Centenary Institute

annual report 05

CENTENARY INSTITUTE
CANCER MEDICINE & CELL BIOLOGY

OUR LOGO

The letter "C" set in sandstone in the logo, has dual symbolism. It reflects our commitment to cancer research and, as the Roman Numeral for 100, it represents our association with the Centenaries of the University of Sydney Medical School and Royal Prince Alfred Hospital.

Our mission

To improve the
quality of life
for all Australians through
excellence in medical
research


HAND AND FACE
PROTECTION
MUST BE WORN

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2005 Highlights

Major equipment upgrade

In June 2005 Centenary took delivery of three new flow cytometers from BD Biosciences valued at $1.7 million, significantly enhancing the research capacity of its flow cytometry facility and offering its researchers with unrivalled access to state-of-the-art equipment with very wide-ranging applications. This purchase was made possible due to a grant from the Federal Department of Health, as well as funds raised at the 2004 Centenary Raceday and Luncheon and a generous donation from one of Centenary's supporters.

Centenary recently purchased an IVIS small imaging system valued at $350,000. The system will allow researchers to use real-time imaging to non-invasively monitor and record cellular and genetic activity within a living organism. This purchase was made possible by funding from the University of Sydney (NHMRC Equipment Grant and USyd Major Equipment Scheme), Clive and Vera Ramaciotti Foundation and the James N Kirby Foundation.

Another valuable purchase was a KODAK Image Station 4000MM valued at $82,000. This provides Centenary researchers with a versatile resource for the analysis of data from a wide range of experimental systems used in our laboratories. The purchase was made possible by funding from the Cancer Institute of New South Wales and the James N Kirby Foundation.

3rd Australian B Cell Dialogue

In August Centenary hosted the 3rd Australian B Cell Dialogue which brought together 62 delegates from across Australia to share the latest research findings on B Cell function in health and disease. The event was a great success.

Awards and Grants

- Professor Geoff McCaughan, head of the Liver Immunobiology group was awarded the Gastroenterology Society of Australia 2005 Distinguished Research Prize to acknowledge the liver group's pioneering and continuing work in the field of liver disease pathogenesis and treatment.
- Dr Jamie Triccas of the Vaccine Development unit within the Mycobacterial Research group, was appointed to a Lectureship in Medical Microbiology within the Department of Infectious Diseases and Immunology at the University of Sydney.
- Dr Alex Bishop of the Liver Transplantation group was appointed Guest Professor at the Second Military Medical University of Shanghai.
- Associate Professor Chris Semsarian, head of Centenary's Agnes Ginges Centre for Molecular Cardiology, was the runner-up in the 2005 Royal Prince Alfred Research Medal presentations. His talk was entitled "Genetic Basis of Sudden Death".

The following grants were awarded to our researchers:

- ARC Discovery Grant (The role of neutral amino acid transport in normal physiology) - Professor John Rasko in collaboration with S Broer, G Halliday and JD Pollard
- Cancer Institute NSW Research Infrastructure Grant
  - Dr John Allen, Dr Mark Gorrell, Dr Rosetta Martiniello-Wilks in collaboration with S Clarke and J Arnold
- Cancer Institute NSW Research Infrastructure Grant
  - Dr Stuart Tangye
- Equipment Grant from Rebecca L Cooper Foundation
  - Professor John Rasko
- Equipment Grant from Rebecca L Cooper Foundation
  - Professor Warwick Britton, Professor Geoff McCaughan, Dr Mark Gorrell and Dr John Allen
- Ferring Research Project Grant (Liver Fibrosis)
  - Dr Mark Gorrell
- Guidant Australia Training and Research Fellowship
  - Associate Professor Chris Semsarian
- Ian Potter Foundation Travel Award
  - Dr Jamie Triccas
- Juvenile Diabetes Foundation International Grant (Understanding How Pathogenic B Cells are Generated in Type 1 Diabetes)
  - Dr Pablo Silveira
- Leukaemia Foundation Equipment Grant
  - Professor John Rasko
- Leukaemia Foundation Research Grant (MicroRNA's in primate haemopoiesis)
  - Professor John Rasko
- National Heart Foundation Project Grant (Novel insights into the genetic basis of hypertrophic cardiomyopathy: candidate genes related to calcium handling)
  - Associate Professor Chris Semsarian
- NHMRC Principal Research Fellowship Grant for 2005-9
  - Associate Professor Barbara Fazekas de St.Groth
- NHMRC Program Grant (Molecular and cellular pathogenesis of liver disease)
  - Professor Geoff McCaughan, Dr Mark Gorrell, Dr Patrick Bertolino, Dr Nick Shackel in collaboration with colleagues at the Westmead Millennium Institute

- NHMRC Project Grant (Environmental influences on allergic airways disease from birth to 8 yrs: long-term outcomes of a randomised trial (CAPS))
  - Professor Warwick Britton in collaboration with GB Marks, A Kemp, E Tovey, S Leeder and A Jones
- NHMRC Project Grant (Genetic basis of sudden cardiac death in the young)
  - Associate Professor Chris Semsarian
- NHMRC Project Grant (Overcoming resistance of human melanoma to chemotherapy)
  - Dr John Allen in collaboration with P Hersey and MM Zhang (Uni of Newcastle)
- NHMRC Project Grant (RNA interference in normal and neoplastic myelopoiesis)
  - Professor John Rasko
- NHMRC Project Grant (Role of P2X7 in innate and adaptive immunity to mycobacterial infections)
  - Dr Bernadette Saunders and Professor Warwick Britton in collaboration with JS Wiley (USyd) and E Sluyter (Nepean)
- NSW Cancer Council Grant (Development and function of anti-tumour cytotoxic lymphocytes in health and disease)
  - Dr Stuart Tangye
- NSW Cancer Institute Career Development Fellowship (Interactions of multidrug transporters and new anticancer drugs, and their regulation by MYC oncogenes)
  - Dr John Allen
- Perpetual Trustees Equipment Grant
  - Professor Antony Basten
- Perpetual Trustees Equipment Grant
  - Professor Warwick Britton, Professor Geoff McCaughan, Dr Mark Gorrell and Dr John Allen
- Perpetual Trustees Grant
  - Associate Professor Chris Semsarian
- Pharma Applied Research Grant (Compound selectivity from DPIV)
  - Dr Mark Gorrell
- Roche Organ Transplantation Research Foundation Project Grant
  - Dr Alexandra Sharland, Dr Mark Gorrell in collaboration with M Sandrin and D Christiansen
- University of Sydney Early Career Development Award
  - Dr Tri Phan
- University of Sydney Major Equipment Scheme
  - Professor Warwick Britton
- University of Sydney Research and Development Grant
  - Professor Geoff McCaughan and Dr Mark Gorrell

Patents

A/Prof Barbara Fazekas de St.Groth (T Cell Biology) developed a new method for identifying human regulatory T cells for which a provisional patent has been submitted. The method is under development with a major commercial partner for diagnostic and therapeutic use.

Student Awards

- Dr Tri Phan (PhD student, B Cell Biology) was the recipient of the New Investigator Award at the 35th Annual Scientific Meeting of the Australasian Society for Immunology in Melbourne in December (see photo overleaf).
- Ms Alex Spencer (PhD student, T Cell Biology) was a finalist in the BD Science Communicator Prize at the 35th Annual Scientific Meeting of the Australasian Society for Immunology in Melbourne in December.
- Dr David Gracey (PhD student, T Cell Biology) was awarded a travel grant from the American Transplant Society to give an oral presentation at the 2005 American Transplant Congress in Seattle, USA. He was also awarded a travel grant and selected to present in the President's Prize symposium at the 2005 Scientific Meeting of the Transplantation Society of Australia and New Zealand in Canberra.
- Mr Shaun Cordoba (PhD student, Liver Immunobiology) was selected to present his work at the President's Prize symposium at the Scientific Meeting of the Transplantation Society of Australia and New Zealand.
- Mr Anthony Ryan (PhD student, Mycobacterial Research) was awarded a Faculty of Medicine (USyd) Travel Grant.
- Ms Teresa Wozniak (PhD student, Mycobacterial Research) was awarded a Keystone Symposia Travel Grant.
- Ms Alex Spencer (PhD student, T Cell Biology) was awarded a Keystone Travel Scholarship to attend the "Determinants of Host Resistance, Susceptibility or Immunopathology to Pathogens" conference at Steamboat Springs, Colorado, in January 2006.
- Ms Sioh-Yang Tan (PhD student, T Cell Biology) was awarded a Keystone Travel Scholarship to attend the "Tolerance, Autoimmunity and Immune Regulation" conference at Breckenridge, Colorado in March 2006.

Dr Tri Phan (second from right) with other finalists of the New Investigator Award at the presentation ceremony.

- Ms Alessandra Doolan (PhD student) and Ms Jodie Ingles, both of the Molecular Cardiology Group, were awarded travel grants from the Cardiac Society of Australia and New Zealand (CSANZ). Ms Jodie Ingles also received a National Heart Foundation Travel Grant to present her work at the Scientific Sessions of the American Heart Association (AHA) in Dallas, USA.

Scholarships

Ms Sandra Gardam (B Cell Biology) was awarded the inaugural NHMRC/Merck Sharp & Dohme John Shaw Postgraduate Research Scholarship. Ms Lauren Holz (Liver Immunobiology) was awarded a NHMRC Dora Lush Postgraduate Research Scholarship. Dr Silvia Ling (Cancer Drug Resistance) received an Anthony Rothe Foundation Scholarship. Dr Stephen Larsen (Gene Therapy), Mr Adam Cook (B Cell Biology) and Ms Kim Good (Lymphocyte Differentiation) were recipients of Cancer Institute NSW Scholarships.

Publications

2005 was a very successful year for the Centenary Institute with respect to publications in high impact journals. Researchers published a total of 57 manuscripts, books and chapters throughout the year.

From the Director

2005 has been an eventful year for Centenary. In March an external review was conducted by a committee including Professor Herman Waldmann FRS (Director of the Sir William Dunn School of Pathology in Oxford), Professor Pat Holt FAA (Deputy Director of the Telethon Institute for Child Health Research in Western Australia), Dr Ian Blackburne FTSE (Chairman of ANSTO Board), and Professor John Funder (Chair). Their report found no fault with the research portfolio, but did come up with a number of recommendations on our modus operandi which were implemented. The review paved the way for my departure from the directorship and initiation of the search for a replacement. In the meantime, Professor David Burke FAA (Dean of Research and Development, College of Health Science, University of Sydney) has assumed the position of interim director, a role he is well qualified to play given his years of administrative exposure and his fine personal reputation as a biomedical scientist of distinction.

It has been a privilege for me to serve as the Director for the past 16 years and I wish Centenary and its staff every success in the future.

My views on Centenary's research strategy were enunciated in last year's annual report (go to www.centenary.org.au) and do not bear repetition other than to emphasise that adequate infrastructure remains the key to ongoing productivity and achievement.

In terms of achievements in 2005, the staff performed at their customary high standard in terms of peer reviewed grants, publications and presentations at meetings (see below). Moreover we were joined by Professor Jon Sprent, Fellow of the Royal Society, from the Scripps Research Institute in San Diego. Professor Sprent was granted a prestigious Burnet Award from the National Health and Medical Research Council, worth $2 million over five years.

Awards and grants

This year Dr Jamie Triccas was appointed to a Lectureship in Medical Microbiology within the department of Infectious Diseases and Immunology at the University of Sydney. Jamie is currently Project Leader of the Vaccine Development Unit within the Mycobacterial Research Group. I would like to congratulate Jamie on this noteworthy achievement.

Congratulations also go to Professor Geoff McCaughan who heads the Liver Immunobiology Group for being awarded the Gastroenterology Society of Australia 2005 Distinguished Research Prize. He adds this to the Royal Prince Alfred Hospital Research Prize which he received in 2000.

I would like to commend the many researchers who were successful in their applications for NHMRC Fellowships, Program Grants, Project Grants and other Equipment Grants in 2005, as well as our postgraduate students who received travel awards and prestigious PhD scholarships (see 2005 Highlights).

In June 2005 Centenary took delivery of three new flow cytometers from BD Biosciences valued at $1.7 million, significantly enhancing the research capacity of the flow cytometry facility. This purchase was made possible due to a grant from the Federal Department of Health, as well as funds raised at the 2004 Centenary Raceday and Luncheon and a generous donation from one of our supporters.

Australian B Cell Dialogue Meeting

In August this year, Centenary hosted the second Australian B cell Dialogue meeting which was attended by 62 participants interested in the role of B cell function in health and disease. The meeting was a great success thanks to the efforts of the organising committee which included Dr Stuart Tangye, Dr Robert Brink, Dr Pablo Silveira, and Dr Chris Jolly.

Fundraising

This year's End of Tax Year Appeal raised $53,500 towards Professor John Rasko's research aimed at using adult stem cells to repair damaged heart tissue. Through the generosity of those who supported our 2005 Christmas Library Appeal, we have also raised $31,146 to help cover the purchase of journals for the library in 2006.

On Saturday 22 October, Centenary held its 12th Annual Raceday and Luncheon. The day was another great success with over $75,000 net being raised. Our thanks go to the wonderful efforts of the Raceday Committee chaired by Malcolm Noad, organiser Sue Finn and the General Manager. Special presentations were made to Malcolm Noad, Graham McNeice (Master of Ceremonies) and Peter Baldwin (Auctioneer) for their contributions over the past decade.

Professor Antony Basten AO FAA FTSE
Executive Director

Farewell to Professor Antony Basten

Professor Basten's career has been exceptional to say the least. After graduating from Adelaide University in 1964, he undertook his doctoral studies in Oxford with Professors Sir Paul Beeson and Sir James Gowans, following which he joined the research unit of Professor Jacques Miller AC at the Walter and Eliza Hall Institute. His time there was highly productive and he was to forge strong scientific and research links with colleagues which he has retained to this day. In 1972 he took up a conjoint position as Senior Lecturer in Immunology at the University of Sydney and Consultant Physician at the Royal Prince Alfred Hospital. In 1975 he was appointed the first Chair in Immunology at the University of Sydney, aged 36.

In 1980 Professor Basten was the first recipient of the Inaugural Wellcome Australia Medal for 'distinguished discovery and its demonstrated use' and in 1983 he was listed as one of only seven Australians in the top 1,000 Scientists from all disciplines in the Citation Index. His accomplishments earned him an international reputation which was recognised by an appointment as Officer in the General Division of the Order of Australia for services to Medicine in 1988. In 1996 his contribution to medical research was once again recognised with the Rotary International Award for Vocational Excellence.

As a physician Professor Basten is a Fellow of the British Royal College of Physicians (London), the Royal Australian College of Physicians and the Royal College of Pathologists of Australia. As a scientist he has the distinction of being elected as a Fellow both of the Australian Academy of Science and the Australian Academy of Technological Sciences and Engineering.

He has embraced numerous roles in his research career including teacher and mentor to over 50 students and clinical trainees; Chair of several scientific, medical and university committees; member of the Editorial Board of 11 national and international journals; invited participant to over 40 international scientific conferences; author and co-author of over 250 publications.

In 1982 the Federal Government designated Professor Antony Basten's Immunology Research Unit in the University of Sydney's Faculty of Medicine as one of the ten Centres of Excellence in Australian Research. The Centenary Institute of Cancer Medicine and Cell Biology was conceived to commemorate the centenaries of the University of Sydney Medical School and the Royal Prince Alfred Hospital, one of Sydney's oldest teaching hospitals, and incorporated under the New South Wales Government legislation in recognition of the value to the community of an internationally competitive research centre in 1985.

Professor Basten was appointed the Founding Director of Centenary in 1989 and his team of young scientists became the core of the Institute. Their goal was to use the understanding of disease to develop more effective ways of dealing with health problems through new vaccines, better diagnostic tests and innovative forms of treatment. Their mission: to improve the quality of life for all Australians through excellence in medical research.

It was not until 1994 - when Centenary moved into a new six-storey research facility on the Royal Prince Alfred Hospital campus, purpose-built to accommodate up to 150 staff, thus enabling the diversification of its research

programme to encompass molecular medicine as well as immunology - that Professor Basten's dream was fully realised.

Under Professor Basten's leadership, the Centenary Institute quickly flourished to become a leading centre in immunology. In 1990, the NH&MRC Review Committee described the Centenary Institute as "....one of the two principal flag bearers for Australian immunology..." alongside the Walter and Elisa Hall Institute in Victoria. Recognising that "...the Centenary Institute should greatly strengthen basic biomedical research in New South Wales....(its) studies on autoimmunity are undoubtedly the most exciting findings in immunology originating from an Australian source over the past ten years....". In 1997 Nobel Laureate Professor Peter Doherty AC described the Centenary Institute as "Australia's premier immunology research centre".

In 2001 Centenary's biotechnology company, Cen*Tec* Ltd, was created for the purpose of developing projects with commercial potential. Whilst still in its infancy and under the leadership of Professor Basten as Chief Scientist, the company became the recipient of two Federal Government Biotechnology Innovation Fund Grants - one for developing a human antibody technology and another for developing a preventative vaccine for type 1 diabetes.

Twenty years on, Centenary has dramatically expanded its research profile, now housing an internationally competitive, multidisciplinary research team comprising of some of the very best scientists from major centres overseas as well as Australian researchers who have studied and/or completed fellowships on international campuses. It maintains its focus of delivering the highest standard of research to the prevention, diagnosis and treatment of common diseases of today such as cancer, diabetes, asthma, tuberculosis and heart disease.

Professor Basten is one of Australia's leading medical researchers and clinical immunologists. Throughout his distinguished career he has been a leader in his field. He is known amongst his peers as one of the rare breed of immunologists who has successfully balanced the demands of clinical medicine whilst leading an internationally competitive research team.

Professor Basten's decision to step down as Executive Director of an organisation which he has moulded from its inception has been received with much sadness, eternal gratitude and eager anticipation for what can only be a bright future ahead following a short but rich history of remarkable achievements and a powerful vision to create a better life for all Australians.

Professor Basten has accepted a position as Visiting Fellow Commoner in Trinity College which will take him to Cambridge in 2006 and will enable him to return to full-time research. His wisdom and leadership is held in the highest of regard by all who have had the pleasure of making his acquaintance. We wish him every success and happiness in his future endeavours and well-deserved retirement.

From the Interim Director

Professor David Burke AO FAA FTSE commenced as Interim Director of the Centenary Institute on the 1st of November 2005. He is a clinical neurologist and was one of the scientists responsible for the creation of the Prince of Wales Medical Research Institute, NSW, where he was Director of Clinical Research from 1991-2002. He is currently President of the Australian Association of Neurologists and is Professor and Dean, Research and Development in the College of Health Sciences at the University of Sydney.

The last few months have seen a number of developments within Centenary. In May, Professor Antony Basten AO FAA FTSE announced his intention to stand down as Executive Director after 16 years. This occurred in late October and I have since taken up the position of Interim Director. I am proud to have been selected to lead Centenary during its search for a new director.

Tony will be a difficult man to replace. He has close personal relationships with staff, supporters and stakeholders, and he has had an extremely distinguished career, recognised nationally and internationally as an outstanding physician, researcher, and teacher. The process of finding someone of the same calibre to lead Centenary into the future while holding onto the values which embody the core of its existence will take some time. A primary objective for the new Director will be to foster and enhance Centenary's many strengths in research and collaborative associations.

It is my duty to ensure that until such a person is appointed, we continue to grow and prosper. I believe that, with the support of Centenary's Board of Governors and our committed Management team, we will meet challenges of the next few months and that this transition will prove to be a positive experience.

Centenary's research portfolio has diversified to include molecular medicine, gene therapy and cardiovascular research, as well as the creation of a biotechnology company, Cen*Tec*, in 2001. Led by a dedicated group of enthusiastic scientists committed to excellence in medical research, their many achievements over the years showcase their outstanding talents. Centenary staff and students have been the recipients of some of the most prestigious awards in science and medical research, including the NSW Young Tall Poppy Awards, RPA Foundation Prize, Centenary Medals, NH&MRC Development Awards, Clinical and Scientific Fellowships, University Medals and Program Grants.

Continued support from members of the Research Society and the general public remains an integral part of our development. The core funding provided through the unwavering generosity of our supporters allows us to continue our important research. It is imperative that we work to strengthen our ties with members of our community to achieve the goal of improving the quality of life for all Australians. I look forward to building meaningful relationships with our supporters and stakeholders.

Perhaps the most recognisable and satisfying achievement for any Director is the ability to act as mentor to the younger generation of future leaders of our society. Tony has been this and much more to many young scientists who have sought his wisdom and guidance throughout their careers and succeeded as leaders in their fields. We are all indebted to him for his hard work, dedication and guidance over the last two decades, and I am sure that all of our supporters will join with us in wishing him the very best in his future endeavours.

I envision a bright and exciting future for Centenary. It has gone from strength to strength in its first two decades and will continue to prosper and attract talented and dedicated staff from around the world to produce research advances of the highest international standard. As we move into our twenty-first year, we look forward to the year ahead with optimism.

David Burke AO FAA FTSE
Interim Director

Board Governors

The Honourable Michael Egan was appointed as Chairman of the Board of Governors in September 2005, as a nominee of the Vice Chancellor of the University of Sydney, Gavin Brown. He is the former Treasurer of NSW and has held a number of ministerial positions. Mr Egan was a Member of Parliament for 25 years and is the longest serving Treasurer of NSW (1995-2005) since the introduction of responsible Government in 1856.

Professor Tony Basten AO FAA FTSE was appointed Governor ex officio in 1989 at the time of his appointment as Founding Director of Centenary Institute. He holds the Chair of Immunology at the University of Sydney, is a consultant physician at Royal Prince Alfred Hospital and Chief Scientist of Cen*Tec* Limited. On retiring as Director in October he also resigned from the Board.

Professor David Burke AO FAA FTSE was appointed Governor in November 2005 at the time of his appointment as Interim Director of the Centenary Institute. He is Dean of Research & Development, College of Health Sciences at the University of Sydney and a Neurologist at the Institute of Clinical Neurosciences, Royal Prince Alfred Hospital.

The Honourable John Brown AO FAMI was appointed as a Governor in 2001. Formerly the Member for Parramatta in the Federal House of Representatives for thirteen years from 1977, during which time he held various Ministerial portfolios including Arts, Sports, Environment and Territories. In 1986 Mr Brown was named Australian of the Year by the Australian Newspaper. Mr Brown is the Emeritus Chairman of the Tourism Task Force and is the Founder and Patron of the Sport and Tourism Youth Foundation.

Professor Andrew Coats was appointed as a Governor in 2004 in his capacity as the Dean of the Faculty of Medicine, University of Sydney. He is a member of the Board of a number of Institutes affiliated with University of Sydney including the Woolcock Institute, Heart Research Institute, George Institute of International Health and the Menzies School of Health Research and is Chairman of the Australian Health Informatics Council.

Mr Alastair Davidson MICA (Scot) was appointed as a Governor in 2004. He has held executive positions in the banking and financial services industry for 15 years in the UK, USA and Australia including Salomon Smith Barney in Sydney for eight years as co-head of its new product group, specialising in equity derivatives. He is currently Managing Director of Aurora Funds Management based in Sydney.

Mr Paul Harris ASIA was appointed as a Governor in 1998. He has worked in the securities market in Australia for nearly 30 years holding a number of senior positions in merchant banks and stockbrokers. Mr Harris is a member of the Australian Stock Exchange and a Director of various companies including Ten Group Ltd, Gresham CEA Management Ltd and Stadium Australia Club Ltd. He resigned from the Board in December.

Ms Jan Hogan MAPs was appointed as a Governor in 1998. She is a Psychologist and Family Therapist with an active practice. Ms Hogan holds directorships in several private companies and is a Trustee of the Centenary Institute Medical Research Foundation. She resigned from the Board in December.

Dr Diana G Horvath AO was appointed as a Governor in 1993 in her capacity as Chief Executive Officer of the former Central Sydney Area Health Service. Dr Horvath is currently CEO of the South Western Sydney Area Health Service which is affiliated with the Centenary Institute.

Mr Jim Longley FCPA FAICD was Chairman of the Board between 2002 and August 2005. He has been a Governor since 1997 and served as Treasurer between 1999 and 2002. Formerly the State Member for Pittwater for almost 10 years, Mr Longley held various ministerial portfolios in the NSW Government between 1992-1995 and was the Chief Executive Officer of Anglican Retirement Villages, Diocese of Sydney between 1996-2000. Mr Longley is currently Head of Government Finance with Business Development at Commonwealth Bank of Australia. He resigned from the Board in August.

Professor John Mathews AM was appointed as a Governor in October 2000. He was the Founding Director of the Menzies School of Health Research in Darwin for fifteen years until 2000 when he was appointed Head of the National Centre for Disease Control, Health and Aged Care as well as a Visiting Professor of the University of Sydney. Professor Mathews has been a member of numerous advisory and review groups for the NHMRC and the Federal Government.

Ms Sam Mostyn was appointed as a Governor in 2003. She has an extensive background in law, corporate affairs, human resources and politics, and was a senior advisor (communications) to the former Australian Prime Minister, The Hon PJ Keating. Ms Mostyn is Group Executive of Culture and Reputation at IAG and serves on the Academic Advisory Board of the Australian Institute of Management and the Boards of the NSW Premier's Council on Active Living and the Sydney Festival. She is a Trustee of the Australian Museum and is a Director of Insurance Australia Group Services Pty Limited, NRMA Life Limited and NRMA Staff Superannuation Pty.

Mr Malcolm Noad was appointed as a Governor in 1995. He held the position of Chairman between 1999-2002 and was Deputy Chairman until 2005. Mr Noad has an extensive background in newspaper publishing. Since joining News Ltd in 1973 he has held various executive management positions and was appointed to the News Ltd Board in 1992. Mr Noad is a former Chairman of the National Rugby League and is currently Chief Executive Officer of the 2004 Premiership NRL team, Mitsubishi Electric Canterbury - Bankstown Bulldogs. Mr Noad has been a Trustee of the Centenary Institute Medical Research Foundation since 1994. He resigned from the Board in August.

Professor Michael Reid was appointed Governor in 2005. He is Director General of the recently-formed Ministry for Science and Medical Research, which has overall responsibility for planning and coordinating science, innovation and medical research in NSW. He was formerly Director of the Policy and Practice Program at the George Institute for International Health, University of Sydney. He held the position of Director General of NSW Health for five years and prior to that was Managing Director of a consulting company with government and NGO projects in Australia, Asia and the Pacific.

Mr John Samaha was appointed as a Governor in 2003. He has an extensive background in law specialising in litigation, regulatory investigations and risk management strategies, which often involve mediation outside the formal court process. He joined Malleson Stephen Jaques in 1998 and in 1992 was seconded to the Chairman's Office, Australian Securities Commission as adviser to the Director of Enforcement. He is Partner in the Dispute Resolution Group, Malleson Stephen Jaques.

Our History

The Centenary Institute was conceived in 1982 to commemorate the Centenaries of the University of Sydney Medical School and the Royal Prince Alfred Hospital. In 1989 it became a functioning entity under an Act of the NSW Parliament based on the Founding Director's, Professor Antony Basten, Federal Centre of Excellence. Formal affiliations with the University and Hospital promote opportunities for students to become involved in research as well as the translation of basic discoveries into clinical practices. Centenary is located in the grounds of Royal Prince Alfred Hospital adjacent to the Medical School and University campus. It is housed in a purpose built facility capable of accommodating a research team of up to 150 career investigators, trainees and support staff. Facilities include a specific pathogen free grade animal house, mouse cardiac physiology and function facility, transgenic service, a state of the art flow cytometry facility, library with online capability and a lecture theatre.

Centenary has an internationally competitive, multidisciplinary research team comprising some of the very best young scientists from major centres overseas as well as Australian researchers who have studied and/or completed fellowships on international campuses. Centenary has published in excess of 730 articles in refereed journals and books, its staff have in excess of 1100 presentations at international and national conferences since 1992, and it has attracted over $84.5 million dollars in grant funding to the campus.

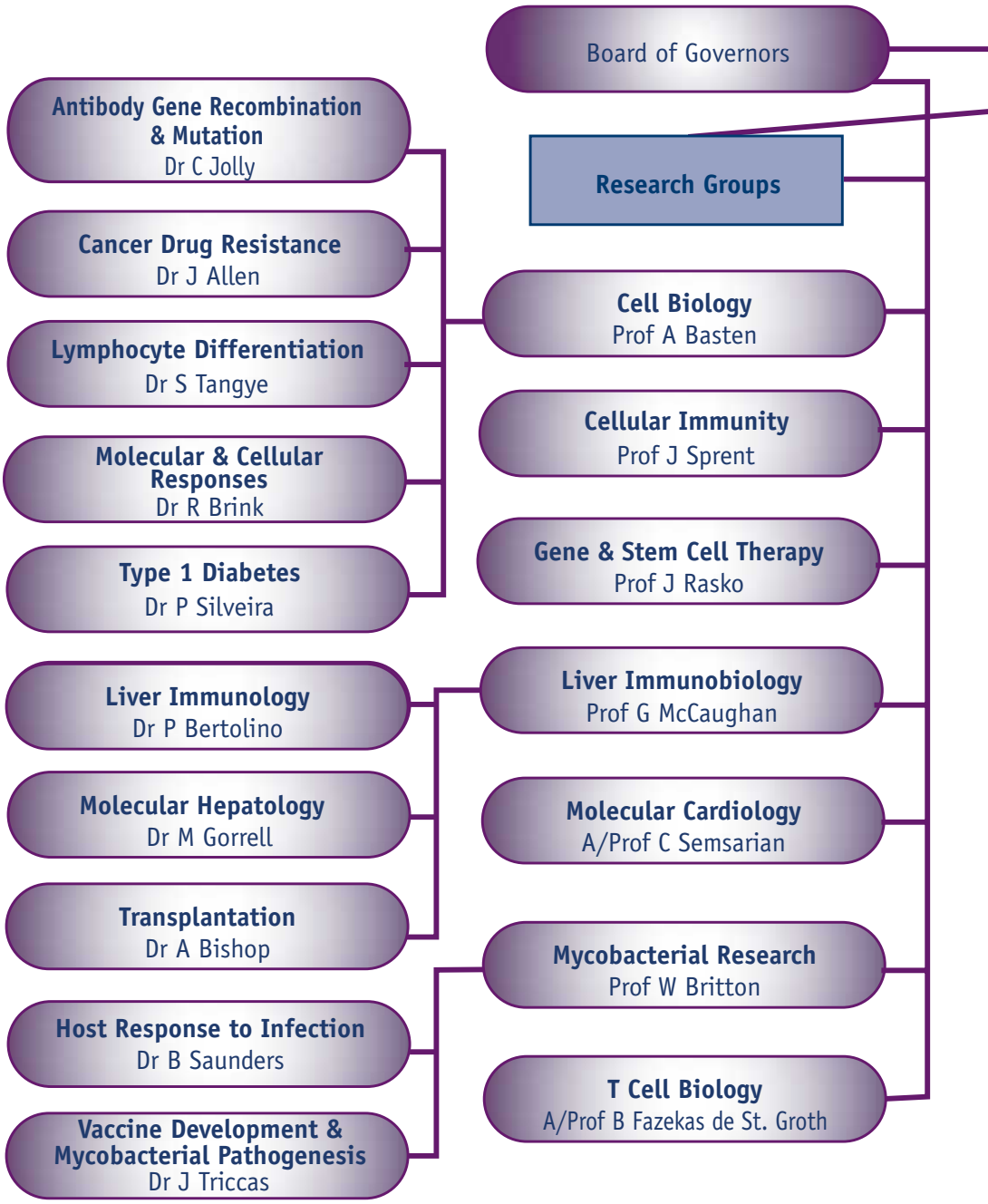
Centenary has a proud record of training PhD students. Since 1992 Centenary has produced 47 graduates. On completion of their PhDs, students have gone on to successful post doctoral studies at many of the world's leading institutions.

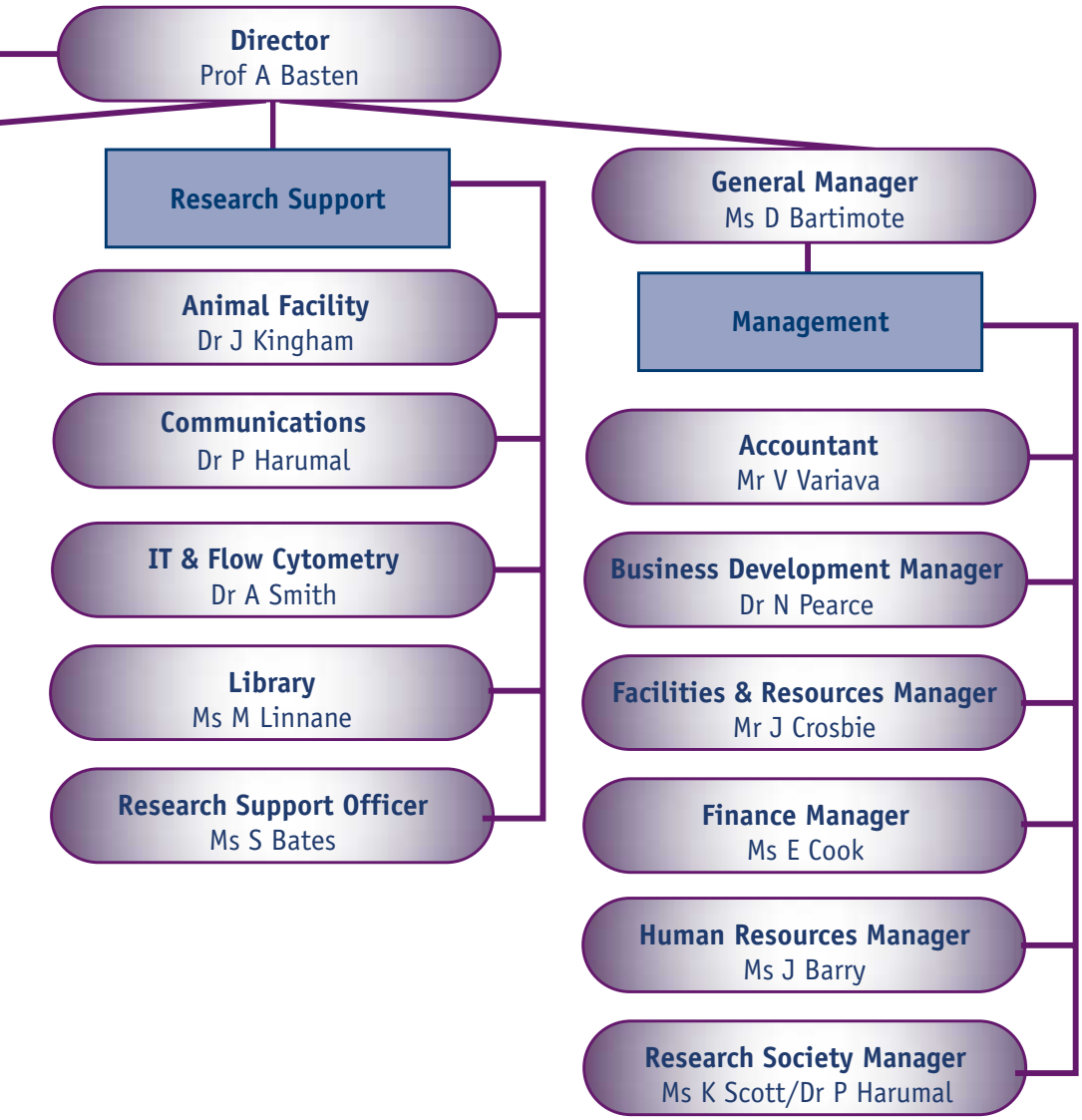
Centenary has a strong commitment to commercialising products of its research and has set up a biotechnology company, Cen*Tec* Ltd for this purpose. Two industry grants have been obtained to date by the company for developing a human antibody technology and a preventative vaccine for type 1 diabetes

Defining milestones in the history of the Centenary Institute:

- Appointment of Professor Antony Basten as the Founding Director of the Centenary Institute.
- Commencement of the new $21.5 million building, which enabled Centenary to quadruple staff numbers to the current level of 120 and to diversify the research programme to encompass molecular medicine as well as immunology.
- Creation of Centenary's spin out company, Cen*Tec* Ltd, in 2001 for the purpose of developing projects with commercial potential. The company has been the recipient of two Federal Government Biotechnology Innovation Fund grants.
- Recruitment in 2005 of Professor Jonathon Sprent FRS who has received a highly prestigious Burnet Award from the NHMRC to bring him back to Australia after a brilliant 30 year research career in the USA and Europe. Prof Sprent is described by his referees as one of the two or three leading experts in the world on T cell biology.

Organisational Chart




Director
Prof A Basten
Research Support
Animal Facility
Dr J Kingham
Communications
Dr P Harumal
IT & Flow Cytometry
Dr A Smith
Library
Ms M Linnane
Research Support Officer
Ms S Bates
General Manager
Ms D Bartimote
Management
Accountant
Mr V Variava
Business Development Manager
Dr N Pearce
Facilities & Resources Manager
Mr J Crosbie
Finance Manager
Ms E Cook
Human Resources Manager
Ms J Barry
Research Society Manager
Ms K Scott/Dr P Harumal

Research Groups

Centenary's research programme is based on a combination of cell biology, molecular medicine and immunology. Research is carried out by nine teams within Centenary, namely B Cell Biology (the Director's lab), Cancer Drug Resistance, Cellular Immunity, Gene and Stem Cell Therapy, Liver Immunobiology, Lymphocyte Differentiation, Molecular Cardiology, Mycobacterial Immunity, and T Cell Biology.

Cell Biology

Group Head: Professor Antony Basten

The research activities of the Director's group, also known as the Cell Biology Laboratory encompasses five different programs managed by independent scientists with the overall support and leadership of the Director.

Dr Robert Brink of the Molecular and Cellular Responses Project investigates the signals inside cells, which are responsible for cell survival versus death. The Antibody Gene Recombination & Mutation Project led by Dr Chris Jolly investigates the mechanisms involved in immunoglobulin class switching and somatic hypermutation, which produce the diversity of antibodies in our immune system. Dr Pablo Silveira's Type I Diabetes Project investigates the white cells responsible for destroying the insulin secreting apparatus in the pancreas

of patients with diabetes. Dr John Allen's Cancer Drug Resistance lab investigates the mechanisms of resistance to anticancer drugs and ways in which this problem can be overcome. The Lymphocyte Differentiation lab led by Dr Stuart Tangye investigates the regulation of the human immune system and how it responds to infection.

Antibody Gene Recombination and Mutation

Project Leader: Dr Chris Jolly

Antibodies form our first line of defence against most infections and are secreted into circulation by B cells. Their production is elicited by infection or immunisation. High quality antibodies provide protection (immunity) against re-infection for life, so they are essential for health. All antibodies have the same basic structure, but each B cell produces an antibody subtly different from every other B cell, and specific for a particular infectious agent. This unique specificity is achieved by the process of "hypermutation". The major focus of our group is to understand the largely unknown mechanism of antibody gene hypermutation.

The hypermutation process is fascinating in its own right, because it is unprecedented in nature. In some ways the mutation and selection of improved antibodies is a time-lapse model of evolution itself. Even though our capacity to mount effective immune responses to infections requires antibody hypermutation, the B cell hypermutation machinery can occasionally cause cancer by mutating the wrong gene. We now know that many very aggressive leukaemias and lymphomas (for instance, multiple myeloma and Burkitt's lymphoma) are initiated when the B cell hypermutation machinery accidentally modifies a cancer-causing gene.

Understanding of the antibody hypermutation process will help us to develop better ways of making effective antibody-based drugs. Furthermore, because DNA mutation

and repair of DNA mutation are processes central to development and prevention, respectively, of cancer, our research adds to the pool of knowledge that will produce more effective anti-cancer therapeutics.

We are about to publish work that demonstrates how one particular DNA repair pathway is used by B cells to minimise the risk that the antibody hypermutation process will initiate cancer-causing DNA damage. We have also recently developed a method that now allows us to definitively and quickly test the role of any gene in the hypermutation process. Previously, such tests would have taken 1 to 2 years per gene, but we will now be able to reduce that to a few weeks or months per gene. At the moment we are using our new method to resolve a major controversy in the field about how mutation "spreads" from a starting point in antibody genes to nearby DNA.

In addition to our hypermutation studies, we have also been attempting to develop a new biotechnology that will harness the process of antibody hypermutation in large scale cell cultures in order to isolate new antibodies that could be given to patients as exquisitely specific drugs for diseases such as cancer or rheumatoid arthritis.

Highlights:

- Demonstrated that the DNA-dependent protein kinase acts to inhibit gene recombination during antibody V region hypermutation.
- Established a model experimental system, using retroviral transduction of primary B cells, that allows the rapid investigation in vivo of the role of any gene in antibody affinity maturation.

Cancer Drug Resistance

Project Leader: Dr John Allen

Just over half of all cancer patients are cured, mainly by a combination of surgery, radiotherapy and chemotherapy. In cases where chemotherapy is the main treatment option, such as advanced metastatic cancer or disseminated cancers of the blood, the long term survival rate is often much lower because tumours respond poorly to the available drugs or else respond initially but then acquire resistance and regrow.

The Cancer Drug Resistance Group aims to identify new mechanisms of resistance to anticancer drugs, to evaluate their clinical significance, and to identify and pursue ways of overcoming drug resistance. We focus on resistance to new and promising anticancer drugs that are being applied to treating common, recalcitrant tumours, including melanoma, multiple myeloma and prostate cancer.

Our comprehensive *in vitro* models allow identification of candidate cellular mechanisms relevant to drug resistance or the related issues of drug pharmacokinetics and toxicity. Findings are followed up in preclinical mouse models and by analysis of molecular changes in patient tumour samples that can be related to outcomes of drug treatments.

Interactions of new anticancer drugs with multidrug transporter proteins

Multi-drug transporter proteins remove toxins encountered in the diet or produced by normal metabolism, from cells and from the body as a whole. Many anti-cancer drugs resemble such toxins, so the multidrug transporter proteins interfere with drug uptake into the body and into cancer cells. We are systematically investigating how the multi-drug transporter proteins affect the efficacy of promising new anti-cancer drugs. Some of these beneficial new drugs have low toxicity compared to traditional anti-cancer drugs and may be taken daily over long periods of time with obvious benefits for the management of cancer. Under this type of treatment, however, the emergence of drug resistance is much more likely. We collaborate in this work with the Sydney Cancer Centre, Royal Prince Alfred Hospital, The Children's Cancer Institute Australia, several other research centres, and pharmaceutical companies.

Contribution of defective apoptosis pathways to drug resistance in melanoma

Australia has the world's highest incidence of melanoma. It is one of the cancers most resistant to chemotherapy. Left too long untreated, melanoma is invariably fatal. In the last year, we began investigation of drug resistance in melanoma, focusing on the failure of melanoma cells to undergo apoptosis when damaged by anticancer drugs. This work is a collaboration with leading apoptosis groups at the Hall Institute in Melbourne and the melanoma group at the University of Newcastle.

Drug resistance in haematological cancer

Multiple myeloma is an incurable cancer of cells responsible for producing antibodies to fight infection. These cells have a revved-up mechanism for dealing with mistakes during the production of antibodies, a quality control and garbage disposal system known as the "Unfolded Protein Response". We suspect that this is what makes myelomas resistant to many drugs but susceptible to a class of new drugs, the proteasome inhibitors. Tests of this possibility are underway. If it proves correct, it will be possible to test the activity of a protein, XBP-1, that regulates the unfolded protein response and this may enable haematologists to better tailor their treatments for this difficult disease.

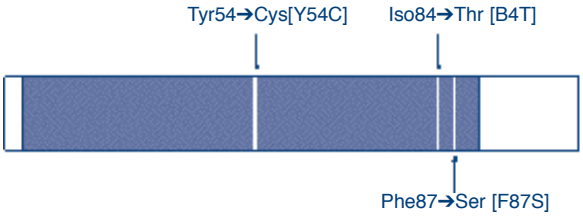
Highlights:

- Establishment of a mouse melanoma model for investigating the contribution of defective apoptosis pathways to drug resistance in this recalcitrant cancer.
- A multidrug resistance gene, MRP4, is directly upregulated by oncogenes of the MYC family, which are frequently over-active in common cancers.
- A side effect of daily use of the new drug for chronic myeloid leukaemia (CML), Imatinib, is that it could promote photosensitivity and other toxicities as a result of abnormal retention of porphyrin.

Lymphocyte Differentiation

Project Leader: Dr Stuart Tangye

Research performed in our laboratory is focused on understanding the regulation of the human immune systems, both in normal individuals, as well as in individuals with defined diseases, such as immunodeficiencies; i.e. individuals who have defects in their ability to mount a sufficient immune response, and are thus susceptible to infection with specific pathogens, such as viruses. We are particularly interested in understanding the mechanism by which the immune system responds following infections or vaccinations, thereby providing us with a "memory" of the initial response so that following subsequent exposure to the same infection, our immune systems will respond more rapidly. The immunodeficiency that we study is called X-linked lymphoproliferative disease (XLP). XLP is a very rare disease, affecting ~ 1-2/10^6 males. It is caused by mutations in the SH2D1A gene which encodes the intracellular adaptor protein SAP. Through collaborations with labs in the USA and Italy, we have identified 15 patients from 10 different families affected by XLP, and have characterized the mutation in their SAP gene that is responsible for this disease.



SAP mutations detected in different XLP patients

Highlights:

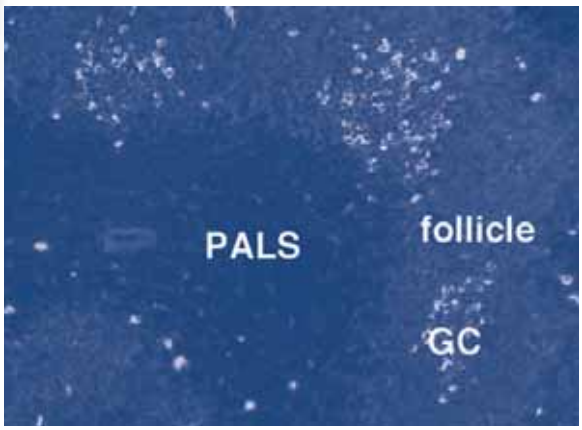
- Identified and characterised human transitional B cells, an important stage of lymphocyte development and differentiation, and found that these cells may contribute to the inability of some individuals to produce normal levels of protective antibodies.
- Identified distinct mechanisms for the generation of different types of human memory B cells.
- Established an important role for the cytokine IL-21 in the proliferation and differentiation of human B-cell subsets.
- Awarded a 3-year project grant from the Cancer Council NSW to continue studies into the immunodeficiency X-linked lymphoproliferative disease.

Molecular and Cellular Responses

Project Leader: Dr Robert Brink

The B cells of the immune system are a subset of white blood cells that produce the antibodies that recognise and eliminate invading micro-organisms. Because of the destructive power of antibodies, their production is carefully regulated to ensure that autoantibodies which recognise the body itself are not produced. Our group studies the cells, molecules and genes that regulate antibody production and how they may malfunction to give rise to autoimmune disease, immunodeficiency or cancer. For this purpose a powerful mouse model (SWHEL mice) is used which allows us to follow antigen-specific B cell responses within immunised mice. These mice produce B cells that have a uniform high affinity for the well characterised protein antigen hen egg lysozyme (HEL).

A particular focus of our research is the role of the tumour necrosis factor receptor (TNFR) family and how these cell surface receptors transmit molecular signals into cells. Separate lines of genetically modified mice form the primary tools for our studies of how signalling through members of the TNFR superfamily are regulated *in vivo*. TNFR molecules are critical regulators of immune responses and many other physiological systems. The TNFR associated factors (TRAFs) are a family of intracellular proteins that transmit signals from TNFRs following ligand binding. To determine the precise functions of the different TRAF proteins, mice have been produced that carry specifically inactivated TRAF genes.



The fate of the anti-HEL B cells can be tracked *in vivo* by flow cytometry and immunohistology

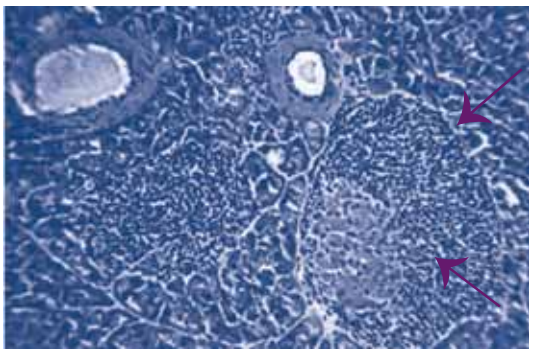
Highlights:

- Demonstrated that antigen affinity determines whether a B cell produces a rapid antibody response.
- Visualised for the first time the process of affinity maturation of the antibody response *in vivo*.
- Showed that inactivation of the TRAF2 gene in B cells restores responsiveness to B cells lacking CD40.
- Showed that the TRAF2 and TRAF3 proteins both negatively regulate B cell survival.

Type 1 Diabetes

Project Leader: Dr Pablo Silveira

Type 1 diabetes (T1D) is a disease that occurs when the body's own immune system mistakenly attacks and destroys the insulin producing beta cells of the pancreas. This is detrimental since insulin is an essential hormone used to regulate sugar levels in the blood. Currently, the disease affects more than 100,000 Australians and its incidence is increasing at an alarming rate in this country as well as in other developed nations. Using an animal model, our research has demonstrated that a class of immune cell, termed B cells, play an important role in the early stages of T1D. We are currently investigating the role of these dangerous B cells and why they are produced in diabetes-prone individuals. We hope this may eventually lead to the development of new therapies aimed at preventing the development of T1D.



Immune cell infiltrate destroying B cells in the pancreas

The non-obese diabetic (NOD) mouse develops a form of Type 1 Diabetes (T1D) which closely resembles the human disease. As a model for the disease, it has led to many important discoveries about the immune basis of T1D. One important discovery revealed that a class of immune cell, termed T cells, are responsible for most of the damage to the insulin producing beta cells in patients who develop T1D.

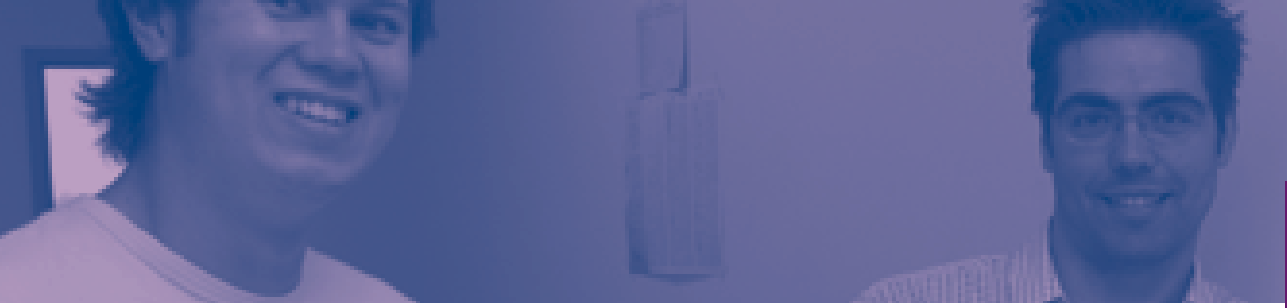
Our research is attempting to identify the faulty immune mechanism/s responsible for the development of an aberrant population of B cells in NOD mice which are capable of taking up and presenting proteins from insulin secreting beta cells.

We are also interested in determining if some of the T1D susceptibility genes may be the same or similar to those conferring predisposition to other autoimmune diseases such as systemic lupus erythematosus or autoimmune gastritis.

By discovering the mechanisms that break down in order to produce self reactive B cells in NOD mice and identifying the genes and molecules that regulate the development and actions of this cell type, we hope to provide the basis for new therapies in humans designed to prevent immune mediated destruction of insulin producing beta cells in T1D susceptible individuals.

Highlights:

- In a collaboration with researchers from the Jackson Laboratory (USA), we published a paper in Genes and immunity which confirms the location of two diabetes susceptibility genes in a mouse model of the disease.
- Jessica Stolp completed her Honours thesis, in which she described her important research showing how certain diabetes susceptibility genes can contribute to the erratic production of B cells that aid in the development of disease.
- In a collaboration with Dr Shane Grey from the Garvan Institute (Sydney), we have been able to better characterise phases in the development of Type 1 Diabetes where B cells play a critical role.



Cellular Immunity

Group Head: Professor Jonathon Sprent

Within the thymus, immature T cells are subjected to a number of interactions which impart the capacity to discriminate between self- and foreign- molecules (antigen). Consequently, when allowed to access the rest of the body, mature T cells do not react to self-antigen, but mount an immune response to foreign antigen. These immune responses, initiated by contact with antigen-presenting cells (APC), are associated with prominent proliferation and differentiation of the T cells into effector cells, followed by elimination of the specific antigen. Later exposure to the same antigen induces a memory response, characterised by heightened immune reactivity. Some T cells, if primed correctly, can also destroy virus-infected cells and tumour cells.

Research conducted in the Cellular Immunity laboratory focuses on the requirements for inducing optimal responses by T cells, with particular emphasis on their application to anti-tumour immunotherapy. Toward this end, we have been examining the contributions made by individual molecules within the T cell/APC interaction necessary to generate effector cells. We have also been investigating the suitability of using plasma membrane fragments from mechanically disrupted APCs to act as antigen presenting microdomains for immunotherapy.

Highlights:

- Under defined conditions, antigen presenting microdomains expressing a high density of costimulatory/adhesion molecules can stimulate an immune response both in *vivo* and *in vitro* and can prime T cells for rejection of tumour cells.

Gene & Stem Cell Therapy

Group Head: Professor John Rasko

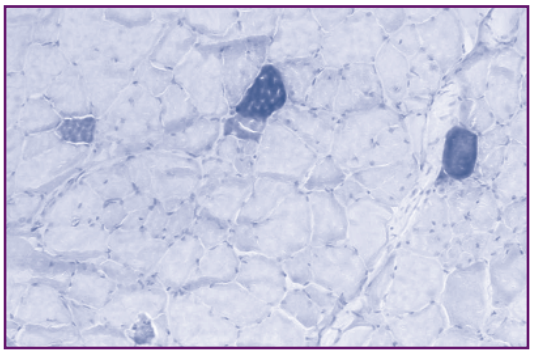
The broad aims of the Gene & Stem Cell Therapy Group are to overcome the barriers to successful human gene therapy, develop models to understand the biology of adult stem cells and shed light on disease mechanisms including cancer and genetic disorders. The group undertakes research in five areas, namely gene therapy, stem cell biology, gene silencing, genetic disorders and cancer biology.

The safe introduction of healthy genes into patients with genetic disorders could effectively cure inherited genetic disorders such as some cancers, haemophilia, and immunodeficiency disorders as well as infectious diseases such as HIV. The overall focus of our work continues to be to improve gene delivery to the precursor cells of all blood cells, known as haemopoietic stem cells (HSCs) and other adult stem cells such as mesenchymal stem cells.

One of the major problems limiting stem-cell based therapies is the absence of a clear understanding of the composition of the stem cell pool in humans. The right cell must be targeted for the right application or therapy. Haemopoietic stem cells have the capacity to divide to produce billions of progeny cells throughout a lifetime and it is these progeny that form the basis of our immune system. We have a well-established program studying HSCs and adult mesenchymal stem cells which are also present in the bone marrow. This is integrated with a model we have developed for autologous haemopoietic stem cell transfer in non-human primates.

Models of systemic and stem cell gene delivery

We have established mouse and nonhuman primate models to test novel agents for their ability to mobilize haemopoietic progenitors and stem cells. Using this model we can investigate means to improve the mobilisation of haemopoietic stem cells (HSCs) and other stem cell populations into the peripheral blood. We have established the SCID-repopulating cell (SRC) assay using NOD/SCID mice to evaluate different mobilisation regimens and to investigate the long-term repopulating ability of different HSC subsets, including HSCs purified by the Hoescht side population method. We have developed protocols for differentiating non-human primate mesenchymal progenitors into cells of adipogenic, chondrocytic and osteogenic origin. In both HSCs and mesenchymal progenitors we are working to optimise gene transfer using retroviral and adeno-associated vectors. We have achieved the successful introduction of gene-modified cells into small animal models to study therapies for diseases of blood and muscle.



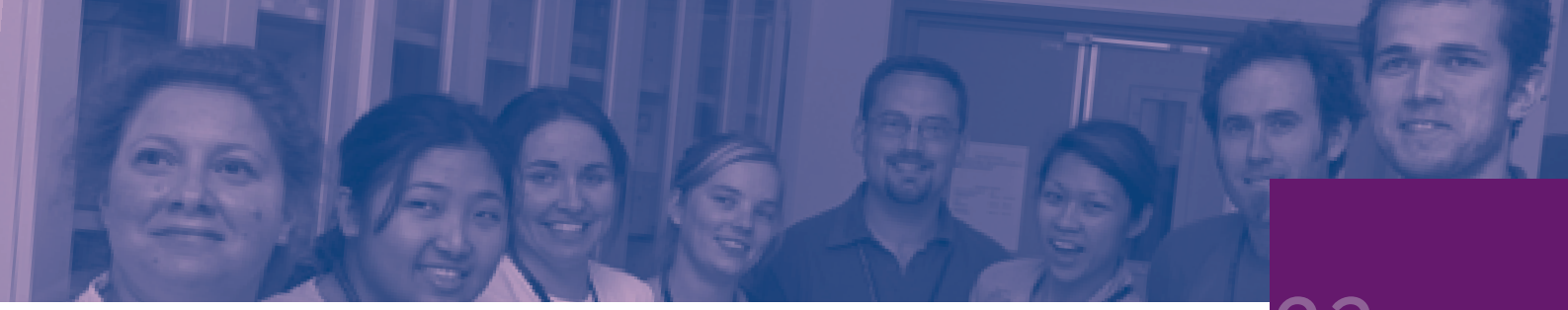
Gene-marked mesenchymal stem cells proliferating in damaged mouse muscle

Gene silencing and mechanisms of gene expression control

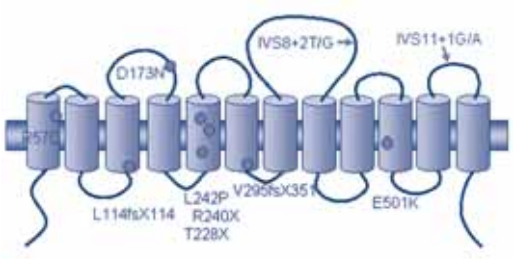
An understanding of the way haemopoiesis is regulated in the body has widespread relevance to diseases like leukaemia and the way they are treated. MicroRNAs recently identified in the phenomenon of gene silencing are found to be intricately involved in the control of cell development and differentiation. The role of microRNAs in normal and malignant haemopoiesis is only now being revealed. We are studying the importance of this new class of regulatory molecules in order to discover their previously hidden functions in normal blood cells and leukaemia in humans. Already we have developed a number of exciting molecular techniques for identifying and quantifying microRNA expression in cells. Ultimately this project may lead to novel treatments involving gene therapy and bone marrow transplantation.

Hartnup disorder

Hartnup disorder is an inborn error of renal and gastrointestinal neutral aminoacid transport. In 2004 we



described a breakthrough in this field by cloning and characterising the gene responsible for Hartnup disease, SLC6A19. This work was performed by our laboratory in collaboration with two groups from Canberra and its importance has been recognised by successful peer reviewed grants from both the NHMRC and ARC. During 2005 we further dissected the various mutations involved in Hartnup disease and reported the results of further functional studies in several publications. The mutations found in SLC6A19 were shown either to completely abolish or impair amino acid transport. We have also embarked on a wider analysis of other diseases affecting aminoacid transport to provide a clearer understanding of these intriguing inborn errors of metabolism.



Mutations (dots) indentified in neutral amino acid transmembrane transporter responsible for Hartnup Disease

Highlights:

- Clarification of the genetic basis for Hartnup disease we reported in Nature Genetics.
- Refined techniques to study transcription factors and a new set of molecular control molecules (microRNAs) present in normal and cancerous human cells.
- Optimised and characterized adult stem cell collection technologies and their therapeutic use in diseases of the blood and muscle.
- Consolidated gene transfer technologies using adenovirus, adeno-associated virus, retrovirus and lentivirus vectors.
- Completed an international clinical- and laboratory-based study of liver-directed gene therapy for haemophilia shedding light on the immune obstacles which must be overcome for this revolutionary technology to be successful.

Liver Immunobiology

Group Head: Professor Geoffrey McCaughan

The Liver Immunobiology Group has three distinct research programmes. Dr Patrick Bertolino leads the Liver Immunology programme, Dr Mark Gorrell the Molecular Hepatology programme and Dr Alex Bishop the Transplantation programme.

Transgenic, genomic and post-genomic advanced technologies are applied to understanding the molecular pathogenesis of liver injury, the biochemistry and biology of prolyl oligopeptidase in liver diseases, and the cellular basis of liver immune responses and non-responsiveness in infection and transplantation.

A major highlight for the group in 2005 was the commencement of our NHMRC Program Grant and the awarding of the Gastroenterology Society of Australia Distinguished Research Prize to Professor McCaughan for the liver group's pioneering and continuing work in the field of liver disease pathogenesis and treatment.

Liver Immunology

Project Leader: Dr Patrick Bertolino

The research of our group is focused on the liver, an organ with unique tolerogenic properties. In many species, liver transplants are spontaneously accepted across a complete MHC mismatch and some viral infections, such as the one by the Hepatitis C virus (HCV), become chronic suggesting that the virus exploits this liver property to persist in the host. The mechanisms involved in these processes remain unknown. The broad aims of our group are to understand the interactions between T lymphocytes and hepatic cells, the parameters that determine the balance between tolerance and immunity in the liver as well as those leading to chronic hepatitis.

We are particularly interested in dissecting complex mechanisms of liver-induced tolerance of CD8+ T cells, which are responsible for graft rejection and virus clearance. We have demonstrated for the first time that unlike other solid organs, naïve T cells (cells that have never "seen" their antigen) can also be directly activated within the liver. Primary activation of T cells within a solid organ challenges the current dogma and implies that mechanisms of tolerance to liver antigens are more intricate than initially thought as the liver may compete with lymph nodes (LN) for recruitment/retention of antigen-reactive T cells. Our recent results suggest that the outcome of an immune response is determined by the site where immune responses are initiated. Unlike immune cells primed in the lymph nodes that promote hepatitis, immune responses generated in the liver are abortive and do not cause liver damage. This model explains for the first time how the liver can induce immune unresponsiveness while maintaining the ability to generate an effective immune response to several pathogens. Our findings have important implications for transplantation studies and for the development and treatment of immune-mediated liver disease. This year we published an opinion review article in Trends in Immunology on the importance of these findings for chronic HCV infections. In collaboration with Prof Alf Hamann (Berlin, Germany), we have also used radiolabeling techniques and intravital microscopy to investigate adhesion molecules and chemokines that are important in early retention/activation within the liver. Our results, published in Hepatology this year indicate that ICAM-1/LFA-1 molecules play an essential role in these events. Finally, in collaboration with David Lecouteur and Alessandra Warren (Concord Hospital, NSW), we have shown that intrahepatic lymphocytes can contact antigen-bearing hepatocytes through cytoplasmic extensions penetrating the fenestrae of the liver sinusoidal

endothelial cells. We believe that this type of interaction might play an important role in hepatotropic viral infections such as Hepatitis C in which hepatocytes represent the main antigen presenting cells.

We are currently characterizing the phenotype, function and fate of T cells activated in the liver compared to those activated in the LN. We believe that these studies will provide important clues to understand mechanisms associated with the "liver tolerance effect".

Highlights:

- We have proposed a new model to explain the mechanisms regulating intrahepatic immunity that might play an important role in establishing chronic hepatitis C infection.
- We have demonstrated for the first time that early antigen-specific T cell retention and primary T cell activation in the liver is predominantly ICAM-1/LFA-1 dependent.
- We have identified a new type of interaction between T cells and hepatocytes through liver sinusoidal endothelial cell fenestrations.

Molecular Hepatology

Project Leader: Dr Mark Gorrell

Chronic liver diseases injure liver tissue and usually result from hepatitis B and C infection, iron storage disorders, autoimmune disease, disregulated lipid metabolism or chronic alcohol abuse, causing liver fibrosis (scarring) and ultimately cirrhosis and sometimes cancer. We are focused on understanding the biological roles and cell biology and biochemistry of molecules potentially important in liver diseases and disorders and harnessing that knowledge to improve human health.

The molecules that we study include enzymes of the prolyl oligopeptidase (POP) gene family, annexin II, Discoidin Domain Receptor 1 (DDR1), osteopontin and a matrix-controlling protein called EMMPRIN.

The POP family of enzymes consists of dipeptidyl peptidase IV (DPIV), DP8, DP9, fibroblast activation protein (FAP) and prolyl endopeptidase (PEP). DPIV inhibitors are under development by more than two dozen pharmaceutical companies as a novel therapy for type 2 diabetes. Our role is principally to understand the activities and overall biological roles of the POP family enzymes so that we can predict effects of targeting individual enzymes or groups of enzymes in humans. Liver levels of DP8 and DP9 vary greatly between patients, suggesting roles for these enzymes in liver function.

Cell adhesion and movement are crucial in organ development, inflammation, tumour growth and wound healing. Our *in vitro* approach to gain evidence that a gene is involved in these processes is to force cells to make a protein in cell culture in such a way as to identify each cell that makes the protein and quantify the altered behaviour of that cell. We have done that by tagging each molecule of interest with green fluorescence. In some cases molecules were altered to understand how they work. In this way we discovered extra-enzymatic effects of DPIV, DP8, DP9 and FAP.

Discoidin Domain Receptor 1 (DDR1) is a collagen - responsive cell surface protein that has a kinase enzyme activity in its tail. We have shown that DDR1 is made by liver cells in increased amounts after hepatocyte injury and that the size and excitation state of DDR1 alters in injured human liver.

The group also studies the immunobiology of chronic hepatitis C infection. These studies have been in two particular areas. (1) Analysis of liver biopsy material in patients with chronic hepatitis C at different stages of liver injury. These studies have included serum analysis of antioxidant levels in the peripheral blood as well as hepatic gene expression using gene array technology. The gene array data has identified novel molecules that may be important in the pathogenesis of steatosis, fibrosis and inflammation. For example, we have identified a strong correlation between the expression of the chemokine CCL21 with portal tract inflammation and Claudin 10 with hepatic fibrosis. This work involves a major collaboration with the Storr Liver Unit at Westmead and the bioinformatician Dr Rohan Williams of UNSW . (2) The second area has been the study of hepatitis C infection following liver transplantation. Hepatitis C related infection is much more aggressive in this setting. We have previously documented the intrahepatic inflammatory response against the virus in this situation. More recent studies have examined viral levels in approximately 90 patients following liver transplantation including 500 samples and have identified poor outcomes associated with early peak viral levels.

Highlights:

- DPIV and DP9 make epithelial cells less adherent and slower to migrate and DP9 can stimulate cell death. In contrast, FAP causes increased liver stellate cell migration and adhesion *in vitro*.
- FAP and DPIV gene deficient mouse livers exhibited less fibrosis and less inflammation, which greatly adds to our accumulated data that strongly indicates that FAP has an important pro-fibrotic role in the liver.
- Completed cloning of DPL2 (DPP10) showed that it lacks enzyme activity, even when modified (collaboration with C Abbott, Flinders University).
- Discovered that DP8 has two enzyme activities.
- Crystallised DPIV protein (collaboration with O El Kabbani, Monash University).
- Interesting genes including osteopontin, claudin 10 and annexin II are associated with human alcoholic liver disease (collaboration with PS Haber, Royal Prince Alfred Hospital).
- Dr Mark Gorrell was appointed Principal Research Fellow by the University of Sydney.

Transplantation

Project Leader: Dr Alex Bishop

The goal of the Liver Transplantation group is to identify natural treatments to prevent rejection of transplanted organs so as to minimise use of the powerful but dangerous drugs that are used to treat transplant patients. To achieve this goal we have been examining animal models where a transplanted organ is not rejected. This outcome is most unusual as almost all organs are rejected unless the recipient is given drugs, called immunosuppressives. There are two models where completely mismatched organs are accepted without the recipient being given any treatment. One is where a liver is transplanted in a rat model and the other is where a kidney is transplanted in mice. We have previously found that liver transplant acceptance is associated with rapid and paradoxical immune activation of the recipient's rejection response, which then exhausts itself. This has led to our findings that some of the immunosuppressive drugs that are given to transplant recipients can block long-term acceptance and thus lead to a situation where they cannot be discontinued lest the graft is rejected. This, in combination with our findings that donor leukocytes are required for liver transplant acceptance, has led to our examining a novel treatment protocol in a large animal model. This involves administration of donor leukocytes in combination with optimised immunosuppression that will not inhibit tolerance.

The other model of transplant acceptance involves transplantation of a kidney in a mouse model and although the outcome is similar to the rat liver transplant model, the mechanism by which this occurs appears to be different. Acceptance in the mouse model does not depend on donor leukocytes but instead appears to be associated with much higher levels of a marker of regulatory T cells in the kidney. Comparison of kidney acceptance with rejection of a heart in the same donor/recipient combination showed a marked increase in the forkhead box p3 transcription factor, which is closely associated with a population of immune cells that is capable of suppressing an immune response. In collaboration with Dr Stephen Alexander at the Children's Hospital, Westmead, we are examining this mechanism for transplant acceptance.

Highlights:

- Establishment of a large animal model to investigate novel treatment protocols for inducing transplant acceptance.
- Identification of a mechanism for kidney transplant acceptance in mice that differs from the mechanism of liver transplant acceptance in rats.
- Identification of the patterns of gene expression in liver transplant tolerance compared to rejection.
- Selection of the work of PhD student Shaun Cordoba for presentation in the President's Prize symposium at the Scientific Meeting of the Transplantation Society of Australia and New Zealand.
- Appointment of Alex Bishop as Guest Professor at the Second Military Medical University of Shanghai.

Molecular Cardiology

Group Head: Associate Professor Chris Semsarian

The Agnes Ginges Centre for Molecular Cardiology is focused on the integration of basic laboratory research in heart disease and clinical cardiology. While there are several lines of integrated research within the laboratory, the unifying main focus is the study of cardiovascular disorders which are caused by underlying genetic abnormalities. There are now over 40 cardiovascular diseases which have been identified to be directly caused by primary genetic abnormalities.

Despite the escalation in our knowledge of the genetic causes of cardiac disease, little is known about the molecular steps which determine how a defect in the DNA leads to the clinical disease we see in patients. Furthermore, studies have shown marked variability in the degree of clinical expression of the abnormal gene. There are many examples of affected individuals within the one family, who are carrying the same gene (DNA) defect, having vastly different clinical features and outcomes. This suggests modifying factors, both environmental (e.g. exercise, diet) and secondary genetic influences, play an important role in modifying the clinical phenotype in genetic cardiac disorders.

The aims of this laboratory are to understand the molecular basis of how gene mutations lead to cardiac disease and how these pathogenic mechanisms are influenced by modifying factors. These aims are being addressed in an integrated research program utilising three concurrent sets of studies; in isolated cells, in genetically-modified mice, and in humans with inherited cardiovascular disorders attending the Genetic Heart Disease Clinic at RPAH. Two particular areas of interest are understanding the genetic basis and triggers of sudden cardiac death in the young, with a specific focus on the most common structural cause of sudden death, Hypertrophic Cardiomyopathy (HCM, Figure 1). HCM is characterised by marked thickening of the heart muscle and occurs in approximately 1 in 500 people, making it the commonest genetic heart disorder known. Our research program has seen and collected clinical information and DNA in over 300 HCM families to enable genetic studies to be performed. To complement the studies in humans, our laboratory has developed two unique transgenic models of HCM, as well as cell culture models to evaluate the cellular effects of specific gene mutations.

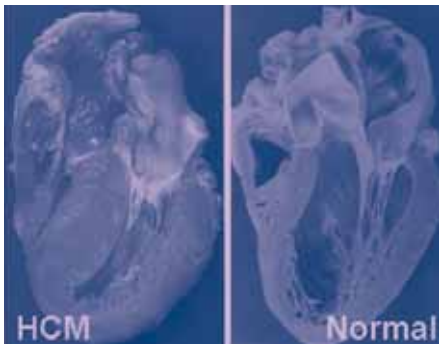


Figure 1

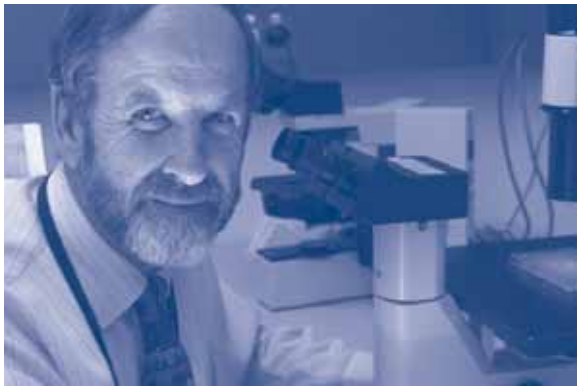
Understanding the basic biology of heart muscle function and therefore defining novel ways to treat heart muscle disorders clearly has wider implications for a variety of cardiovascular disorders, including cardiomyopathies, heart rhythm disorders and coronary artery disease. The potential therapeutic boundaries are limitless. Integration of molecular biology, genetic technologies and clinical medicine will ultimately reduce human heart diseases and prolong life. It is the focus of our research to realise these goals in the coming years.

Highlights:

- Early identification of young patients with genetic heart disease at high risk of sudden death and successful prevention of sudden death by treatment with implantable cardioverter defibrillators.
- Discovery of multiple gene mutations (i.e. 2 disease gene defects), associated with more severe disease, within families with hypertrophic cardiomyopathy.
- Identification of both clinical and genetic differences between males and females with inherited heart muscle diseases.
- Development and investigation of genetically-engineered mouse models of human heart disease.
- Ms Christine Chiu, a research assistant in the laboratory, awarded a prestigious NHMRC - National Heart Foundation of Australia co-funded scholarship to commence her PhD studies in 2006 investigating genetic mechanisms in inherited heart diseases.

Mycobacterial Research

Group Head: Professor Warwick Britton



The Mycobacterial Research Group studies various aspects of the immunological control of tuberculosis and leprosy. This includes the study of lymphocyte recruitment and cytokine production required to control pulmonary tuberculosis, and the development of subunit and live vaccines against pathogenic mycobacteria. More recently the group has studied the gene responses of macrophages to mycobacterial and HIV infection and genetic factors influencing the development of tuberculosis and leprosy.

A major focus of the Mycobacterial Research Program is investigating ways of improving subunit vaccines against tuberculosis and the biology of mycobacterial proteins. There are over 430 proteins of the estimated 3,900 proteins in *Mycobacterium tuberculosis* which have secretory signal sequences suggesting they are exported across the membrane of mycobacteria. A number of these secreted proteins have important functions in the assembly and activity of mycobacterial cell walls, however, the majority have no identified function. We are studying a family which have secreted proteins which have homology with cutinase, an enzyme which is a virulence factor in pathogenic fungi. Dr Nicholas West in the group has expressed four of these 7 proteins and successfully refolded these so that they have enzymatic activity. He has discovered that a number of the cutinases have different enzyme functions suggesting they play a variety of roles in the cell wall metabolism. In related studies, we examined the protective effect of the seven cutinase proteins when delivered in the form of DNA vaccines. Four of the cutinases induced protection against aerosol infection with virulent *Mycobacterium tuberculosis*, and we are now concentrating on immune responses to these four antigens. Dr West has established a collaboration with Dr Joel Mackay in the School of Molecular and Microbial Sciences, University of Sydney, to study the structure of one of the protective cutinase proteins.

We have previously shown that DNA vaccines expressing a single mycobacterial secreted protein induced partial protection against aerosol tuberculosis infection in mice. In a collaboration with Dr Scott Thompson at John Curtin School of Medical Research, ANU, we have developed novel vaccines called SAVENES which contain the antigenic sequences of multiple proteins of *M. tuberculosis*. We have recently demonstrated that one of these SAVENE vectors expressing four secreted proteins of *M. tuberculosis* is protective in the mouse model of experimental tuberculosis. Over the coming year we will examine in detail the immunological and protective properties of these SAVENE vaccines.

Ms Teresa Wozniak is continuing to explore the virology of cytokines which stimulate a Th1 type of cellular immunity necessary for protection against tuberculosis. She has shown that plasmids expressing interleukin-12 and IL-23, but not another cytokine, IL-27, when delivered with DNA vaccines expressing the immunodominant tuberculosis antigen 85B, enhanced the T cell response to the mycobacterial protein. This increased T cell response was associated with a significant increase in protection when either IL-12 or IL-23 were co-administered. Teresa has then examined the effects of these cytokine adjuvants in mice which are deficient for a protein chain common to IL-12 and IL-23. These IL-12p40 gene-deficient mice are unable to develop a protective immune response against tuberculosis because the mice fail to develop T cells reactive of the organism. In addition, the IL-12p40 gene-deficient mice are unable to mount a protective immune response to BCG vaccine, which is the only currently licensed vaccine against tuberculosis, as well as the novel DNA vaccines. When IL-12 or IL-23 were delivered as plasmid with the DNA vaccines, a cellular immune response developed. This was associated with the release of interferon-gamma which is the critical protective cytokine against tuberculosis infection. The level of response to the DNA vaccine with the cytokine adjuvants were similar to that seen in wild-type mice given the vaccine alone. This translated into an improved protective response against experimental tuberculosis infection. These studies indicate that IL-23 is able to complement deficiency of IL-12 in the initiation of a Th1 T cell response when previously it was thought that IL-12 was essential for this to develop. We are now examining the long term protective effects of these cytokines.

A new study initiated in 2005 was the study on mycobacterial lipoproteins. Frank Kao, an honours student in the laboratory, developed cell lines expressing toll-like receptor molecules. Toll-like receptor 2 and Toll-like receptor 4 molecules are present on dendritic cells, which are essential for their early response to foreign infection. Cell lines expressing TLR2 or TLR4, and a combination of TLR1 and TLR2, have been developed. These cell lines will allow us to study the adjuvant properties of a number of novel adjuvants. In addition, we can study the effects of components of mycobacteria on stimulating innate immune responses to mycobacteria.

Dr West and Ms Sultana Mahmuda have expressed a mycobacterial lipoprotein which may be one candidate for stimulating toll-like receptors. The gene encoding this protein, MPT83, is a component of genetic vaccines developed in the laboratory, and we shall use the soluble refolded protein to examine immune responses to this protective antigen of avium mice and humans.

Ms Gabriella Ige completed a collaborative study with colleagues at Westmead Millennium Institute on the interaction of *M. tuberculosis* and HIV infection on human macrophages. *M. tuberculosis* dominates the cellular gene response to co-infection with both pathogens.

Highlights:

- Definition of the function and protective effect of cutinases of *Mycobacterium tuberculosis*.
- Delineation of the adjuvant effects of IL-12 and IL-23 on improving vaccines against tuberculosis.
- Demonstration that *M. tuberculosis* dominates the gene response of macrophages co-infected with HIV and *M. tuberculosis*.

Host Response to Infection

Project Leader: Dr Bernadette Saunders

Our group is examining the host response to mycobacterial infection in humans as well as utilising mouse models to examine key components of this immune response. The overall aims of our research are to understand how protective immunity to tuberculosis (TB) is generated and maintained, and to develop alternative therapies and treatments for combating this disease.

This year has seen the expansion of our research into the genetic control of mycobacterial infection. Suran Fernando, who is currently completing his PhD, has continued his research, into the function of the P2X7 receptor. ATP stimulation of the P2X7 receptor induces a calcium flux within macrophages and activates a number of cellular functions including caspase activation and phago-lysosome fusion, which can result in mycobacterial killing. In collaboration with Professor James Wiley at Nepean Hospital and Dr Guy Marks at the Woolcock Institute we have shown that a number of single nucleotide polymorphisms in the P2X7 gene significantly reduce ATP mediated mycobacterial killing. During 2005 we completed a 4 year study to examine the frequency of one of these loss-of-function polymorphisms, the 1513A-C. We have screened two separate cohorts of TB patients and controls in Sydney and have determined that expression of the 1513C allele increases susceptibility to extrapulmonary TB.

We are continuing these studies, along with investigations to identify other polymorphisms that may be risk factors for the development of tuberculosis disease.

We have also continued our studies examining the function and mechanism of action of members of the TNF superfamily in control of experimental tuberculosis and *Listeria* infection. We have shown that both TNF and lymphotoxin are essential for normal granuloma formation and resistance to these intracellular pathogens. Further work has now shown that, in the absence of soluble TNF, transmembrane TNF can control acute tuberculosis infection, and low dose *Listeria* infection and is sufficient for complete protection against secondary infection. We have now also shown that another TNF superfamily member, known as LIGHT, plays a role in the early control of tuberculosis infection, but is not essential for resistance to either tuberculosis or *Listeria* infection.

We have also extended collaborations with colleagues in the USA and Nepal studying genetic susceptibility to Leprosy, which is caused by another member of the mycobacterial family, *Mycobacterium leprae*, and the role of TNF superfamily members in the control of this pathogen.

Highlights:

- Demonstrated that a single nucleotide polymorphism in the gene encoding the P2X7 receptor is associated with increased susceptibility to extrapulmonary tuberculosis.
- Determined that transmembrane TNF alone is sufficient for induction of primary and secondary protective immunity against *Listeria* infection.
- Awarded NHMRC funding for a new, collaborative project between the Mycobacterial Research Programme and Professor John Rasko and Dr Charles Bailey in the Gene and Stem Cell Therapy Programme to design and test alternative therapies to treat TB.

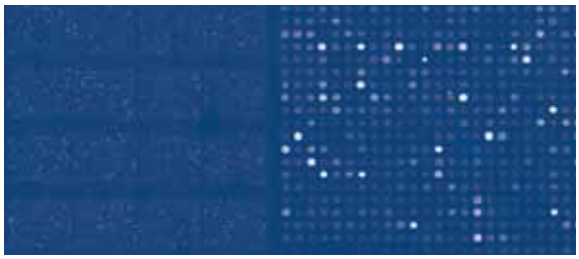
Vaccine Development and Mycobacterial Pathogenesis

Project Leader: Dr James Triccas

A major research focus of the group aims to develop anti-tuberculosis strategies more effective than the current vaccine, *M. bovis* BCG. One approach under investigation is to over-express important *M. tuberculosis* antigens in BCG, either those lacking from the vaccine or those demonstrated to invoke protection. Work by Umamainthan Palendira has shown that recombinant BCG secreting two dominant *M. tuberculosis* antigens stimulated stronger protective immunity than BCG alone. This BCG strain is currently under evaluation as part of the NIH Tuberculosis Vaccine Testing Contract at the University of Colorado. BCG is also being engineered to produce mammalian molecules important in the host immune response, such as cytokines and chemokines, which may enhance the effectiveness of BCG-based vaccines and therapeutic agents. A PhD student in the laboratory, Mr Anthony Ryan, has demonstrated that secretion of chemokines by BCG can markedly improve the ability of the vaccine to control tuberculosis in mice. These studies were performed with Professor Mike O'Donnell from the University of Iowa and the vaccine strains are being prepared for pre-clinical testing at the University of Colorado. Mr Ryan and Miss Joanne Spratt have also constructed a new series of protein expression vectors to facilitate the development of new mycobacterial vaccine strains.

On-going collaborative studies with Professor Thomas Leyh at the Albert Einstein College of Medicine investigate sulphur metabolism in mycobacteria and its role in virulence. This work has resulted in a recent joint publication in the Journal of Biological Chemistry. Dr Rachel Pinto, a former PhD student in the Mycobacterial Research Group, is now undertaking postdoctoral studies in the laboratory of Professor Leyh in New York.

The laboratory is also broadening it focus by investigating host/pathogen interactions of other medically important micro-organisms. Collaborations have recently been established with Professor Peter Reeves and Dr Dee Carter from the School of Molecular and Microbial Biosciences at the University of Sydney, investigating the host response to *Salmonella* and *Cryptococcus* infections.



A microarray slide showing the response of cells to infection with *Mycobacterium tuberculosis*.

Highlights:

- A new tuberculosis vaccine developed in our laboratory has been selected for pre-clinical testing at the University of Colorado, USA as part of a global vaccine testing programme.
- Collaborative studies with Professor Tom Leyh in New York have further defined the pathway of sulphur utilisation in *Mycobacterium tuberculosis*.
- We have developed a new series of gene expression vectors that will markedly improve the ability to develop new mycobacterial vaccine strains and produce recombinant antigens for vaccine studies.
- Dr Triccas was awarded a prestigious NMHRC RD Wright Biomedical Career Development Award to further his work into bacterial pathogenicity and vaccine development.

T Cell Biology

Group Head: Associate Professor Barbara Fazekas de St.Groth

The T Cell Biology Research Program aims to understand the early interactions between T cells and dendritic cells. These interactions are crucial for the subsequent control of the immune response, and it is likely that the major defects that predispose to allergic, autoimmune and immunoinflammatory disease involve these early processes. By understanding how they are controlled, we hope to provide a basis for new therapies to prevent and treat immunological diseases, which are becoming increasingly common in Western communities and now affect at least 20% of the population.

Dendritic cell function *in vivo*

Our dendritic cell research program, led by Dr Elena Chklovskaia, has established novel methods for tracking the function of individual dendritic cell subsets *in vivo*. By using transgenic models expressing cognate T cell receptors and MHC under the control of various promoters, we can restrict presentation of specific antigen to particular subsets of dendritic cells. In particular, we are studying the function of dendritic cells derived exclusively from either lymphoid-restricted or myeloid-restricted haemopoietic progenitor cells. In a second model, antigen presentation is restricted to the Langerhans cells of the skin. These approaches are indicating that many of our assumptions about the ability of different dendritic cell subsets to generate immunological memory may not be valid.

Dendritic cell subsets in lymph node, identified using immunohistochemistry

A second area of interest is the ability of dendritic cells to exchange pre-formed antigen-MHC complexes *in vivo*. By injecting labelled dendritic cells loaded with peptide, we have shown that peptide-MHC derived from the injected cells is able to rapidly travel deep into the T cell area of the draining lymph node, while the donor cells are still located superficially. This mechanism distributes antigen-MHC to all the T cells in the node, rather than the small number that actually come into contact with injected dendritic cells. We believe that this mechanism is used to increase the speed with which the T cell repertoire can be scanned for high affinity cells of appropriate specificity. Our current studies are aimed at elucidating the cell biology of peptide-MHC exchange.

Dendritic cells (white arrows) entering a lymph node

Regulatory T cells

CD4+CD25+ regulatory T cells have been implicated in prevention of immunological disease in both mouse and man. Our murine studies have focused on the requirement for IL-2 and CTLA-4 for maintenance of normal regulatory T cell number and function. When regulatory T cells are deficient, mice become susceptible to inflammatory bowel

disease because T cells respond to endogenous antigen that they would normally ignore. Increased expression of costimulatory molecules by dendritic cells appears to contribute to this abnormal response. Regulatory T cells can control the level of costimulation, and regulatory T cell deficits therefore allow abnormally high costimulation.

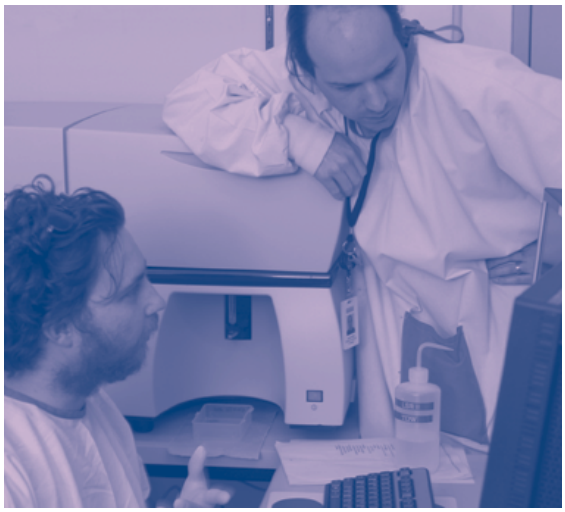
To test whether regulatory T cells are also deficient in patients with inflammatory bowel disease, we have measured the number of regulatory T cells in blood, mesenteric lymph nodes and bowel mucosa of patients with Crohn's disease and ulcerative colitis. To do this, we had to develop a new method to identify human regulatory T cells. This method, which is being developed as a test for clinical laboratories, was patented recently. Young patients with inflammatory bowel disease showed a selective deficit in naïve regulatory T cells, irrespective of disease type, activity or therapy. This deficit was apparent at the age of peak disease onset, strongly suggesting that it serves as a susceptibility factor for inflammatory bowel disease.

Highlights:

- Developed new methods for selective reconstitution of murine dendritic cell subsets, to allow precise tracking of individual dendritic cell function *in vivo*.
- Demonstrated that preformed peptide-MHC complexes can be transferred between dendritic cells *in vivo*, speeding up screening for antigen-specific T cells within the draining lymph node.
- Demonstrated that CD4+ T cells compete with each other for access to peptide-MHC complexes, but not for access to other cell surface molecules or dendritic cells themselves.
- Developed and patented a new method for identifying human regulatory T cells.
- Identified primary deficits in regulatory T cells in patients with Inflammatory Bowel Disease.
- Demonstrated that memory T cells are essential for organ graft rejection, underlining the importance of targeting new therapies to memory cells rather than naïve cells.

Core Facilities

Flow Cytometry Facility



Flow Cytometry involves the high speed measurement of multiple characteristics of cells in a stream of fluid that moves past a focused beam of light. As a cell passes the beam, light is both scattered from the cell and emitted from any fluorescent molecules incorporated in or attached to that cell. By collecting this light, information can be gathered about the type of cells that are present and the state they are in. Furthermore, some flow cytometers incorporate the ability to sort the cells into different fractions at high speeds thus enabling the purification of rare cell populations for further study.

Flow cytometry and cell sorting are key technologies that are used extensively by most of the groups at Centenary. In June 2005 Centenary took delivery of three new flow cytometers from Becton Dickinson (BD) Biosciences valued at $1.7 million. Without a doubt we are now one of the top two flow cytometry facilities in Australia, offering our researchers with unrivalled access to state-of-the-art equipment with very wide-ranging applications. Centenary's facility is very well equipped with three cell sorters - the new BD FACSAria (equipped with 3 lasers and capable of using up to 11 different fluorescent markers for analysis and sorting of up to 25,000 cells/second at purities of over 99%), a BD FACSVantageDiVa (equipped with 3 lasers, and capable of simultaneous measurement of 10 parameters and sorting cells at up to 20,000 per second) and a BD FACStarPlus (2 lasers, 7 parameters). In addition the facility houses four flow analysers - a new BD FACSCanto (2 lasers, 8 parameters), a new BD LSR-II (4 lasers, 15 parameters), a BD FACSCalibur (2 lasers, 6 parameters) and a BD FACScan, (1 laser, 5 parameters).

Microinjection Facility

The use and development of the latest transgenic (overexpression of a single gene) and knockout (deletion of a single gene) technology has for many years been a high priority for Centenary. The first transgenic mice at Centenary were created in the mid 1980s, the first knockout mice in the mid 1990s and the facility continues to produce new strains every year. Centenary's transgenic and knockout mice are the subject of hundreds of scientific publications. Mouse sperm freezing techniques are also performed at the facility enabling the storage of mouse strains in liquid nitrogen for future use without the ongoing costs of maintaining a mouse colony.

Mouse Cardiac Physiology and Function Facility

In evaluating the cardiac phenotype in genetically-engineered mice, the Agnes Ginges Centre for Molecular Cardiology at Centenary has developed a facility which allows *in vivo* analysis of several cardiac parameters including:

- Blood pressure measurement (tail-cuff)
- Electrocardiography (ECG)
- Electrophysiological stimulation studies
- Echocardiography

In addition, there is a mouse exercise facility (running and swimming) which allows the role of exercise on the cardiac phenotype to be evaluated.

PC3 Laboratory

Centenary houses a PC3 containment facility that allows work on level 3 pathogens such as *Mycobacterium tuberculosis*. The facility contains equipment permitting cell culture, genetic manipulation of bacteria and aerosol exposure system for animal infection models.

Animal Facility

Genetically modified mouse lines are bred under Level 2 Specific Pathogen Free conditions in the Centenary Institute Animal Facility. Climate control, strict hygiene and sterilisation procedures, the provision of quality irradiated feed and environmental enrichment provide an optimal environment for the mice. The PC2 approved facility offers differing levels of containment with dedicated areas for immunodeficient mice, infectious studies and quarantine. The facility is an Australian Quarantine approved premise.

Postgraduate Training Programme

An objective of the Centenary Institute is the development of the next generation of research leaders through our student programme. The Centenary Institute is closely affiliated with the University of Sydney and Royal Prince Alfred Hospital. Conveniently located on the grounds of the hospital adjacent to the University's main campus, we provide students with access to facilities, support and opportunities available at both of these organisations.

Our student body is made up of a group of students from diverse ethnic and academic backgrounds with the common goal of achieving excellence. This year the student body at Centenary comprised of 33 PhD and 13 Honours students. Our PhD students have the opportunity in their final year to visit laboratories overseas to establish connections and seek placements for their scientific careers.

Centenary's Student Affairs Subcommittee oversees the activities of PhD students at Centenary. Every year the Committee assesses the progress of PhD students who are half way through their candidature (approximately 18 months for full-time students). For their Midpoint Review, candidates must submit a report on their work to the Committee and are subsequently interviewed on the contents of their report. The purpose of the interview is to examine the overall strategy of the project, data obtained to date and future directions. In this way any problems which have arisen or are likely to arise can be identified and discussed. Thus the interview acts as a medium for constructive suggestions for both candidates and supervisors.

Centenary hosts Postgraduate Seminars as part of its student programme, providing students with a broader exposure to immunology than the area of their studies. These seminars are held between May and November each year and are presented by Centenary researchers as well as invited national and international scientists. Students are encouraged to fully participate in the discussions during these and other Centenary presentations. The 2005 Postgraduate Research Workshops were sponsored by ASI NSW. Many thanks to PhD students Dr Tri Phan and Ms Cindy Ma for organising the seminars.

Our thanks go to Centenary's 2005 Postgraduate Co-ordinators A/Prof Barbara Fazekas de St.Groth (Jan-June) and A/Prof Chris Semsarian (July-Dec) for their hard work. We would like to congratulate all of the candidates who successfully completed their Midpoint Reviews, submitted their Thesis or were awarded their Doctorates in 2005.

Midpoint Reviews

PhD Student	Supervisor(s)	Group
Lye Lin Ho	Prof Antony Basten/Dr John Allen	Cancer Drug Resistance
Jennifer Randall	Prof John Rasko/Prof Antony Basten	Gene & Stem Cell Therapy
Sunmi Song	Dr Mark Gorrell/Prof Geoff McCaughan	Liver Immunobiology

PhD Submissions

Student	Supervisor	Thesis Title
Gabriella Ige	Prof Warwick Britton/Dr Jamie Triccas	Macrophage Gene Responses to *Mycobacterium tuberculosis* and HIV and Genetic Approaches to Vaccine Development
Cindy Ma	Dr Stuart Tangye/Prof Antony Basten	Elucidating the cellular defects in X-linked Lymphoproliferative disease resulting from mutations in SH2D1A
Joohong Park	Dr Mark Gorrell	Expression, purification and characterization of dipeptidyl peptidase 8 and DPIV

PhDs Awarded

Student	Supervisor	Thesis Title
Jennifer Cropley	Prof John Rasko	Epigenetics of retrotransposons in the mouse
Xiao Xuan Huang	Dr Mark Gorrell/ Prof Geoff McCaughan	The cirrhotic transcriptome in hepatitis B and C carcinoma
Tri Giang Phan	Dr Robert Brink	Cellular and molecular aspects of B Cell responses
Rachael Pinto	Prof Warwick Britton/ Dr Jamie Triccas	Genetic approaches to vaccines designed against tuberculosis
Marilyn Thien	Dr Robert Brink/Prof Antony Basten	Analysis of factors regulating self-reactive B cell fate

Masters Submissions

Student	Supervisor	Thesis Title
Vanessa Gysbers	Prof John Rasko	Homology-mediated silencing of retroviral vectors in mammalian stem cells

2005 Postgraduate Research Workshop Programme

Speaker	Title	Date
Prof David Vaux Molecular Genetics of Cancer, Walter & Eliza Hall Institute	Ten rules of thumb for the presentation of your data in publications, and criticism of everyone else's	3rd May
Dr Robert Brink B Cell Biology, Centenary Institute	Knock-in sense into knockouts	18th May
Dr Stephen Adelstein Clinical Immunology, Centenary Institute	Human models of autoimmunity	1st June
Prof Chris Parish Cancer and Vascular Biology, The John Curtin School of Medical Research	The story of CFSE	15th June
Dr Jenny Kingham B Cell Biology, Centenary Institute	All mice are equal but some are more equal than others	29th June
A/Prof Barbara Fazekas T Cell Biology, Centenary Institute	Women and Science	13th July
Dr John Allen Cancer Drug Resistance, Centenary Institute	The great flu pandemic of 1918, and the coming one	27th July
Prof Charles Mackay Immunology and Inflammation Research, Garvan Institute	How to make money in science	7th September
Dr David Fulcher Department of Immunopathology, Westmead Hospital	Human immunodeficiencies and other catastrophes	21st September
Dr Stuart Tangye Lymphocyte Differentiation, Centenary Institute	Immunological memory - deviating from the dogma	19th October
Professor Antony Basten B Cell Biology, Centenary Institute	Serendipity and science	23rd November

2005 Seminar Series

Centenary Institute Seminars are an opportunity for scientists to gather and discuss recent scientific work, and to share ideas and results. Presentations are given by Centenary staff, as well as visiting local and international researchers.

Centenary hosts seminars every Tuesday at 1pm in the Level 6 Lecture Theatre.

We would like to thank our organisers Dr John Allen and Dr Nick West, the sponsors for their generous support, and all the presenters for sharing their knowledge and research findings, making this a most successful 2005 Seminar Series.

Speaker	Title	Date
Ms Marilyn Thien Centenary Institute, NSW, Australia	Excess BAFF creates HEL in the forbidden zones	22nd February
Prof Iain Campbell University of Sydney, NSW, Australia	Cytokine-mediated inflammation and disease-associated signalling circuits in the central nervous system	1st March
Prof Roland Stocker University of New South Wales, NSW, Australia	Atherosclerosis and oxidative processes; where is the link?	15th March
Dr Andrew Katsifis ANSTO	Radiopharmaceuticals and Molecular Imaging - New Tools for an Old Disease	22nd March
Dr Simon Barry University of Adelaide, SA, Australia	Lentiviral vectors for gene delivery and gene validation and the targeting of genes for regulatory T cell function	29th March
Dr Kerstin Meyer Cambridge Institute of Medical Research, UK	Regulation of gene expression and gene conversion at the chicken IgL locus	5th April
Prof Ian MacLennan University of Birmingham, UK	Requirement for antibody and CD4 effectors for protection against salmonella needs a novel vaccine strategy	12th April
Dr Scott Thomson Australian National University, John Curtin School of Medical Research, NSW, Australia	Genetic Based T cell Vaccine Strategies	19th April
Dr Qihan Dong University of Sydney, NSW, Australia	Annexin and phospholipase A2 in prostate cancer	26th April
Prof David Vaux Walter & Eliza Hall Institute, Vic, Australia	Paradigms Lost - Cell death mechanisms of mammalian cells	3rd May
Dr Rachel Kohler Centenary Institute, NSW, Australia	Targeting the migration of T cells: implications for MS research and therapy	17th May
Dr Rebecca Mason University of Sydney, NSW, Australia	Vitamin D - from the sun, for the sun	24th May
Prof Simon Hawke University of Sydney, NSW, Australia	The immunology of prion diseases	31st May
Prof Alan Landay Rush University Medical Centre. Illinois, USA	Innate Immunity in HIV Disease: Potential for Immune Based Therapy	21st June

Prof Julian Rood Monash University, Vic, Australia	The pathogenesis of clostridial myonecrosis	28th June
Dr Tracy Bryan Children's Medical Research Institute, NSW, Australia	Interaction of telomerase with its DNA substrate	5th July
Prof Redwan Moqbel University of Alberta, Canada	Immune deviation in allergy & asthma; role of the eosinophil, IFN-gamma, tryptophan and IDO	11th July
Prof Jan Hendrik Richardus ANZAC Research Institute, NSW, Australia	Pharmacogenomics of drug clearance in cancer: tumour-derived inflammation represses drug metabolism and transport	19th July
Prof Jacob Golenser University of Sydney, NSW, Australia	Oxidative stress and malaria	2nd August
Prof Marc Feldmann Imperial College London, UK	TNF: from mediator of host defense to therapeutic target	12th August
Prof Georges Grau Université de la Méditerranée, France	Importance of Microvesiculation in the pathophysiology of cerebral malaria	16th August
Dr Jamie Triccas Centenary Institute, NSW, Australia	Making better tuberculosis vaccines	6th September
Prof Stephen Harrap University of Melbourne, Vic, Australia	Challenges for Cardiovascular Genetics	13th September
Dr Rosanne Taylor University of Sydney, NSW, Australia	Stem cell, gene transfer and protein replacement therapies in models of inherited neurological disease	20th September
Prof Juergen Reichardt University of Sydney, NSW, Australia	SNPing Away at Human Diseases: A “Renaissance” of Biochemical Genetics	4th October
Prof John Harley University of Oklahoma, USA	Immunochemistry Implicates Epstein-Barr Virus in Systemic Lupus Erythematosus	14th October
A/Prof Lea Dellridge University of Melbourne, Vic, Australia	Big hearts are bad news - cellular insights	25th October
Dr Juergen Götz University of Sydney, NSW, Australia	Alzheimer's disease addressed by transgenesis and functional genomics	1st November
Dr Kevin Francis Xenogen Corporation, Australia,	SYMPOSIUM- *In vivo* bioluminescent imaging i.e. IVIS	8th November
Dr Filip Braet Australian Key Centre for Microscopy & Microanalysis, USyd, NSW, Australia	The hepatic endothelium: a gateway for traversing macromolecules and cancer cells	15th November
Prof Maggie Bassendine University of Newcastle, UK	Hepatitis C; interaction with host lipid metabolism	22nd November
Dr Nina van Sorge UMC Utrecht, The Netherlands	Unraveling post-infectious auto-immune disease - Guillain-Barre syndrome	24th November
Ms Alex Spencer Centenary Institute, NSW, Australia	Nothing but a bit of healthy competition ...between T cells at least	29th November

2005 Publications

1. Adams LA, Bulsara M, Rossi E, Deboer B, Speers D, George J, Kench J, Farrell G, McCaughan GW, Jeffrey GP (2005) Hepascore: An Accurate Validated Predictor of Liver Fibrosis in Chronic Hepatitis C Infection. Clin Chem, 51:1867-1873.
2. Allen JD, Zhang XD, Scott, C.L, Boyle GM, Hersey P, Strasser A (2005) Is Apaf-1 expression frequently abrogated in melanoma? Cell Death Differ, 12:680-681.
3. Avery DT, Ellyard JI, Mackay F, Corcoran LM, Hodgkin PD, Tangye SG (2005) Increased expression of CD27 on activated human memory B cells correlates with their commitment to the plasma cell lineage. J Immunol, 174:4034-4042.
4. Bandara P, George J, McCaughan G, Naidoo D, Lux O, Salonikas C, Kench J, Byth K, Farrell GC (2005) Antioxidant levels in peripheral blood, disease activity and fibrotic stage in chronic hepatitis C. Liver Int, 25:518-526.
5. Baxter AG, Jordan MA, Silveira PA, Wilson WE, Van Driel, IR (2005) Genetic control of susceptibility to autoimmune gastritis. Int Rev Immunol, 24:55-62.
6. Bertolino P, Bowen D, Zen M, McCaughan G (2005) Autoimmune hepatitis in transgenic mouse models: what lessons can be learnt?: Series: Falk Symposium, Vol. 142 Dienes HP, Leuschner U, Lohse AW, Manns, MP (Eds). Ch 8:60-72.
7. Bertolino P, Schrage A, Bowen DG, Klugewitz K, Ghani S, Eulenburg K, Holz L, Hogg N, McCaughan GW, Hamann A (2005) Early intrahepatic antigen-specific retention of naive CD8+ T cells is predominantly ICAM-1/LFA-1 dependent in mice. Hepatology, 42:1063-1071.
8. Bohmer C, Broer A, Munzinger M, Kowalczuk S, Rasko JE, Lang F, Broer S (2005) Characterization of mouse amino acid transporter B0AT1 (slc6a19). Biochem J, 389:745-751.
9. Bowen DG, McCaughan GW, Bertolino P (2005) Intrahepatic immunity: a tale of two sites? Trends Immunol, 26:512-516.
10. Britton WJ, Gilbert GL, Wheatley J, Leslie D, Rothel JS, Jones SL, Bradley P (2005) Sensitivity of human gamma interferon assay and tuberculin skin testing for detecting infection with *Mycobacterium tuberculosis* in patients with culture positive tuberculosis. Tuberculosis (Edinb), 85:137-145.
11. Broer S, Cavanaugh JA, Rasko JE (2005) Neutral amino acid transport in epithelial cells and its malfunction in Hartnup disorder. Biochem Soc Trans, 33:233-236.
12. Dahlke M, Loi R, Warren A, Holz L, Popp FC, Weiss DJ, Piso P, Bowen DG, McCaughan GW, Schlitt HJ, Bertolino P (2005) Immune-mediated hepatitis drives low-level fusion between hepatocytes and adult bone marrow cells. Journal of Hepatology, 44:334-341.
13. Demangel C, Zhou J, Choo AB, Shoebridge G, Halliday GM, Britton WJ (2005) Single chain antibody fragments for the selective targeting of antigens to dendritic cells. Mol Immunol, 42:979-985.
14. Dilda PJ, Don AS, Tanabe K, Higgins VJ, Allen JD, Dawes IW, Hogg PJ (2005) Mechanism of selectivity of an angiogenesis inhibitor from screening a genome-wide set of *Saccharomyces cerevisiae* deletion strains. Journal of the National Cancer Institute, 97:1539-4157.
15. Doolan A, Tebo M, Ingles J, Nguyen L, Tsoutsman T, Lam L, Chiu C, Chung J, Weintraub RG, Semsarian C (2005) Cardiac troponin I mutations in Australian families with hypertrophic cardiomyopathy: clinical, genetic and functional consequences. J Mol Cell Cardiol, 38:387-393.
16. Dupre L, Andolfi G, Tangye SG, Clementi R, Locatelli F, Arico M, Aiuti A, Roncarolo MG (2005) SAP controls the cytolytic activity of CD8+ T cells against EBV-infected cells. Blood, 105:4383-4389.
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22. Gorrell MD (2005) Dipeptidyl peptidase IV and related

enzymes in cell biology and liver disorders. Clin Sci (Lond), 108:277-292.

23. Gorrell MD and Yu DMT (2005) Diverse functions in a conserved structure: The dipeptidyl peptidase IV gene family. In Robinson, JW (ed.) Trends in Protein Research. Nova Biomedical Books, New York pp. 1-78.

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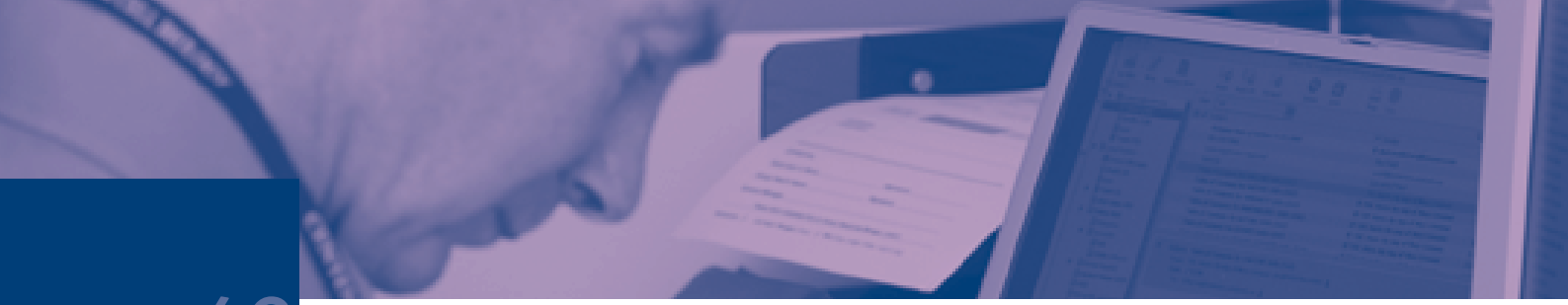

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45. Semsarian C, Seidman JG (2005) Animal models of hypertrophic cardiomyopathy: relevance to human disease. Molecular Mechanisms for Cardiac Hypertrophy and Failure. Parthenon Publishing Group Ltd.

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52. Vinuesa CG, Tangye SG, Moser B, Mackay CR (2005) Follicular B helper T cells in antibody responses and autoimmunity. Nat Rev Immunol, 5:853-865.

53. Wang C, Li J, Cordoba SP, McLeod DJ, Tran GT, Hodgkinson SJ, Hall BM, McCaughan GW, Bishop GA (2005) Posttransplant interleukin-4 treatment converts rat liver allograft tolerance to rejection. Transplantation, 79:1116-1120.

54. Wang XM, Yu DMT, McCaughan GW, Gorrell MD (2005) Fibroblast activation protein increases apoptosis, cell adhesion, and migration by the LX-2 human stellate cell line. Hepatology, 42:935-945.

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56. Wolf CM, Moskowitz IP, Arno S, Branco DM, Semsarian C, Bernstein SA, Peterson M, Maida M, Morley GE, Fishman G, Berul CI, Seidman CE, Seidman JG (2005) Somatic events modify hypertrophic cardiomyopathy pathology and link hypertrophy to arrhythmia. Proc Natl Acad Sci USA, 102:18123-18128.

57. Zahir H, McLachlan AJ, Nelson A, McCaughan G, Gleeson M, Akhlaghi F (2005) Population pharmacokinetic estimation of tacrolimus apparent clearance in adult liver transplant recipients. Ther Drug Monit, 27:422-430.

2005 Presentations

International

Invited presentations

1. Basten A (2005) BCR signalling thresholds in plasma cell differentiation: role of affinity. 10th Annual Australasian Autoimmunity Workshop, Daydream Island.
2. Bertolino P (2005) Role du foie dans la reponse Immunitaire. ENS-Lyon, Lyon, France.
3. Bertolino P (2005) The liver: an immunological oddity. MRC Centre for Immune Regulation, Birmingham University Medical school, UK.
4. Bishop GA (2005) Tolerance induction in clinical liver transplantation. Second Military Medical University of Shanghai. Guest Professor Award, Shanghai, China.
5. Britton WJ (2005) Gaps in our understanding of the disease leprosy. 40th US-Japan Tuberculosis and Leprosy Research Conference, Seattle, USA.
6. Britton WJ (2005) Manipulating the cytokine environment to enhance responses to vaccines against tuberculosis. Keystone Symposium on Tuberculosis. Whistler, Canada.
7. Fazekas de St.Groth B (2005) Transfer of intact peptide-MHC II complexes between dendritic cells *in vivo*. Keystone Symposium 'Dendritic cells', Vancouver, Canada.
8. Gorrell M (2005) Structure and function in dipeptidase peptidase IV and related proteins. Dipeptidyl Aminopeptidases: Basic science and clinical applications. Magdeburg, Germany.
9. Gorrell M (2005) Recent discoveries on the prolyl oligopeptidase gene family. Ferring Research Institute. Southhampton, England.
10. McCaughan GW (2005) Functional genomics and proteomics and the study of liver disease. Digestive Diseases Week. Chicago, USA.
11. McCaughan GW (2005) Gene arrays and liver disease. American Association for the Study of Liver Diseases. San Fransisco, USA.
12. McCaughan GW (2005) Immunobiology of HCV recurrence post liver transplant. International Liver Transplant Society Meeting. Los Angeles, USA.
13. McCaughan GW (2005) Liver transplant for HCV infection. Asia Pacific Association for the Study of Liver. Bali, Indonesia.
14. McCaughan GW (2005) Pathogenesis of HCV recurrence and allograft injury post liver transplant. 41st Annual meeting of Japanese Transplant Society. Niigata, Japan.
15. Rasko JEJ (2005) A Non-Human Primate Stem Cell Model. AVI BioPharma, Corvallis, OR, USA.
16. Rasko JEJ (2005) Gene and Stem Cell Therapy Down Under. Klinik und Poliklinik für Chirurgie, Regensburg University, Germany.
17. Rasko JEJ (2005) Gene Transfer and Virus Receptors. Institut Gustave Roussy, Paris, France.
18. Rasko JEJ (2005) Non-human Primate Models to Study Stem Cell Mobilization. Amgen Thousand Oaks, USA.
19. Tangye SG (2005) Cellular defects resulting from inactivating mutations in SH2D1A, the gene responsible for X-linked lymphoproliferative disease.
20. Tangye SG (2005) Plasma cell differentiation in humans. Keystone Conference: B cell development, function and disease; Steamboat Springs, Colorado, USA. Institute for Gene Therapy, Milan, Italy.
21. Tangye SG (2005) Tracking human B cell differentiation *in vivo* and *in vitro*. University of Birmingham, Alabama, USA.
22. Tangye SG (2005) Tracking human B cell differentiation *in vivo* and *in vitro*. Children's Hospital of Boston, Massachusetts, USA.
23. Tangye SG (2005) Tracking the fate and differentiation of subsets of human B cells *in vivo* and *in vitro*. MD Anderson Cancer Centre, Houston, Texas, USA.

Abstracts, oral and poster presentations

1. Azmanov DN, Rasko JEJ, et al. (2005) Analysis of the SLC6A19 D173N allele in Hartnup Disease. 55th Annual Meeting of The American Society of Human Genetics Salt Lake City, Utah, USA.
2. Aung HT, Flamant S, Lu DP, Read RL, Humphreys DT, Tan SA, Rajasekhar M, Martin DIK, Rasko JEJ (2005) A refined RT-PCR based quantitative technique to identify and characterize new micro RNAs, RNAi and Related Pathways, Keystone Meeting, Vancouver, Canada.
3. Banavara M, Kable EPW, Braet F, Wang XM, Gorrell MD and Cox G (2005) Detection of Collagen by Second Harmonic Microscopy as a Diagnostic Tool for Liver Fibrosis. Multiphoton Microscopy in the Biosciences VI, San Jose, CA, USA.

4. Britton WJ (2005) Manipulating the cytokine environment to enhance responses to vaccines against tuberculosis. Keystone Symposium on Tuberculosis. Whistler, Canada.

5. Britton WJ, Musicki K, Tran S, Briscoe H and Saunders BM (2005) Differential effects of soluble and transmembrane TNF on the control of tuberculosis and *Listeria* infection. Keystone Symposia Whistler, Canada.

6. Bertolino P, Schrage A, Bowen DG, Klugewitz K, Ghani S, Eulenburg K, Holz L, Hogg N, McCaughan GW and Hamann A (2005) Early intrahepatic antigen-specific retention of naïve murine CD8+ T cells is predominantly ICAM-1/LFA-1 dependent. American Association for the Study of Liver Disease, San Francisco, USA.

7. Bryant V, Hodgkin PD and Tangye SG (2005) IgM memory B cells exhibit phenotypic and functional characteristics of naïve and switched memory B cells. Keystone Conference: B cell development, function and disease; Steamboat Springs, Colorado, USA.

8. Cabot MC, Yu JY, Kelly GE, Brown DM, Lucas KM, Tanabe K and Allen JD (2005) Phenoxodiol, a synthetic analog of genistein, generates ceramide and is equipotent in wild-type and multidrug-resistant human tumor cells. American Society of Clinical Oncology Annual Meeting, Orlando FL, USA.

9. Chen T, Gai WP, Chegini F, Park J, Ajami K, Gorrell MD and Abbott CA (2005) Expression and Characterisation of DPL2-S - the Short Form of Dipeptidyl Peptidase Like Protein 2 (DPL2/DP10). Dipeptidyl Aminopeptidases: Basic science and clinical applications, Magdeburg, Germany.

10. Chklovskaia E and Fazekas de St.Groth B (2005) Selective reconstitution of dendritic cell subsets *in vivo*. Keystone Symposium 'Dendritic cells', Vancouver, Canada.

11. Cordoba S, Wang C, Williams R, Sharland A, McCaughan G and Bishop GA (2005). Meta-analysis of transcriptional profiles in three models of transplant tolerance identifies the STAT-1/IRF-1 pathway. Transplantation Society Basic Sciences Symposium, La Baule, France.

12. Cordoba S, Wang C, Wu M, Li J, Bertolino P, McCaughan GW, Alexander SW and Bishop GA (2005) Evidence for suppression rather than deletion, ignorance or immune deviation as the mechanism of spontaneous renal allograft acceptance in a mouse model. Transplantation Society Basic Sciences Symposium, La Baule, France.

13. Fernando S, Baunders B, Sluyter R, Skarratt K, Wiley and Britton WJ (2005) Additive inhibitory effects of Polymorphic alleles of the P2x7 receptor on ATP mediated mycobacterial killing by human macrophages. Keystone Symposia: Tuberculosis: Integrating Host and Pathogen Biology. Banff, Alberta, USA.

14. Good KL and Tangye SG (2005) The molecular mechanisms responsible fore the lower threshold of activation of memory B cells compared to naïve B cells. Keystone Conference: B cell development, function and disease; Steamboat Springs, Colorado, USA.

15. Gracey D (2005) Memory CD4+ lymphocytes are required for the initiation of MHC Class II-dependent skin allograft rejection. American Transplant Congress. Seattle, USA.

16. Grech A, Chan T, Gardam S, Limaye S, Basten A and Brink R (2005) TRAF2 differentially regulates the survival of mature B cells and their progenitors. Keystone Symposium "Survival and Death in Immune Tolerance and Homeostasis", Keystone, CO, USA.

17. Ingles J, Doolan A, Chiu C, Richmond DR, Seidman J, Seidman C and Semsarian C (2005) Identification of compound and double mutations in hypertrophic cardiomyopathy patients: Implications for genetic testing and counselling. American Heart Association Meeting, Dallas, USA.

18. Kable EPW, Cox GC, Boustany S, Wang XM and Gorrell MD (2005) Detection of Collagen by Second Harmonic Microscopy as a Diagnostic Tool for Liver Fibrosis. Microscopy and Microanalysis Conference, Honolulu, Hawaii.

19. Knott HM, Park J, Ajami K and Gorrell MD (2005) Expression, purification, and partial characterisation of Dipeptidyl Peptidase 9. Dipeptidyl Aminopeptidases: Basic science and clinical applications, Magdeburg, Germany.

20. Larsen SR, Chng K, Battah F, Armstrong M, Hayward M, Leung L, Thomson S, Hennessy A, Gibson J, Joshua D and Rasko JEJ (2005) Addition of Pegylated Megakaryocyte Growth Development Factor (pegMGDF) to G-CSF Improves Mobilization of Primitive Haemopoietic Cells. American Society of Hematology, Atlanta, USA.

21. Larsen SJ, Chng K, Battah F, Armstrong M, Hayward M,Leung L, Thomson S, Hennessy A and Rasko JEJ (2005) Cytokine-induced *In vivo* Expansion and Mobilization of Marrow Mesenchymal Stem Cells in Nonhuman Primates. BMT Tandem Meetings, Honolulu.

22. Ma CS, Hare NJ, Nichols KE, Dupre L, Andolfi G, Roncarolo MG, Adelstein S, Hodgkin PD and Tangye SG (2005) Impaired humoral immunity in XLP is due to defective IL-10 production and ICOS expression by

CD4+ T cells. Keystone Conference: B cell development, function and disease. Steamboat Springs, Colorado, USA.

23. Park J, Ajami K and Gorrell MD (2005) Characterization of human dipeptidyl peptidase (DP) 8 produced in insect cells using engineered baculovirus. Dipeptidyl Aminopeptidases: Basic science and clinical applications, Magdeburg, Germany.

24. Park J, Ajami K, and Gorrell MD (2005) Recombinant Human Dipeptidyl Peptidase 8 Has Dipeptidyl Peptidase IV and Prolyl Endopeptidase Activities (Reference Number 402). In. 4th Meeting of the International Proteolysis Society, Quebec City, Canada.

25. Popp FC, Inoue S, Engelhardt N, Kucuk I, Piso P, Geissler EK, Bertolino P, Schlitt HJ and Dahlke MH (2005) Fusion of bone marrow cells with resident hepatocytes occurs under regenerative conditions in inflammatory liver disease. 3rd Annual Meeting ISSCR, San Fransisco, USA.

26. Poustchi H, George J, Labio ED, Coverdale SA, Carney RG, Perry JF, Lee Au, McCaughan GW and Farrell GC (2005) Screening for Liver Cancer: Feasibility of a Randomised Controlled Trial. American Association for the Study of Liver Diseases, San Francisco, USA.

27. Tanabe KM, Millward M, Allen JD (2005) Interactions of patupilone (epothilone B) with multidrug transporter proteins. American Association of Cancer Research 96th Annual Meeting, Anaheim, CA, USA.

28. Tangye SG (2005) Analysis human Ig-secreting cells generated *in vivo* and *in vitro*: requirements for generation and survival. Keystone Conference: B cell development, function and disease; Steamboat Springs, Colorado, USA.

29. Triccas JA (2005) Recombinant forms of BCG as new anti-tuberculosis vaccines. Department of Microbiology, Colorado State University, Colorado, USA.

30. Triccas JA (2005) Targeting dendritic cells as a strategy to improve protective immunity against tuberculosis. Tuberculosis: integrating host and pathogen biology (Keystone Symposium), Whistler, Canada.

31. Wang XM, Yu DMT, McCaughan GW and Gorrell MD (2005) Extra-enzymatic roles of DPIV and FAP in cell adhesion and migration on collagen and fibronectin. Dipeptidyl Aminopeptidases: Basic science and clinical applications, Magdeburg, Germany.

32. Wang XM, Yu DMT, McCaughan GW, and Gorrell MD (2005) The Prolyl Oligopeptidase Fibroblast Activation Protein (FAP) Influences Cell Adhesion, Migration And Apoptosis (Reference Number 386). In. 4th Meeting of the International Proteolysis Society, Quebec City, Canada.

33. Wang XM, Yu DMT, Cordoba S, Marguet D, Rettig W, Schnapp A, McCaughan GW and Gorrell MD (2005) The Role of Fibroblast Activation Protein (FAP) in Cell Adhesion, Migration and Liver Fibrosis. American Association for the Study of Liver Disease, Boston, MA, USA.

34. West N, Wozniak T, Ribeiro J, Valenzuela J, Feng C, Sher A, Britton W (2005) Cutinases Are Novel Secreted Enzymes of Mycobacterium tuberculosis Which Confer Protection Against Murine Aerosol Tuberculosis Infection. Keystone Symposia, Whistler, Canada.

35. Yu DMT, Wang XM, McCaughan GW and Gorrell MD (2005) DP8 and DP9 have extra-enzymatic roles in cell adhesioin, migration and apoptosis. Dipeptidyl Aminopeptidases: Basic science and clinical applications, Magdeburg, Germany.

36. Yu DMT, Wang XM, and Gorrell MD (2005) Extra-enzymatic impairment of cell-extracellular matrix interactions by dipeptidyl peptidases (Reference Number 403). In. 4th Meeting of the International Proteolysis Society, Quebec City, Canada.

National

Invited presentations

1. Allen J (2005) Multidrug transporter MRP4 in drug resistance and prognosis of cancer. Oncology Research Unit, Childrens Hospital Westmead, Sydney.
2. Allen J (2005) The great influenza pandemic of 1918 and the one coming. Centenary Institute Postgraduate Workshop, Centenary Institute, Sydney.
3. Allen J (2005) Multidrug transporters and new anticancer drugs. Immunology and Oncology Unit, Matermisericordiae Hospital, Newcastle.
4. Basten A (2005) Know your ailment. Rotary Club of Chatswood, Chatswood, Sydney.
5. Basten A (2005) Opening Address and Chair, 3rd Australian B Cell Dialogue, Centenary Institute, Sydney.
6. Bertolino P (2005) The liver: an immunological oddity. The Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia.
7. Bertolino P (2005) Early intrahepatic antigen-specific retention of naïve murine CD8+ T cells is predominantly ICAM-1/LFA-1 dependent. ALA Workshop, Victor Harbour.
8. Bertolino P (2005) The balance of intrahepatic immunity is determined by the site of primary T cell activation. 35th Annual Conference of the Australasian Society for Immunology.
9. Bishop GA (2005) Induction of liver transplantation tolerance using donor-derived cells. 7th Australia and New Zealand Liver Transplant Meeting, Sydney.
10. Brink R (2005) Modulation of B cell responses through targeted gene inactivation and variation of antigen affinity. Seminar Program, John Curtin School of Medical Research, Australian National University, Canberra.
11. Brink R (2005) Identifying extrinsic and intrinsic controls over B cell responses. Seminar Program, John Curtin School of Medical Research, University of New South Wales, Sydney.
12. Brink R (2005) Identifying extrinsic and intrinsic controls over antigen-specific B cell responses using an in vivo mouse model. 35th Annual Conference of the Australasian Society for Immunology, Melbourne.
13. Britton WJ (2005) The global challenge of HIV. CRC-VT Annual Scientific Conference, Byron Bay.
14. Britton WJ (2005) Tuberculosis: Understanding and controlling the old scourge. Royal Society of NSW, University of Sydney, Sydney.
15. Fazekas de St.Groth B (2005) CD4+CD25+ regulatory T cells: translation from mouse to man. Ludwig Institute for Cancer Research, Austin Hospital, Melbourne.
16. Fazekas de St.Groth B (2005) Regulatory T cells and autoimmune disease: translation from mouse to man. 16th Annual Scientific and Clinical Meeting of the South Australian Rheumatology Association, Adelaide.
17. Fazekas de St.Groth B (2005) Regulatory T cells and cancer immunotherapy. Tumour Immunology Workshop, 35th Annual Scientific Meeting of the Australasian Society for Immunology, Melbourne.
18. Fazekas de St.Groth B (2005) Regulatory T cells and the maintenance of tolerance. 35th Annual Scientific Meeting of the Australasian Society for Immunology, Melbourne.
19. Fazekas de St.Groth B (2005) Regulatory T cells in human inflammatory bowel disease. Child Health Research Institute, Adelaide.
20. Fazekas de St.Groth B (2005) Regulatory T cells: translation from mouse to man. Centre for Immunology, Sydney.
21. Gorrell M (2005) Roles of the dipeptidyl peptidase IV gene family in liver injury, cell-extracellular matrix interactions and developing novel type 2 diabetes therapeutics. Kolling Institute, North Sydney.
22. Gorrell M (2005) Peptidases as potential novel therapeutic targets for diabetes and fibrosis. LIVER FORUM: BIOLOGY and LIFESTYLE. Research Showcase of University of Sydney NHMRC Liver Programs. Medical Foundation Building, Sydney.
23. McCaughan GW (2005) Autoimmune liver diseases. Royal Australian College of Pathologists Meeting Sydney.
24. McCaughan GW (2005) Intrahepatic gene expression in chronic HCV infection. QIMR Diamond Jubilee Anniversary Meeting, Brisbane.
25. McCaughan GW (2005) Molecular and Cellular Pathogenesis of Liver Disease. Distinguished Research Award Lecture. Australian Gastroenterology Week, Brisbane.
26. McCaughan GW (2005) Pathogenesis of Autoimmune Hepatitis. Hepatology Advanced Training Seminar, Sydney.
27. Rasko JEJ (2005) A funny thing happened on the way


to gene therapy. Barbara Ell Seminar Series Lecturer, Victor Chang Cardiac Research Institute, Sydney.

28. Rasko JEJ (2005) A Non-human Primate Model of Mobilisation and Stem Cell Biology. Bone Marrow Transplant Scientists Association of Australia, Sydney.
29. Rasko JEJ (2005) A non-human primate model of stem cell mobilization. 2nd Annual MMRI Haematopoietic Stem Cell Symposium, Brisbane.
30. Rasko JEJ (2005) A Non-Human Primate Stem Cell Model, Victor Chang Cardiac Research Institute, 7th International Symposium: Development, Differentiation and Disease, Sydney.
31. Rasko JEJ (2005) Gene therapy: are we there yet? Grand Rounds, St George Hospital, Sydney.
32. Rasko JEJ (2005) Clinical trial regulations in Australia. Australasian Duchenne Muscular Dystrophy Trial Meeting, Perth.
33. Rasko JEJ (2005) Gene therapy: worth the wait? Dept. Genetic Medicine, Women's and Children's Hospital, MS McLeod Research Seminar Series, Adelaide.
34. Semsarian C (2005) Genes and hypertrophic cardiomyopathy, Basic Physician Training Course, RPAH, Sydney.
35. Semsarian C (2005) Genes and sudden cardiac death. Cardiology Grand Rounds, St. Vincent's Hospital, Sydney.
36. Semsarian C (2005) Genes and sudden cardiac death. Heart Research Institute Seminar Series, Sydney.
37. Semsarian C (2005) Genes and sudden cardiac death. Cardiology Grand Rounds, Royal North Shore Hospital, Sydney.
38. Semsarian C (2005) Genes in hypertrophic cardiomyopathy. 53rd CSANZ Scientific Meeting, Perth.
39. Semsarian C (2005) Genetic basis of heart failure. 53rd CSANZ Scientific Meeting, Perth.
40. Semsarian C (2005) Getting to the heart of sudden death. Baker Heart Research Institute, Melbourne, Victoria.
41. Semsarian C (2005) Getting to the heart of sudden death. Western Australian Institute of Medical Research (WAIMR), Perth.
42. Semsarian C (2005). Heart problems in young adults, RPA Cardiology update for rural physicians, RPAH, Sydney.
43. Semsarian C (2005). Molecular aspects of cardiac hypertrophy and heart failure: from mice to man, ASCEPt-APSA Scientific Meeting, Melbourne.
44. Semsarian C (2005) Hereditary cardiomyopathies: genetics and screening. Qld Heart Failure Meeting, Brisbane.
45. Semsarian C (2005) How to search for genes in cardiovascular disease. 53rd CSANZ Scientific Meeting, Perth.
46. Semsarian C (2005) Hypertrophic cardiomyopathy: current assessment and management. Qld Heart Failure Meeting, Brisbane.
47. Semsarian C (2005) Lipodystrophies and cardiomyopathy syndromes. RPAH Endocrine Seminar Series, Sydney.
48. Semsarian C (2005) The genetic basis of ischaemic heart disease, Asia-Pacific Interventional Advances Conference, Newcastle, NSW.
49. Semsarian C (2005) The Power of Genomics and Proteomics. Cardiology 2005 PRPAH / Mayo Clinic Meeting , Sydney.
50. Semsarian C (2005) Update on proteomics: applications to cardiovascular disease. ASEANZ Meeting, Melbourne.
51. Tangye SG (2005) Cellular defects resulting from inactivating mutations in SH2D1A, the gene responsible for X-linked lymphoproliferative disease. John Curtin School of Medical Research, ANU, Canberra.
52. Tangye SG (2005) Cellular defects resulting from inactivating mutations in SH2D1A, the gene responsible for X-linked lymphoproliferative disease. University of New South Wales, Kensington, Sydney.
53. Tangye SG (2005) Cellular defects in X-linked lymphoproliferative disease. Australian Institute of Medical Scientists Annual Conference, Sydney.
54. Tangye SG (2005) Expansion of functionally immature transitional B cells is a characteristic of human immunodeficient states. Australasian Society for Immunology 35th Annual Scientific Meeting, Melbourne.
55. Tangye SG (2005) Pathophysiology of X-linked lymphoproliferative disease. 11th Annual Immunopathology Update/Training Workshop, Westmead Hospital, Sydney.
56. Triccas JA (2005) Targeting Components of Host Immunity to Improve Vaccination Against Tuberculosis. Australian Society for Microbiology annual meeting, Canberra.
57. Triccas JA (2005) Defining Immunity to *Mycobacterium tuberculosis* to Improve Vaccination against Tuberculosis. Australasian Society for Immunology annual meeting, Melbourne.

Abstracts, oral and poster presentations

1. Benseler V, Bishop GA, Chng K, Watson J, Wang C, Dahlke M, Koutalistras N, Watts A, Hawthorne W, McKenzie P, Hennessy A, Pleass H, Chadban S, Schlitt H, McCaughan G and Allen R (2005) Development of a primate model to evaluate strategies to achieve long term renal allograft acceptance. Transplantation Society of Australia and New Zealand, Canberra.
2. Bertolino P, Schrage A, Bowen DG, Klugewitz K, Ghani S, Eulenburg K, Holz L, Hogg N, McCaughan GW and Hamann A(2005) Early intrahepatic antigen-specific retention of naïve murine CD8+ T cells is predominantly ICAM-1/LFA-1 dependent. Australian Gastroenterology Week, Brisbane.
3. Britton WJ (2005) Harnessing the immune system to develop new vaccines against tuberculosis. Seminar, Faculty of Pharmacy, University of Sydney, Sydney.
4. Britton WJ (2005) Role of proinflammatory and regulatory cytokines in the host control of TB infection. School of Pathology, University of NSW, Sydney.
5. Britton WJ (2005) The many faces of TNF: its importance in tuberculosis and inflammation. Grand Rounds, Nepean Hospital, Sydney.
6. Bryant VL, Good KL, and Tangye SG (2005) IL-21 has pleiotropic effects on proliferation and differentiation of human B cell subsets. ASI 2005: Australasian Society for Immunology: 35th Annual Scientific Meeting, Melbourne.
7. Chng K, Larsen S, Thomson S, Hennessy A and Rasko JEJ (2005) Specific Serotypes of Adeno-associated Virus Vectors Facilitate Gene Transfer In A Non-human Primate Model of Mesenchymal Stem Cell-Directed Gene Therapy. Australasian Gene Therapy Society, Melbourne.
8. Chklovskaia E, Roediger B and Fazekas de St.Groth B (2005) Antigen presentation by epidermal-derived dendritic cells induces peripheral deletion of CD4+ T cells. Australasian Society for Immunology 35th Annual Scientific Meeting, Melbourne.
9. Chklovskaia E and Fazekas de St.Groth B (2005) Lack of peripheral clonal deletion of CD4+ T cells in lymphopaenia. Australasian Society for Immunology 35th Annual Scientific Meeting, Melbourne.
10. Cordoba S, Wang C, Li J, Bertolino P, McCaughan GW, Alexander SW and Bishop GA (2005) Examination of immune mechanisms in a mouse model of spontaneous renal allograft acceptance. Transplantation Society of Australia and New Zealand, Canberra.
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12. Cuss AK, Avery DT, Nichols KE, Shaw PJ and Tangye SG (2005) Expansion of functionally immature transitional B cells is a characteristic of human immunodeficient states. Australasian Society for Immunology 35th Annual Scientific Meeting, Melbourne.
13. Dilda PJ, Don AS, Tanabe KM, Higgins VJ, Allen JD, Dawes IW and Hogg PJ (2005) Mechanism of selectivity of an angiogenesis inhibitor from screening a genome-wide set of Saccharomyces cerevisiae deletion strains. Australian Vascular Biology Society Annual Meeting, Darling Harbour, Sydney.
14. Dilda PJ, Don AS, Tanabe KM, Higgins VJ, Allen JD, Dawes IW and Hogg PJ (2005) Mechanism of selectivity of an angiogenesis inhibitor from screening a genome-wide set of *Saccharomyces cerevisiae* deletion strains. ComBio, Adelaide Convention Centre, Adelaide.
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16. Chiu C, Ingles J and Semsarian C (2005) Brain natriuretic peptide gene analysis in patients with hypertrophic cardiomyopathy. 53rd CSANZ Annual Scientific Meeting, Perth.
17. Chiu C, Ingles J and Semsarian C (2005) Gender-related differences in patients with hypertrophic cardiomyopathy. 53rd CSANZ Annual Scientific Meeting, Perth 2005.
18. Doolan A, Langlois N and Semsarian C (2005) Post-mortem genetic analysis of the KCNQ1 gene in sudden unexplained death in the young. 53rd CSANZ Annual Scientific Meeting, Perth.
19. Doolan A, Tebo M, Ingles J, Nguyen L, Tsoutsman T, Lam L, Chiu C, Chung J, Weintraub RG, Semsarian C (2005) Cardiac troponin I mutations in Australian families with hypertrophic cardiomyopathy: clinical, genetic and functional consequences. 53rd CSANZ Annual Scientific Meeting, Perth.
20. Gardam S, Grech A, Basten A and Brink R (2005) Diverse roles for TRAF2 and TRAF3 in NF-∫ pathways. 35th Annual Conference of the Australasian Society for Immunology, Melbourne.

21. Good KL and Tangye SG (2005) Differential expression of cell cycle regulators modulates the behaviour of naïve and memory B cells. Australasian Society for Immunology: 35th Annual Scientific Meeting, Melbourne.

22. Gracey D (2005) Memory CD4+ lymphocytes are required for the initiation of MHC Class II-dependent skin allograft rejection. TSANZ, Canberra.

23. Holz L, Benseler V, Gengos M, Newton R, McCaughan GW and Bertolino P (2005) Intrahepatic immunity is influenced by the site of primary T cell activation. 35th Annual Conference of the Australasian Society for Immunology, Melbourne.

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28. Lam L, Tsoutsman T, Chung J and Semsarian C (2005) The effect of dietary caffeine in normal and cardiomyopathic mice. 53rd CSANZ Annual Scientific Meeting, Perth.

29. Limaye S, Grech A, Basten A and Brink R (2005) Positive and negative regulation of T-dependent B cell responses by TRAF2. 3rd Australian B Cell Dialogue, Centenary Institute of Cancer Medicine and Cell Biology, Sydney.

30. Ling S, Poulos V, Allen J (2005) A Pilot Study of the Effect of Imatinib Mesylate on Porphyrin Elimination. Haematology Society of Australia and New Zealand 2005 Annual Scientific Meeting, Darling Harbour, Sydney.

31. Park J, Ajami K and Gorrell MD (2005) Comparative enzymology of human dipeptidyl peptidase (DP) 8 and the prospective type 2 diabetes therapeutic target DPIV. Australian Gastroenterology Week, Brisbane.

32. Park J, Ajami K, and Gorrell MD (2005) Recombinant Human Dipeptidyl Peptidase 8 Has Dipeptidyl Peptidase IV And Prolyl Endopeptidase Activities. Liver Forum: Biology and Lifestyle. University of Sydney Medical Foundation Building, Sydney.

33. Paus D, Phan T, Chan TT, Gardam S, Basten A and Brink R (2005) Antigen affinity governs plasma cell differentiation in vivo. 3rd Australian B Cell Dialogue, Centenary Institute of Cancer Medicine and Cell Biology, Sydney.

34. Phan T, Paus D, Chan T, Gardam S, Basten A and Brink R (2005) Visualising B cell responses to protein antigens of varying affinity *in vivo*. 35th Annual Conference of the Australasian Society for Immunology, Melbourne.

35. Rasko JEJ (2005) Gene therapy and stem cells: it takes two to tango. Australian Institute of Medical Scientists (AIMS) 2005 National Scientific Meeting, Sydney.

36. Roediger B and Fazekas de St.Groth B (2005) Dendritic Cell Transfer of MHC complexes *in vivo*. Australasian Society for Immunology, NSW Branch Meeting, Weisemans Ferry.

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41. Seth D, Gorrell MD, McCaughan GW and Haber PS (2005) Intrahepatic gene expression profiling in human alcoholic hepatitis and alcoholic steatosis. Australian Gastroenterology Week, Brisbane.

42. Silveira P (2005) The pathogenic role of B cells in Type 1 Diabetes can be controlled by diabetes susceptibility genes. 3rd Australian B cell Dialogue, Sydney.

43. Silveira P (2005) Mechanisms whereby Idd genes can affect the diabetogenic capacity of B cells. 10th Australasian Autoimmunity Workshop, Hamilton Island.

44. Song S, Shackel NA, Wang XM, Ajami K, McCaughan GW and Gorrell MD (2005) Intrahepatic discoidin domain receptor 1 (DDR1/CD167A) expression in human cirrhosis. Australian Gastroenterology Week, Brisbane.

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46. Spencer A and Fazekas de St.Groth B (2005) CD4+ T cells require antigen during both the activation and expansion phases of the response. Australasian Society for Immunology, NSW Branch Meeting, Wisemans Ferry.

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48. Tan S-Y (2005) B7-deficient non-regulatory T cells show an impaired response to regulation. Australasian Society for Immunology, NSW Branch Meeting, Wisemans Ferry.

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54. Yu DMT, Wang XM, and Gorrell MD (2005) Extra-enzymatic impairment of cell-extracellular matrix interactions by dipeptidyl peptidases. Liver Forum: Biology and Lifestyle. University of Sydney Medical Foundation Building, Sydney.

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2006 - The Year Ahead

Dr Fiona Warner will join the Liver Immunobiology Group in January where she will be investigating the role of angiotensin-converting enzyme 2 in liver injury. Dr Warner completed a CJ Martin NHMRC Fellowship at Monash University in Melbourne. Dr Warner has been awarded a Rolf Edgar Lake Fellowship from the University of Sydney Faculty of Medicine.

Dr Joanne Lind of the Molecular Cardiology Group was one of only five recipients of a 2006 Individual Grant from the Layne Beachley Aim for the Stars Foundation. The grants are awarded to ambitious and dedicated women each year to help them achieve their goals.

NHMRC Project Grants Commencing 2006

- Professor John Rasko is co-recipient of a five year, $2 million NHMRC Enabling Grant awarded to the Prince of Wales Medical Research Institute for the establishment of Genetic Repositories Australia (GRA), a national facility for the distribution and long-term secure storage of human genetic samples from a variety of sources.
- Dr Bernadette Saunders, Professor Warwick Britton and Professor John Rasko were awarded grant funding for their project entitled "Genetic Modulation of the host response to pulmonary TB".
- Dr Jamie Triccas and Professor Warwick Britton were awarded grant funding for their project entitled "Manipulating immunity to *Mycobacterium tuberculosis* with novel vaccines and immunotherapeutics".
- Professor John Rasko was awarded grant funding for his project entitled "Diseases of Aminoacid Transport: Genetic, Molecular and Biochemical Studies" in collaboration with JA Cavanaugh, S Broer.
- Dr Fiona Warner was awarded a New Investigator's Project Grant entitled "Regulation of Angiotensin-Converting Enzyme 2 Expression in Liver Injury".

NHMRC Fellowships

Dr Robert Brink (B Cell Biology) was awarded a Senior Research Fellowship. Dr Jamie Triccas (Mycobacterial Research) is the recipient of an RD Wright Biomedical Career Development Award. Dr Tri Phan (B Cell Biology) received a CJ Martin (Overseas) Fellowship.

Other grants commencing 2006

- National Heart Foundation Project Grant
  - A/Prof Chris Semsarian
- USyd NHMRC Equipment Grant
  - Prof Geoff McCaughan, Dr Mark Gorrell, Dr Alexandra Sharland, A/Prof Paul S Haber, Dr Bret W Church, Dr Patrick Bertolino
- USyd NHMRC Equipment grant
  - Prof John Rasko
- USyd Major Equipment Scheme Grant
  - Prof John Rasko

Postgraduate Scholarships

Ms Christine Chiu from the Molecular Cardiology Group was awarded a prestigious NHMRC/National Heart Foundation Dora Lush (Biomedical) Scholarship for her PhD.

PhD Students Dr Lye Lin Ho and Dr Silvia Ling, both of the Cancer Drug Resistance Group, and Dr Stephen Larsen of the Gene & Stem Cell Therapy Group were recipients of Cancer Institute NSW Research Scholar Awards. Mr Robin Mihrshahi who will be joining the T Cell Group in 2006 has been awarded a prestigious Alumni Scholarship for Health Sciences and an Australian Postgraduate Award for his PhD.

Fundraising

12th Annual Raceday and Luncheon

Centenary held its 12th Annual Raceday at Rosehill Gardens on Saturday October 22, 2005. The perfect spring day set the scene for our most successful Raceday raising over $120,000 through the generosity of sponsors and luncheon guests. This year's event focused on raising funds for Associate Professor Barbara Fazekas de St.Groth's (T Cell Biology) research into developing a simple blood screening test to determine which children are most at risk of developing asthma and type 1 diabetes.

Our sincere thanks and appreciation go to the Raceday Steering Committee chaired by Mr Malcolm Noad, Event Manager Ms Sue Finn, all our many sponsors and to all those who, by their presence, contributed to a very special and most successful Raceday.

Young Winemaker of the Year Awards

The Wine Society's Young Winemaker of the Year Award was held on Saturday 19 November, 2005, at a Gala Dinner at the Four Season's Hotel. The evening was hosted by Sky News Australia's senior anchorman, Mr John Mangos. Guests were presented with a selection of 20 fine wines produced by the 10 finalists for tasting. Our congratulations go to Amanda Kramer from Wise Wine who was named the 2005 Young Winemaker of the Year for her Single Vineyard Chardonnay 2003, and also to Jane Donat from Petersons Winery who won the Member's Choice Award for her Petersons Griffith Botrytis Semillon 2004.

Over $16,000 was raised through a raffle, mystery envelopes and a silent auction. The funds will be used to support research projects at Centenary. Particular thanks go to Ms Eva Gero of the Wine Society for organising the event and all those who generously gave of their time to assist with the fundraising. Centenary is most grateful to the Wine Society for their ongoing support of our research.

End of Tax Year Appeal

The generosity of those who supported our most recent special initiative fundraising activity is particularly appreciated. This year's End of Tax Year Appeal raised over $50,000 towards Professor John Rasko's research aimed at using adult stem cells to repair damaged heart tissue.

We would be delighted if you would consider supporting us.

There are many ways in which you can support Centenary's research programme depending on your own particular interests. All donations are tax deductible and acknowledged in the Centenary News published twice a year.

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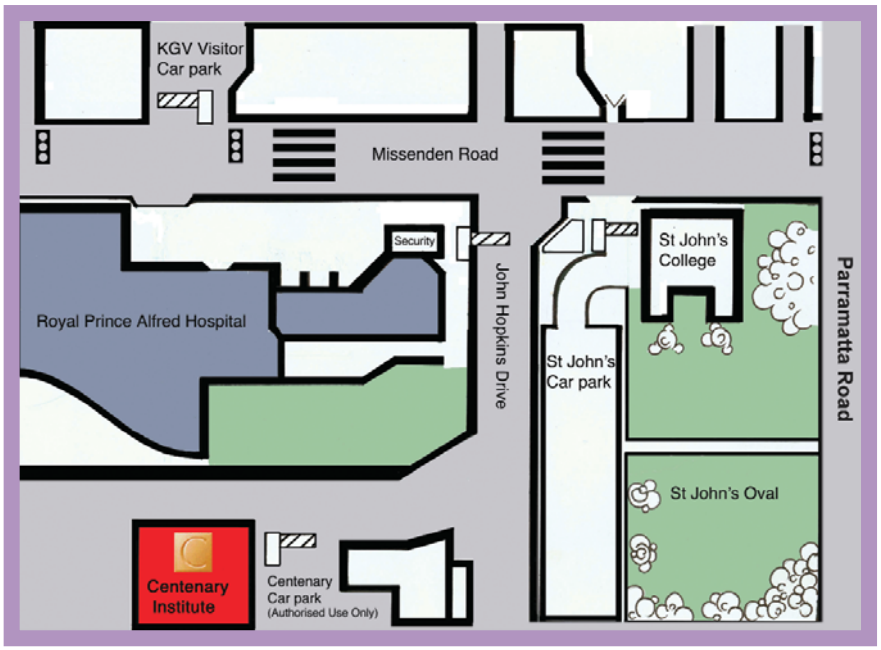

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