW Parker. Structural studies of amyloid precursor protein. NHMRC Project Grant. (3-year support)

MW Parker. Structural studies of glutathione transferases: a model system for functional genomics and drug design. ARC Discovery Grant. (3-year support)

TJ Martin, MT Gillespie and MW Parker. Small molecule inhibitors of parathyroid hormone-related protein action: treatment for hypercalcemia and bone metastases. NHMRC Development Grant. (1-year support)

VIROLOGY

FELLOWSHIPS AND PRIZES

Chan Lay was awarded a Student Poster Award during St. Vincent's Hospital's Research Week.

GRANTS

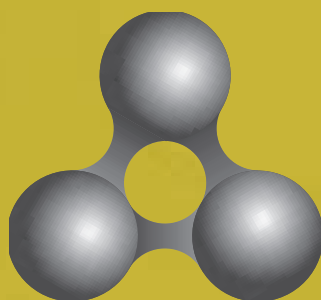
H Drummer and A Poubourios. Structure and function of hepatitis C virus glycoproteins. NHMRC Project Grant (3-year support)

H Drummer, R French and A Poubourios. Development and validation of neutralising antibody assays to hepatitis C virus. Australian Centre for HIV and Hepatitis Research (1-year support)

NATIONAL SEROLOGY REFERENCE LABORATORY'

GRANTS

E Johnson, K Wilson and D McPhee. Comprehensive investigation of humoral and cellular immune responses to structured treatment interruption in HIV infection Australian Centre for HIV and Hepatitis Research (1-year support)

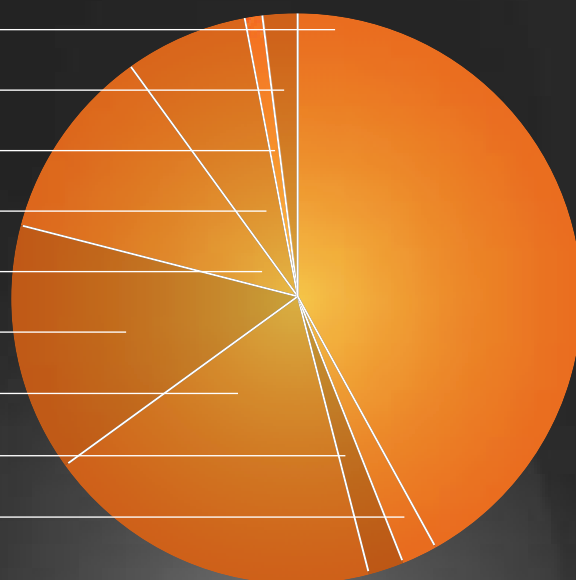


FINANCIAL REPORT

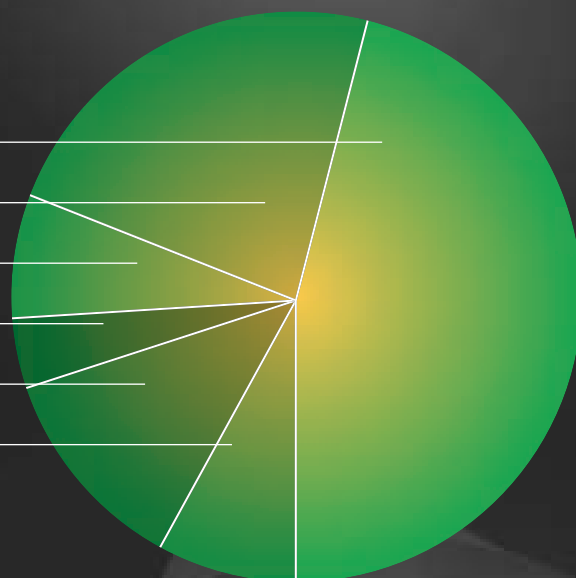
St Vincent's Institute **2003 Annual Report**

FINANCIAL SNAPSHOT

INCOME	\$ 000's	%
Competitive Research Grants	6,717	42
Other	326	2
Interest and Dividends	185	1
Victorian Govt Infrastructure	1,194	7
Legacies and Donations	1,720	11
Leasehold Write-back	2,306	14
Commonwealth Govt & State Govt Building Grants	3,037	19
Industry	287	2
Commonwealth Govt Service Contract	269	2
TOTAL	16,041	100



EXPENDITURE	\$ 000's	%
Research Salaries	4,096	46
Direct Research Expenses	2,045	23
Transfers to Collaborators	617	7
Direct Infrastructure	385	4
Infrastructure (Admin & Tech Support)	1,065	12
Depreciation	760	8
TOTAL	8,968	100



DIRECTORS' FINANCIAL REPORT

Your Directors present their report on the company for the financial year ended 31 December 2003.

1. Board of management

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

Prof James D Best	Ms Nicole M Feely
Mr Charles A Griss	Mr Barry J Jackson
Mr Ian D Reid	Ms Brenda M Shanahan
Mr Douglas A Wright	

Ms Sue M Alberti (from 14 April 2003)	Prof Thomas WH Kay (from 14 April 2003)	Ms Marcia Griffin (retired 14 April 2003)
Prof James A Angus (from 18 August 2003)	Ms Ruth A O'Shannassy (from 14 April 2003)	Prof Richard G Larkins (retired 31 March 2003)
Mr Jeff Clifton (from 14 April 2003)	Dr Laurence Clemens (retired 14 April 2003)	Mr Graham EN Rogers (retired 14 April 2003)
Sr Mary Fankhauser (from 14 April 2003)		

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

2. 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.

3. Operating results

The operating surplus of the company was \$7,073,259.

4. Dividends

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

5. Review of operations

During the financial year the company's \$9.88 million building extension and refurbishment program was completed within budget and by the scheduled completion date of 26 September 2003. The company also made significant equipment purchases during the year, totalling \$1,288,442. The net surplus of \$7,073,259 was in part the result of a change in accounting policy (refer note 1) which transferred to income \$2,305,973 of leasehold improvements previously treated as expenditure in 2002. The most significant impact on income was the capital fund raising efforts in 2003 and these funds were allocated to the company's building project and equipment fit-out. In 2004 the company will continue its endeavours to raise the funds necessary to meet the total cost of the building project.

The research expenditure increased by 32% on last year, reflecting a general increase in activity and the addition of new research groups. The additional building accommodation has been instrumental in enabling the research programs to advance.

Administration and laboratory support for the research has increased by 16% and reflects the increased costs of supporting the research. In 2003 the number of staff and students increased from 89 to 102. In addition the company, which acts as the host institute for the National Serology Reference Laboratory (NSRL), provides administration and research support to the 29 NSRL staff.

6. Significant changes in state of affairs

The following significant changes in the state of affairs of the company occurred during the financial year:

A revised constitution was approved by the Members at the special meeting, dated 14 April 2003, at which the members were reduced from 38 to 3. This change did not impact on the Institute's status as a company limited by guarantee or its financial performance.

7. 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.

8. Future developments

The likely developments in the operations of the company and the expected results of the operations in future financial years are as follows: During 2003 the company made progress towards establishing a Foundation, whose main objective will be to attract financial support to provide research funds for the activities of the company. The Foundation will be established as a separate legal entity in 2004.

9. 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 2003 to the date of this report, this company has complied with the requirements of the Environmental Protection Act.

DIRECTORS' FINANCIAL REPORT

10. Meetings of directors

During the financial year, 29 meetings of directors (including committees) were held. Attendees were:

	Directors' Meetings		Committee Meetings					
	Number eligible to attend	Number Attended	Appeal		Finance		Building	
	Number eligible to attend	Number Attended	Number eligible to attend	Number Attended	Number eligible to attend	Number Attended	Number eligible to attend	Number Attended
SM Alberti	5	3	7	6	—	—	—	—
JA Angus	2	2	—	—	—	—	—	—
JD Best	6	6	—	—	—	—	—	—
L Clemens	1	0	—	—	—	—	—	—
J Clifton	5	3	—	—	—	—	—	—
Sr M Fankhauser	5	4	—	—	—	—	—	—
NM Feely	6	2	—	—	—	—	—	—
M Griffin	1	0	—	—	—	—	—	—
CA Griss	6	6	—	—	6	6	8	8
BJ Jackson	6	5	—	—	—	—	—	—
TWH Kay	5	5	7	6	3	3	5	5
RG Larkins	1	0	—	—	—	—	—	—
RA O'Shannassy	5	3	—	—	2	1	—	—
ID Reid	6	5	—	—	6	6	8	7
GEN Rogers	1	0	—	—	2	1	—	—
BM Shanahan	6	4	9	8	4	3	8	3
DA Wright	6	5	9	7	—	—	—	—

11. 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: S M Alberti, JA Angus, JD Best, L Clemens, J Clifton, Sr M Fankhauser, NM Feely, M Griffin, CA Griss, BJ Jackson, TWH Kay, RG Larkins, R A O'Shannassy, ID Reid, GEN Rogers, BM Shanahan, DA Wright.

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

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



Director

BM Shanahan

Director

CA Griss

Dated this 19th day of April 2004, Melbourne, Australia

STATEMENT OF FINANCIAL PERFORMANCE FOR THE YEAR ENDED 31 DECEMBER 2003

	Note	2003 (\$)	2002 (\$)
Revenues from ordinary activities	2	16,041,336	10,188,119
Consumables used		(1,590,967)	(1,201,208)
Employee benefits expense		(5,160,775)	(3,983,487)
Depreciation and amortisation expenses	3	(759,859)	(877,304)
Other expenses from ordinary activities		(1,456,476)	(3,305,273)
Net surplus from ordinary activities	14	7,073,259	820,847
Total changes in equity		<u>7,073,259</u>	<u>820,847</u>

The accompanying notes form part of these financial statements.

STATEMENT OF FINANCIAL POSITION FOR THE YEAR ENDED 31 DECEMBER 2003

	Note	2003 (\$)	2002 (\$)
CURRENT ASSETS			
Cash assets	8	1,176,245	5,683,110
Receivables	7	1,094,858	694,541
TOTAL CURRENT ASSETS		<u>2,271,103</u>	<u>6,037,651</u>
NON-CURRENT ASSETS			
Receivables	7	250,000	250,000
Other financial assets	9	415,088	366,708
Property, plant & equipment	10	12,397,507	1,981,861
TOTAL NON-CURRENT ASSETS		<u>13,062,595</u>	<u>2,598,569</u>
TOTAL ASSETS		<u>15,333,698</u>	<u>8,976,220</u>
CURRENT LIABILITIES			
Payables	11	376,217	804,121
Funds held in trust for NSRL accrued leave		138,280	138,280
Provisions	12	717,467	511,688
Other	13	1,401,223	1,824,690
TOTAL CURRENT LIABILITIES		<u>2,633,187</u>	<u>3,278,779</u>
NON-CURRENT LIABILITIES			
Provisions	12	96,903	167,092
TOTAL NON-CURRENT LIABILITIES		<u>96,903</u>	<u>167,092</u>
TOTAL LIABILITIES		<u>2,730,090</u>	<u>3,445,871</u>
NET ASSETS		<u>12,603,608</u>	<u>5,530,349</u>
EQUITY			
Retained surplus	14	12,603,608	5,530,349
TOTAL EQUITY	16	<u>12,603,608</u>	<u>5,530,349</u>

The accompanying notes form part of these financial statements.

STATEMENT OF CASH FLOWS FOR THE YEAR ENDED 31 DECEMBER 2003

	Note	2003 (\$) Inflows (Outflows)	2002 (\$) Inflows (Outflows)
CASH FLOW FROM OPERATING ACTIVITIES			
Grants received		10,737,210	9,006,598
Payments to suppliers and employees		(8,544,797)	(6,107,564)
Donations, legacies and bequests		1,809,975	1,108,448
Other revenue		224,405	1,195,768
Interest received		170,848	153,133
Dividends		21,203	8,390
Leasehold improvements	1(l)	-	(2,305,973)
Net cash used in operating activities	20 (b)	6,724,816	3,058,800
CASH FLOW FROM INVESTING ACTIVITIES			
Purchase of plant and equipment		(1,288,441)	(219,680)
Leasehold improvements	1(l)	(9,887,062)	-
Payments for investments		(56,178)	(1,611)
Net cash used in investing activities		(11,231,681)	(221,291)
Net Increase/(decrease) in cash held		(4,506,865)	2,837,509
Cash at the beginning of the year		5,683,110	2,845,601
Cash at the end of the year	20 (a)	1,176,245	5,683,110

The accompanying notes form part of these financial statements.

NOTES TO THE FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2003

NOTE 1: STATEMENT OF SIGNIFICANT ACCOUNTING POLICIES

The financial report is a general purpose financial report that has been prepared in accordance with Accounting Standards, Urgent Issues Group Consensus Views, other authoritative pronouncements of the Australian Accounting Standards Board and the *Corporations Act 2001*.

The financial report covers St Vincent's Institute of Medical Research, a company limited by guarantee, incorporated and domiciled in Australia. The financial report has been prepared on an accrual basis and is based on historical costs and does not take into account the changing money values or, except where stated, current valuations of non-current assets. Cost is based on the fair values of the consideration given in exchange for assets. The following is a summary of the material accounting policies adopted by the company in the preparation of the financial report. The accounting policies have been consistently applied, unless otherwise stated.

(a) Income Tax

The company is granted exemption from income tax under Subdivision 50-B of the Income Tax Assessment Act 1997 because of the charitable nature of the business within which it operates.

(b) Property, Plant and Equipment

Plant and equipment are carried at cost, less, where applicable, any accumulated depreciation or amortisation. The company does not own property. The Directors annually review the plant and equipment, to ensure the carrying amount is not in excess of the recoverable value of these assets. The recoverable amount is assessed on the basis of the expected net cash flows, which will be received from the assets' employment and subsequent disposal. The expected net cash flows have not been discounted to their present values in determining recoverable amounts.

NOTES TO THE FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2003

(c) Leasehold Improvements

In 2002 and 2003 the company extended and refurbished the existing building, which is leased by the company from the Sisters of Charity Healthcare Australia Limited. The building lease arrangement provides the company with both a future economic benefit and control over that future economic benefit. The cost of the leasehold improvement has been capitalised and appears in the Statement of Financial Position.

(d) Depreciation

Depreciable assets with a cost in excess of \$2,000 are capitalised and depreciation has been provided over their estimated useful lives using the diminishing value method for pre 1 January 1998 and straight-line method for assets purchased after this date. The depreciation rates used for Plant and Equipment range from 10% to 33%. Leasehold Improvement depreciation rate is based on the 15 year term of the lease.

(e) Foreign Currency Transactions and Balances

Foreign currency transactions during the year are converted to Australian currency at the rates of exchange applicable at the dates of the transactions. Amounts receivable and payable in foreign currencies at balance date are converted at the rates of exchange ruling at that date. The gains and losses from conversion of short-term assets and liabilities, whether realised or unrealised, are included in the surplus from ordinary activities as they arise.

(f) Employee Benefits

Provision is made for the company's liability for employee benefits arising from services rendered by employees to balance date. Employee benefits expected to be settled within one year together with benefits arising from wages and salaries and annual leave, which will be settled after one year, have been measured at their nominal amount. Other employee benefits payable later than one year have been measured at the present value of the estimated future cash outflows to be made for those benefits. Contributions are made by the company to employee superannuation funds and are charged as expenses when incurred. The company's long service leave liability of \$273,037 represents a gross liability of \$510,385 offset by net present value contractual obligations of \$237,348 from National Health and Medical Research Council (NHMRC), applicable up to 31 December 2001. This payment will be receivable upon payment of long service leave by the company on behalf of eligible employees. NHMRC reimburse long service leave payments on a pro-rata basis for the period of their grant support.

(g) Cash

For the purpose of the statement of cash flows, cash includes cash on hand and at call deposits with banks or financial institutions, investments in money market instruments maturing within less than two months and net of bank overdrafts.

(h) Revenue

Grant income is recognised upon performing the research associated with the specific grant. Donation income is recognised upon receipt or when spent, if funds were received for a specific purpose. Interest income is recognised as it accrues. Dividend revenue is recognised when the dividend is received. All revenue is stated net of the amount of Goods and Services Tax (GST).

(i) Equipment Purchases

The company's revenue generated from ordinary activities includes funds raised for the purchase of assets. In the financial year ending 31 December 2003, asset purchases totalled \$1,288,442

(j) National Serology Reference Laboratory

The company is the host company for the National Serology Reference Laboratory (NRL). In this role the company provides administration services to the 29 employees. The NRL financial reporting is separate from the company and reported on a 30 June financial year basis to the Commonwealth Government.

(k) Goods and Services Tax (GST)

Revenues, expenses and assets are recognised net of the amount of GST, except where the amount of GST incurred is not recoverable from the Australian Tax Office. In these circumstances the GST is recognised as part of the cost of acquisition of the asset or part of an item of the expense. Receivables and payables in the statement of financial position are shown inclusive of GST.

(l) Change in Accounting Policy

The company changed its accounting policy in regard to leasehold improvements, whereby the building improvements are now being capitalised as a non-current asset rather than being treated as an expense. This is on the basis that, although the company does not own the building they do have control over the future economic benefit of the building. The directors believe that the change in accounting policy will improve the relevance and reliability of the company's financial report. The financial effect of this change in accounting policy has been to recognize \$2,305,973 as revenue in the profit from ordinary activities for the year.

NOTES TO THE FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2003

NOTE 2: REVENUE

	Note	2003 (\$)	2002 (\$)
Operating activities			
- grants	4-6	10,225,070	7,462,536
- infrastructure support (Victorian State Government)		1,194,298	882,225
- contract services		269,207	320,618
- legacies and bequests		718,503	846,967
- donations		1,001,228	357,725
- dividends	(a)	21,203	8,390
- interest	(b)	163,400	167,374
- royalty		53,691	-
- conference		-	19,716
- write back of leasehold improvements expenditure		2,305,973	-
- other		88,763	122,568
Total revenue		16,041,336	10,188,119
<i>(a) Dividends from:</i>			
- other corporations		21,203	8,390
<i>(b) Interest from:</i>			
- other corporations		163,400	167,373

NOTE 3: SURPLUS FROM ORDINARY ACTIVITIES

	2003 (\$)	2002 (\$)
Surplus from research activity has been determined after:		
<i>(a) Expenses</i>		
Direct cost of research activities:		
Direct research expenses		
- consumables	1,446,927	1,169,719
- salaries and on costs	4,095,693	3,096,550
- other	598,290	395,453
	<u>6,140,910</u>	<u>4,661,722</u>
Transfer of funds to external joint collaborators	617,330	272,231
Infrastructure cost of research activities:		
- administration	347,483	295,836
- salaries and on costs (includes laboratory technical support)	1,065,082	908,883
- other	37,412	45,323
	<u>1,449,977</u>	<u>1,250,042</u>
Depreciation of non-current assets		
- Plant and Equipment	593,500	877,304
Amortisation of non-current assets		
- leasehold improvements	166,359	-

(b) Significant Revenue and Expenses:

The following revenue and expense items are relevant in explaining the financial performance.

- Leasehold improvements	(2,305,973)
- write back of leasehold improvements expenditure	2,305,973
- Revenue raised for asset purchases	105,379 212,402
- Revenue raised for building refurbishment and extension	<u>4,599,830 2,353,181</u>

NOTE 4: GRANTS — COMMONWEALTH GOVERNMENT

	2003 (\$)	2002 (\$)
National Health and Medical Research Council	4,350,720	3,040,857
Australian Research Council	201,206	194,920
Department of Health and Aging	1,965,000	1,535,000
	<u>6,516,926</u>	<u>4,770,777</u>

NOTE 5: GRANTS — VICTORIAN STATE GOVERNMENT

	2003 (\$)	2002 (\$)
Department of Innovation, Industry & Regional Development	1,000,001	818,181
Department of Human Services	72,000	-
	<u>1,072,001</u>	<u>818,181</u>

NOTES TO THE FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2003

NOTE 6: GRANTS — OTHER

	2003 (\$)	2002 (\$)
Assoc. International Cancer Research	-	22,417
Biota Holdings Ltd.	79,618	60,985
Chugai Pharmaceuticals Co.	172,898	288,285
Gastroenterological Society of Australia	-	27,258
Juvenile Diabetes Research Fdn.	341,726	147,118
Kidney Foundation — Australia	5,366	-
Max Planck Research Award	54,716	100,352
National Breast Cancer Foundation	53,217	-
National Heart Foundation of Australia	121,655	86,880
National Heart, Lung & Blood Institute	203,626	-
National Institutes of Health	263,220	88,914
Servier Laboratories International	-	11,260
St. Vincent's Hospital, Melbourne	15,218	13,399
Susan G. Komen Cancer Fdn.	244,201	164,305
The Cancer Council of Victoria	61,015	152,115
University of Melbourne	244,594	10,760
US Army Medical Research Command	48,663	-
Victorian Breast Cancer Research Consortium	400,000	458,587
Wellcome Trust	-	17,198
Victoria Department of Education	9,607	25,000
Transfer from other Institutes	153,049	57,784
Other	163,754	704
	<u>2,636,143</u>	<u>1,873,578</u>

NOTE 7: RECEIVABLES

	2003 (\$)	2002 (\$)
CURRENT		
Grants and reimbursements	1,094,858	694,541
NON-CURRENT		
St. Vincent's Hospital - Imprest Advance	250,000	250,000
	<u>1,344,858</u>	<u>944,541</u>

NOTE 8: CASH ASSETS

	2003 (\$)	2002 (\$)
Cash at bank and on hand	1,008,188	3,671,789
Debentures — At cost		
- ANZ Bank Term Deposit	-	923,532
Deposits at call		
- Perpetual Trustees	-	926,807
- Macquarie Treasury Fund	168,057	160,982
	<u>1,176,245</u>	<u>5,683,110</u>

NOTE 9: OTHER FINANCIAL ASSETS

	2003 (\$)	2002 (\$)
Non-current		
Shares in listed Corporations — At cost	415,088	366,708
Market value of listed Corporations	500,511	386,568

NOTE 10: PROPERTY, PLANT & EQUIPMENT

	2003 (\$)	2002 (\$)
Plant and equipment at cost	5,562,999	4,692,745
Less accumulated depreciation	2,886,196	2,710,884
Written down value	2,676,803	1,981,861
Total plant and equipment	<u>2,676,803</u>	<u>1,981,861</u>
Leasehold improvements at cost	9,887,063	-
Less accumulated amortisation	166,359	-
Written down value	9,720,704	-
Total leasehold improvements	<u>9,720,704</u>	<u>-</u>
Total Property, Plant and Equipment	<u>12,397,507</u>	<u>1,981,861</u>

Movements in Carrying Amounts:

Movement in the carrying amounts for each class of property, plant and equipment between the beginning and end of the current financial year.

Balance at the beginning of the year for plant and equipment	1,981,861	2,646,763
Additions	1,288,442	212,402
Disposals/write off	-	(264,374)
Depreciation expense	(593,500)	(612,930)
Carrying amount at the year end	<u>2,676,803</u>	<u>1,981,861</u>
Balance at the beginning of the year for leasehold improvements	0	-
Additions	9,887,063	-
Depreciation expense	(166,359)	-
Carrying amount at the year end	<u>9,720,704</u>	<u>-</u>

NOTE 11: PAYABLES

	2003 (\$)	2002 (\$)
CURRENT		
Trade creditors	343,848	682,314
Sundry creditors	32,369	121,807
	<u>376,217</u>	<u>804,121</u>

NOTES TO THE FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2003

NOTE 12: PROVISIONS

	Note	2003 (\$)	2002 (\$)
CURRENT			
Employee entitlements	(a)	717,467	511,688
		<u>717,467</u>	<u>511,688</u>
NON-CURRENT			
Employee entitlements	(a)	96,903	167,092
		<u>96,903</u>	<u>167,092</u>
(a) Aggregate employee entitlement liability		<u>814,370</u>	<u>678,780</u>

NOTE 13: OTHER

	2003 (\$)	2002 (\$)
Grants in advance	<u>1,401,223</u>	<u>1,824,690</u>

NOTE 14: RETAINED SURPLUS

	2003 (\$)	2002 (\$)
Retained surplus at the beginning of the financial year	5,530,349	4,709,502
Net surplus/(deficit) attributed to the company	<u>7,073,259</u>	<u>820,847</u>
Retained surplus at the end of the financial year	<u>12,603,608</u>	<u>5,530,349</u>

NOTE 15: CAPITAL COMMITMENTS

	2003 (\$)	2002 (\$)
Capital expenditure commitments contracted for:		
- capital expenditure projects	-	8,180,776
		<u>8,180,776</u>
Payable:		
- not later than 1 year	-	8,180,776
		<u>8,180,776</u>

The commitment will be financed from internal funds, grants, fund raising and credit standby facility.

NOTE 16: MEMBERS' GUARANTEE FUNDS

The company is limited by guarantee. If the Company is wound up, each Member of the Company undertakes to contribute to the assets of the Company an amount not exceeding \$100 for payment of debts and liabilities of the Company, including the costs of winding up. This undertaking continues for 1 year after a Member ceases to be a Member of the Company. The number of Members at 31 December 2003 is 3 (2002 : 38).

NOTE 17: SEGMENT REPORTING

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

NOTE 18: RELATED PARTY TRANSACTIONS

Transactions between related parties are on normal commercial terms and conditions no more favourable than those available to other parties unless otherwise stated.

Transactions with related parties:

Ms B Shanahan, a Director, is a Director of a company which provided investment advice during the year at no cost.

NOTE 19: FUNDS HELD IN PERPETUITY

The accumulated funds at the end of the financial year of \$12,603,608 include funds held in perpetuity of \$400,418. The income from these funds is directed to the company's medical research program.

NOTE 20: CASH FLOW INFORMATION

	2003 (\$)	2002 (\$)
(a) <i>Reconciliation of cash:</i>		
Cash at the end of the financial year as shown in the statement of cashflows is reconciled to items in the statement of financial position as follows:		
Cash on hand and cash advances	1,008,188	3,671,789
Deposits at call	<u>168,057</u>	<u>2,011,321</u>
	<u>1,176,245</u>	<u>5,683,110</u>

(b) <i>Reconciliation of cash flows from operations with surplus from ordinary activities:</i>		
Surplus from ordinary activities	7,073,259	820,847
Non-cash flows in surplus from ordinary activities:		
Depreciation - plant and equipment	593,500	877,304
Amortisation of leasehold improvements	166,359	-
Changes in assets and liabilities:		
(Increase)/Decrease in debtors & accrued revenue	(400,317)	(69,909)
Increase/(Decrease) in creditors	(427,904)	637,022
Increase/(Decrease) in other liabilities	(423,467)	1,226,708
Increase/(Decrease) in provision for employee entitlements	135,590	(135,664)
(Increase)/Decrease in non-cash/share transactions	7,796	(297,508)
Cash flows from operations	<u>6,724,816</u>	<u>3,058,800</u>

NOTES TO THE FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2003

(c) Credit Standby arrangement and loan facility:

On the 6th December 2002 the company established a \$3.5m overdraft facility with the Catholic Development Fund as a standby arrangement for funding the building extension. The facility is renegotiable on 30 June 2005 and the overdraft interest rate is variable. At 31 December 2003 \$Nil of this facility was used (2002:\$Nil)

NOTE 21: AUDITOR'S REMUNERATION

	2003 (\$)	2002 (\$)
Remuneration of the auditor of the company for:		
- audit or reviewing the financial report	15,250	10,728
- other services	-	-
	<u>15,250</u>	<u>10,728</u>

NOTE 22: REMUNERATION AND RETIREMENT BENEFITS

	2003 (\$)	2002 (\$)
<i>(a) Directors' Remuneration</i>		
Income paid or payable to all the directors of the company, directly or indirectly, by the company or any related party.	270,164	-
Number of directors whose income from the company and any related parties was within the following bands:	No.	No.
- Executive Directors \$270,000 - \$280,000	1	-
- Non- Executive Directors	-	-
	2003 (\$)	2002 (\$)

(b) Retirement and Superannuation Payments

	2003 (\$)	2002 (\$)
Amounts of a prescribed benefit given during the year by the company or a related party to a director or prescribed superannuation fund in connection with the retirement from a prescribed office.	42,612	-

The names of the company's directors, who held office during the financial year are:

BM Shanahan	S Alberti (from 14 April 2003)
JD Best	JA Angus (from 18 August 2003)
NM Feely	J Clifton (from 14 April 2003)
CA Griss	Sr M Fankhauser (from 14 April 2003)
BJ Jackson	TWH Kay (from 14 April 2003)
ID Reid	R A O'Shannassy (from 14 April 2003)
DA Wright	L Clemens (retired 14 April 2003)
	M Griffin (retired 14 April 2003)
	RG Larkins (retired 31 March 2003)
	GEN Rogers (retired 14 April 2003)

NOTE 23: FINANCIAL INSTRUMENTS

(a) Interest Rate Risk

The company's exposure to interest rate risk, which is the risk that a financial instrument's value will fluctuate as a result of changes in market interest rates and the effective weighted average interest rates those financial assets and financial liabilities, is as follows:

	Weighted Average Effective Interest Rate		2003(\$)	2002(\$)
	2003(%)	2002(%)		
Financial Assets				
Cash at bank and on hand	0.3	0.3	1,008,188	3,671,789
Debentures	-	4.7	-	923,532
Deposits at call	6.5	5.6	168,057	1,087,789
Total Financial Assets			<u>1,176,245</u>	<u>5,683,110</u>
Financial Liabilities				
Funds held in trust	-	-	138,280	138,280
Total Financial Liabilities			<u>138,280</u>	<u>138,280</u>

(b) Credit Risk

The maximum exposure to credit risk, excluding the value of any collateral or other security, at balance date to recognised financial assets is the carrying amount of these assets, net of any provisions for doubtful debts, as disclosed in the statement of financial position and notes to the financial statements. The company does not have any material credit risk exposure to any single debtor or group of debtors under financial instruments entered into by the company.

(c) Net Fair Values

The net fair value of assets and liabilities approximates their carrying value. No financial assets are readily traded on organised markets in standardised form other than listed investments. The aggregate net fair values and carrying amounts of financial assets and financial liabilities are disclosed in the statement of financial position and in the notes to the financial statements.

NOTES TO THE FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2003

NOTE 24: SUPERANNUATION COMMITMENTS

The company contributes to employee superannuation funds managed by external fund managers. Members of the funds are entitled to benefits on retirement, disability or death. Employees contribute to the funds at 7% of their gross salaries and the company contributes 14% of employees' gross salaries. Contributions to the Tertiary Education Superannuation Scheme (TESS) are to meet the company's Superannuation Guarantee and Award obligations to all its employees and currently amount to 9% of employees' gross salaries for employees, who are not members of the employee contribution schemes and 3% for employees, who are members of the employee contribution schemes.

The company is under no legal obligation to make up any shortfall in the fund's assets of the superannuation schemes to meet payments due to employees. 95% of the company's superannuation contributions are made to Unisuper Ltd, which manages the Superannuation Scheme for Australian Universities and TESS. The last actuarial investigation was completed by Mr. Grant Harslett FIA, FIAA and Mr Matthew Burgess FIAA of Towers Perrin on 16 May 2003 and conducted as at 31 December 2002. The figures for the Superannuation Scheme for Australian Universities' Defined Benefits Plan are as at 30 June 2003 (being the latest available information).

	2003 (\$)
Fund assets at net market value	1,962,462
Accrued benefits	1,860,910
Surplus of fund assets over accrued benefits	101,552
Vested benefits	2,227,090
Employer contributions to the various funds by the company for the 12 month period ending 31 December 2003	563,901

The accrued benefits for each member of the Superannuation Scheme for Australian Universities (SSAU) have been calculated as the greater of:

- (a) the present value of future payments of benefits to the member which arise from membership of SSAU up to the reporting date, determined using the actuary's current expectations of earnings on SSAU's assets, future inflation and salary levels and other relevant assumptions, and
- (b) the vested benefits.

Vested benefits are benefits, which are not conditional upon the continued membership of the fund or any factor, other than resignation from the fund.

NOTE 25: COMPANY DETAILS

The registered office and principal place of business of the company is:



St Vincent's Institute of Medical Research
 9 Princes Street
 Fitzroy, Vic 3065

DIRECTORS' DECLARATION

The directors of the company declare that:

1. The financial statements and notes, as set out on pages 49 to 58 are in accordance with the *Corporations Act 2001*:
 - 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 2003 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
CA Griss

Dated this 19th day of April 2004, Melbourne, Australia

INDEPENDENT AUDIT REPORT TO THE MEMBERS OF St VINCENT'S INSTITUTE OF MEDICAL RESEARCH

Scope

We have audited the financial report of St Vincent's Institute of Medical Research for the financial year ended 31 December 2003, comprising the Statement of Financial Performance, Statement of Financial Position, Statement of Cash Flows, Notes to the Financial Statements and Directors' Declaration. The company's directors are responsible for the financial report. We have conducted an independent audit of this financial report in order to express an opinion on it to the members of the company.

Our audit has been conducted in accordance with Australian Auditing Standards to provide reasonable assurance whether the financial report is free of material misstatement. Our procedures included examination, on a test basis, of evidence supporting the amounts and other disclosures in the financial report, and the evaluation of accounting policies and significant accounting estimates. These procedures have been undertaken to form an opinion whether, in all material respects, the financial report is presented fairly in accordance with Accounting Standards and other mandatory professional reporting requirements in Australia and statutory requirements so as to present a view which is consistent with our understanding of the company's financial position and performance as represented by the results of its operations and its cash flows.

The audit opinion expressed in this report has been formed on the above basis.

Audit Opinion

In our opinion, the financial report of St Vincent's Institute of Medical Research is in accordance with:

- a) the Corporations Act 2001 including:
 - i) giving a true and fair view of the company's financial position as at 31 December 2003 and of its performance for the year ended on that date, and
 - ii) complying with Accounting Standards in Australia and the Corporations Regulations 2001; and
- b) other mandatory professional reporting requirements in Australia.



WEBB CALLAWAY PATON
Chartered Accountants

AP MARKS

Dated this 19th day of April 2004, Melbourne, Australia

DONATIONS

Bequests & Donations from Estates & Charitable Trusts

The Ian Potter Foundation	300,000
Helen Macpherson Smith Trust	100,000
John Holt Medical Research Endowment Fund	59,500
Perpetual Trustees - H & L Hecht Trust	50,000
The Jack Brockhoff Foundation	50,000
K & A Bongiorno Medical Research Endowment Fund	38,840
The Marian & EH Flack Trust	27,500
Perpetual Trustees - J & R McGauran Trust	17,000
George Castan Family Charitable Trust	15,000
J & M Carmack Foundation	13,667
Bell Charitable Fund	10,000
Perpetual Trustees - The Teresa Wardell Trust	10,000
M J Polinelli Foundation	15,996
JB Were Foundation	5,000
Trust Private - Estate William George Maxwell	5,000
The William Angliss (Vic) Charitable Fund	1,000

LIST OF DONORS

\$750,000

St Vincent's Health

\$50,000 plus

Alberti AM, S

Shanahan, B

\$20,000 - \$29,999

Anonymous

\$10,000 - \$19,999

Barro Group

Carson, G

Regan, J

\$5,000 - \$9,999

Griffin, M

Jackson, B

Palace Cinemas

Vermont Cancer Research Fund

Young, H

\$1,000 - \$4,999

Anonymous

Aroni, B & R

Bennett, R

Berry, R

Bongiorno, A & A

Burkett, D

Carew, J

Caro, R

Clifton, J

Colorpak Packaging Pty Ltd

Crown Towers

Dale, G

deGruchy, D

Demediuk, Mr & Mrs N

Greene, T

Hale, G

Hart, L & C

Heath, W

Kirby, R

Mahlab, F & E

McHale, JJ

McNaught, G

Michelmore AO, J

Nicoll, G

O'Callaghan, C

O'Day, J & S

O'Shannassy, M & R

Otter, G & D

Reid, I

Rush, B

Salta Properties Pty Ltd/Westgate Logistics Pty Ltd

Schillier, P & J

Smith, C

Smith, P & T

Smith, S

Spry-Bailey, P

Stapleton, M

SVH Emergency Care Centre

SVIMR Construction Site Workers

Swaney, S

Westmore-Peyton, C

Wright, D

Yencken, T

Up to \$1,000

Anonymous
 Attard, C
 Bowen Electronics Pty Ltd
 Brian Cook, Victorian Vending
 Brown, S
 Cale, G
 Campbell, B
 Campbell, M
 Castan, G & F
 Chamberlain, K
 Chappell, J
 Cullen, N
 Dax, EM
 Demediuk, PM
 Demediuk, P
 Douglas, I
 Dunn, K
 Eaton Pty Ltd
 Emerson, APR
 Eves, R
 Falk, G
 Fantech Pty Ltd
 Fox, P
 Gorman, J
 Henderson, K
 Hodder, I
 Hofman, I & R
 Hollis, A
 Hoyle, K
 Hua, C
 John Morris Scientific Pty Ltd
 Karlow Pty Ltd
 Lakes, G
 Le, D
 Loh, K
 Maberly Smith, N
 Mahoney, MT
 Male, A
 McDonald, A
 McGinniss, M
 McMahan, P
 Meyer, A
 Moon, SC
 Newman, P
 Nixon AO, P
 O'Bryan, NM
 O'Loan, R & C
 Peek, A
 Pinskier, N

Purcell, J
 Rees, R
 Robinson, G
 Ritchies Store Pty Ltd
 Santamaria, J
 Savery, D
 Sherlock, A
 Smith, LM
 Tansey, C
 Teasdale, P
 TLC Business & Research Consultants
 Van Dijk, L
 Wantirna Hill Club Patrons
 Woolett, G
 Yu, A

In Memorial Donations

Gifts of remembrance have been made in honour of the following:
 Bernice Mary (Bunny) Arnold
 Emma Smith

Permanent Invested Funds

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.

The Mary Potter Research Grant	90,797
Diane B Jones Endowment	970
Lorna M Miller Endowment	208,651
Albert H Maggs Endowment	100,000



Combating disease requires a team effort

Donors are a vital part of our efforts to raise funds to complete the building project and to support our scientific projects now and in the future. The research philosophy of the Institute has always been collaborative, recognising that through the combined efforts of many, great things are achieved – so it is with donations.

For further information about the Institute and ways to help SVI visit our website or contact us on (03)9288 2480 during business hours.

www.svi.edu.au

St Vincent's Institute
Postal: 41 Victoria Parade Fitzroy Vic 3065
Located at: 9 Princes Street Fitzroy Vic 3065
Telephone: +61 3 9288 2480
Facsimile: +61 3 9416 2676
Email: enquiries@svi.edu.au

The fields of research in which the Institute is engaged touch the lives of many Australians. The scientific research of the Institute is aimed at the treatment and cure of illness and depends heavily on the support of the community.

Your financial support will have a direct effect on the Institute's research. There are many ways in which you can help. These include making single, annual or more frequent gifts, making bequests via a Will, or making a donation in memory of a loved one or esteemed person.

St Vincent's Institute is an endorsed deductible gift recipient and income tax exempt charity.

Contributions are used directly in research, not on administrative or fund-raising costs. Join us in the voyage of continuous discovery and share in the rewards our research will provide.

Enquiries will be welcomed by the Director of the Institute on (03) 9288 2480.

All funds received from bequests and donations are used solely for medical research. However, the Institute will be pleased to use capital and 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 its 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."

DONATION FORM

Please forward to
St Vincent's Institute
41 Victoria Parade Fitzroy Vic 3065
Phone: 03 9288 2480 Fax: 03 9416 2676

I/we would like to support medical research at SVI

Name: _____

Address: _____

_____ Post Code: _____

Phone: _____

Email: _____

Donation: \$ _____

My payment is by: Cheque or money order
payable to St Vincent's Institute

Amex Diners Mastercard

Visa Bankcard

--	--	--	--	--	--	--	--	--	--	--	--	--	--	--	--

Expiry Date: ____ / ____

Signature: _____

All gifts \$1,000 and over will automatically qualify you as a member of the SVI 1000 Club

All amounts of \$2 and over are tax deductible. SVI ABN 52 004 705 640

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THANK YOU FOR YOUR SUPPORT