Celebrating
80
YEARS OF
RESEARCH

Baker Heart Research Institute | **Annual Report 2005**

Baker
Heart Research Institute

Annual Report
2005

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The Baker story...

The Baker's close links with The Alfred, an outstanding hospital specialising in the most complex and serious acute health problems, gives it a special place in cardiovascular research in Australia and puts it among the leading research facilities in the world.

Now in its 80th year, the Baker Heart Research Institute is Australia's most distinguished cardiovascular research centre and one of the world's leading organisations investigating the causes and complications, treatment and prevention of heart, stroke and vascular disease.

At the Baker we are devoted to the prevention and cure of cardiovascular disease. Every research dollar we attract and spend goes into finding out why people are getting sick and dying and the best ways we might help them get better and stay alive. We are finding out more about who is at risk and how we might stop heart attack, stroke, sudden cardiac death and the like from ever happening. In this way, explaining what we do is simple. Why we do it, sadly, is even simpler. The figures remain shocking:

- An Australian dies every 10 minutes from cardiovascular disease, representing more than 40 per cent of all deaths in this country.
- Cardiovascular disease is the leading cause of death and disability, not only in Australia but also around the world. It is on the rise in developing nations and expected to reach epidemic proportions by the middle of this century.
- More than 3.2 million people in Australia are affected by cardiovascular – 67 per cent of all families.
- Throughout the world, cardiovascular disease accounts for more than 16 million deaths every year – more than cancer, and all respiratory, digestive and non-communicable diseases combined.
- Cardiovascular disease is Australia's leading health problem. At a cost of $7 billion a year, it makes up 11 per cent of Australia's total direct health care expenditure.
- Over the last decade, the prevalence of cardiovascular disease in Australia rose by almost 20 per cent.

Our work has never been more important.

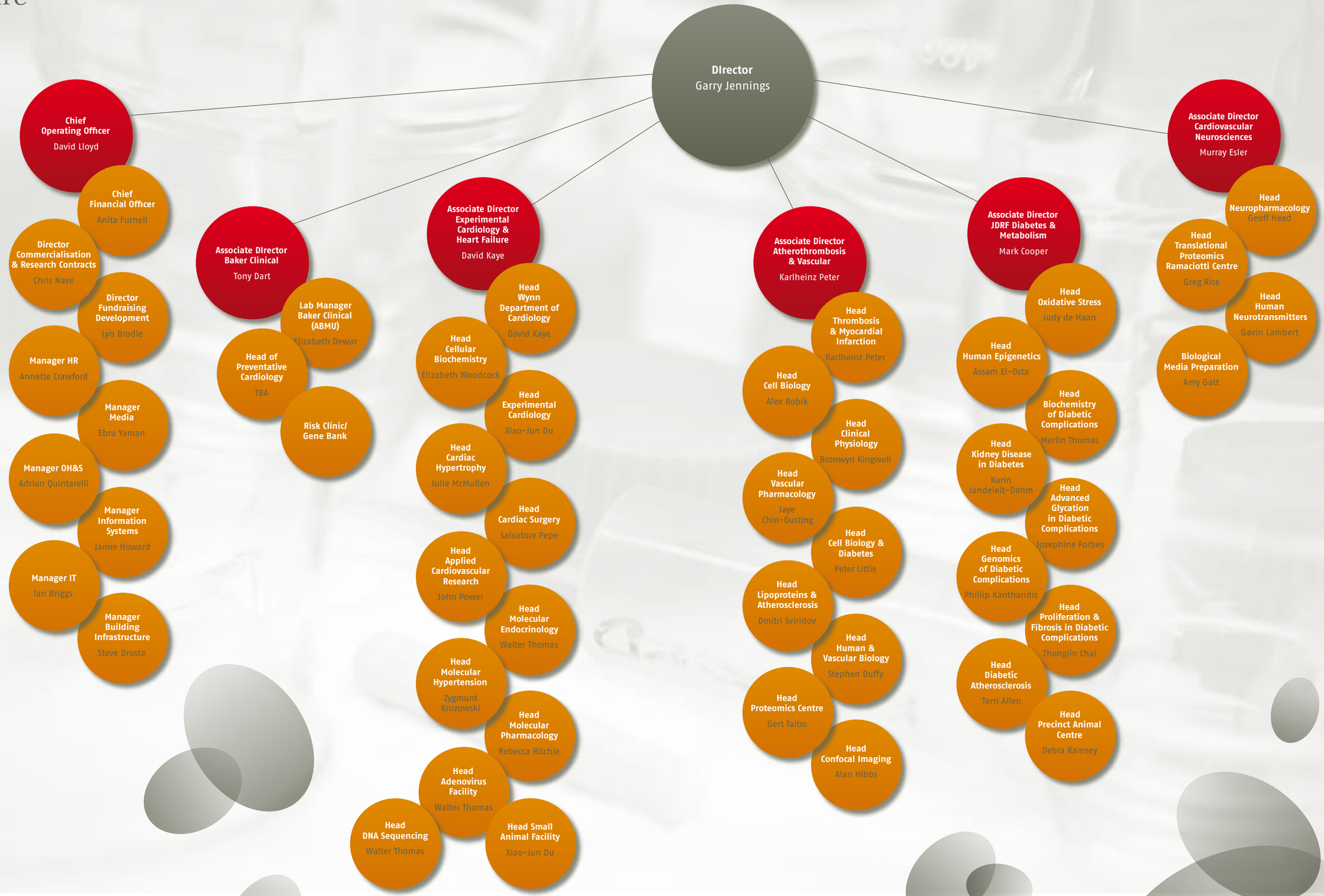
A comprehensive research program with a strategic focus:
Research at the Baker is broadly divided into four divisions: Experimental Cardiology and Heart Failure; Atherothrombosis and Vascular; Diabetes and Metabolism and Cardiovascular Neuroscience. Four associate directors of the Baker, each of them internationally renowned scientists and clinicians, lead these divisions. Together they oversee the research activities of the Baker's 26 laboratories.
A researcher who is at the top of their field in turn heads each of these labs. Their research focus ranges from the study of blood vessels to the complex relationship between molecules, from ways to improve the health of people undergoing or waiting for heart surgery to the organ damage caused by diabetes.

One of the Baker's great strengths is that this disparate research, highlighted in the following pages, is highly collaborative. Together, our specialised staff use state-of-the-art facilities to build a better understanding of the causes and effects of cardiovascular disease than we've ever had.

The Baker's close links with The Alfred Hospital, an outstanding hospital specialising in the most complex and serious acute health problems, gives it a special place in cardiovascular research in Australia and puts it among the leading research facilities in the world. With only a third floor walkway separating the two buildings, the unique relationship between the institute and the hospital is pivotal to the Baker's work. Some of our scientists are also clinicians, and this "wearing two hats" ensures our research remains clinically relevant.

Every day Baker staff witness the effects of cardiovascular disease in Alfred patients and their families. This link is a constant, powerful reminder of the value and the urgency of their work and it keeps the Baker very close to changes in disease trends and treatments. Just as importantly, the Alfred connection gives our researchers access to a huge patient database and to human samples of tissue and cells. In return the clinical services have access to the latest ideas and treatments. The combined effect is a strongly committed, disease-focused, well-informed research community with the highest degree of empathy for those suffering from cardiovascular disease.

Organisational Structure



Director's Report

› Professor Garry Jennings

GROWTH and consolidation have been key for the Baker this year, now 80 years old, but in many ways becoming younger by the day. In part the growth has been organic, driven by outstanding success in grant applications to national and international peer review granting bodies (over $10M in new National Health & Medical Research Council grants), supported by a good year for fundraising and for investment income. Were we not a group of hard-nosed scientists and the like, and aware of the hard work and planning of the Board and staff that got us in this position we might be saying that 2005 was a year when all the stars lined up for the Baker.

We exist in the cause of scientific excellence, especially science that contributes to our community. This involves doing good science now and also training future generations of scientists and clinicians.

Further growth has occurred with the strategic recruitment of new scientific groups – strategic because they not only share the mission of the Baker - to reduce death and disability from heart, stroke and vascular disease, but also because they bring new skills and technologies that match and complement those of our existing groups. Professor Karlheinz Peter relocated from the University of Freiberg in Germany; he brings strengths in thrombosis research and in applying high-class molecular research to the development of new treatments and diagnostic tools for the clinic.

Together with our strong complement of vascular biologists already at the Baker we have formed a new scientific theme, also referred to as a division, working on the link between atherosclerosis and thrombosis. These key events turn an individual who is apparently healthy - albeit with some risk factors like high blood pressure, diabetes, high cholesterol or a family history - into a cardiac emergency, suffering a sudden catastrophic event like a heart attack or major stroke. Understanding the biological processes that occur both in the years when trouble in the arteries is brewing and in the last few minutes before an acute cardiac event is a key Baker objective in the coming years.

Every year, almost 20 million people suffer these events. In Australia, most people who eventually die from cardiovascular disease have previously suffered heart attack or stroke. Our aim at the Baker is to use the new biology to develop predictive tests and treatments that are individualised, more specific and more pre-emptive than tests and treatments that we now have.

Achieving these objectives however will still leave many people in the community living with the combined effects of an ageing and damaged heart. All of us have family members, friends or colleagues in this situation. Heart failure is the most serious manifestation and research on heart failure and advanced disease is another major theme at the Baker involving a large team of molecular scientists, physiologists and cardiologists. Professor David Kaye leads the group, which includes the Wynn Department, established investigators such as Walter Thomas, Elizabeth Woodcock and Xiao-Jun Du as well as some who are developing their careers like Rebecca Ritchie. New arrivals in this division have also hit the ground running, and include Julie McMullen who is working on understanding why heart growth (hypertrophy) from exercise training is good for you, and protects the heart, whereas heart growth due to disease is not.

We exist in the cause of scientific excellence, especially science that contributes to our community. This involves doing good science now and also training future generations of scientists and clinicians. Our 80th anniversary also brings to light the many people, particularly with a scientific background, who have passed through the Baker and now contribute to the community in a variety of ways: in government and industry, in developing policy, in running biotechnology companies or working in occupations such as stock market analysts, as journalists, or in the non-profit sector. Last year we had a record number of students at the Baker, around 70. All were enrolled for postgraduate degrees at Monash University, the University of Melbourne and other universities, and all benefited from a highly active mentoring and support program led by our Scholars Executive, now chaired by Jaye Chin-Dusting.

By now almost everyone is aware that obesity and diabetes will keep cardiovascular disease at the forefront of community health concern for the foreseeable future. But awareness is not enough and we need breakthroughs, more than a few, and at many levels. Professor Mark Cooper leads our diabetes and metabolism theme. He and his large group work on preventing the damage that high sugar levels do to arteries leading to the high risk of heart disease, stroke, vascular disease, blindness and kidney failure that is characteristic of diabetes and the main reason diabetes is such a significant health problem. The award of a Diabetes Complications Centre grant, the only one outside the USA by the New York-based Juvenile Diabetes Research Fund was great news and strong recognition of the international stature of the group.

Exercise, obesity, nutrition, diabetes and other cardiovascular risk factors are closely linked through metabolic pathways, and the Institute is making a major investment in these areas. At the clinical end Professor Kerin O'Dea, one of our most distinguished alumni, has joined us part time to assist us in developing a program of research on nutrition and diabetes. Professor Mark Febbraio will soon establish his Molecular Metabolism laboratory. His work on changes in cell signalling in diabetes and with exercise has had a major impact in the field. The strong collaborations he has already with many existing Baker laboratories will further enhance this research.

Each year the Institute receives a grant from the Thomas Baker Foundation. In 2005, at the suggestion of the trustees, a new initiative was the Thomas Baker Award for Research Excellence, recognising an outstanding piece of research published during the year. The bar was set very high and the winner, Dr Assam El-Osta and his colleagues had their paper featured on the cover of the prestigious journal Nature Genetics. Sam has introduced epigenetics to the Institute - the study of the modification of gene function by chromatin. This has proven important in many of the questions of interest to our laboratories in every division in the Institute and there are many more high impact publications to come.

Most of the diseases we seek to prevent and cure have both genetic and environmental causes and understanding their interaction is a key step in understanding disease. Epigenetic changes as simple as a chemical modification, methylation provides a genetic on/off switch. This may be a critical link between the environment and whether a cell faithfully produces the proteins programmed by its genes.

The applications in the Institute of this epigenetic approach so far range from cancer, to rare inherited forms of autism that appear suddenly in childhood, diabetes, and even to neurogenic hypertension. The latter is a term applied by Professor Murray Esler to a common form of high blood pressure that is caused by overactivity of the nervous system and may be a product of protracted or extreme mental stress. Murray heads our Cardiovascular Neurosciences theme. We all know that there is interdependence between the health of the mind and the body and there has long been a suspicion that in many cases heart attack has a psychological or psychosocial element. Recently expert evidence has accepted depression as a risk factor for heart attack, independent of other risk factors and our Cardiovascular Neuroscience division is pursuing this link using advanced clinical research technologies, many of which were developed here at the Institute.

Our students and postdoctoral fellows did us proud at many national and international conferences during the year as did the eminence gris. Enzo Porelli won the Young Investigators Award of the High Blood Pressure Research Council (HBPRCA). Judy De Haan was successful at a major National Heart Foundation conference and Xiao-Jun Du was their inaugural Ross Hohnen Award recipient for the top rated project in the country. At the same meeting Paul Nestel also received an inaugural award, the NHF Medal for Lifetime Research Achievement. Professor Colin Johnston was recognised for lifetime achievement with the naming of an annual lecture at HBPRCA meetings in his honour.

Four new companies contributed to an important year of progress in the commercialisation of Baker research. V-Kardia Pty Ltd and its US subsidiary V-Kardia Inc are developing the research ideas of Professor David Kaye and Dr John Power. The exciting potential of gene and cell therapy to repair and restore damaged heart muscle can only be realised with the aid of an efficient delivery system that takes the new therapies to the heart without spilling over to other parts of the body. A V-Kardia device is scheduled to go into clinical trials this year. Another company, ElaCor Pty Ltd was formed jointly with the Institute for Molecular Bioscience in Queensland and Geoff Head is leading the research on development of a new drug for heart failure treatment.

Nucleus Network is the Victorian clinical trials platform formed from the merger of Clinical Trials Victoria and the Centre for Clinical Studies. New CEO Andrew Giddy leads a team that is building the clinical trials capability of Australia and helps biotech companies make the transition from pre clinical to human studies, providing regulatory support, education and accreditation as well as a modern early phase clinical trials facility on the Alfred campus.

President's Report

› Mr Robert Stewart

IT has been a tremendous year for the Baker. Our dedicated team of scientists continue to have great success in their pursuit of finding ways to prevent, cure and treat heart disease. Many of their successes are highlighted throughout the pages of this annual report

While I am delighted to be taking over the reins from Norman O'Bryan, who served as Board President for 10 energetic and capable years, I am aware that his is a hard act to follow. It is fitting to be reflecting on some of the Baker's achievements during his presidency in the year of the Baker's 80th anniversary.

Our dedicated team of scientists continue to have great success in their pursuit of finding ways to prevent, cure and treat heart disease.

In his decade as President, Norman saw the Institute through a period of great change. One of the most significant of those changes was the move from the building now known as "the old Baker" to our state-of-the art new building, officially opened in 2002. Our new premises, at the heart of the rapidly expanding AMREP, Melbourne's newest and most exciting medical research precinct, befit the high-tech, leading edge research conducted here. Quite aside from the complex logistics and planning such a move entailed, it would not have been possible without a significant injection of capital. While Norman has previously thanked many of the people and organisations that helped raise those funds, I'd like to extend here our most sincere thanks to him, for his leadership throughout the process and his tireless dedication to the project. It is surely one of his most significant legacies.

But that wasn't the only big change of Norman's decade: it was also during Norman's time that the medical research community underwent the transition from block funding of research to competitive, grant-based funding. At the time the Baker approached this new regime with some trepidation, but it has proven to be a system under which the Baker has excelled. This has been a result of the outstanding leadership of the Institute and the excellence of the scientific and support staff working at the Baker.

And last but not least, Norman has had the privilege of working with two outstanding Baker directors. John Funder's retirement in 2000, after a stellar career and great leadership, ushered in new director Garry Jennings. Garry's steady guidance and inspiring vision has heralded in an exciting new era for the Baker, as this report will attest.

I would like here to report some changes that occurred on the Board in 2005: Gerry Johnson, Philip Munz, and Paula Campbell-Tuckfield all resigned during the year. Gerry had served on the Board for 14 years, including a valuable term as vice president. Philip was a Board member for 10 years, making a particular contribution to the commercialisation of Baker research. Although Paula had only been on the Board for a short period her contribution during that time was well valued. We thank them for their service and wish them well in their future endeavours.

New appointments to the Board include Lindsay Maxsted who has joined our ranks as Treasurer, John Allen, Justin Arter and the newly appointed Chief Operating Officer of the Institute, David Lloyd. I am delighted that Paula Dwyer has agreed to take on the role of Vice President, after serving as Treasurer for three years. The very strong financial performance of the Institute in 2006 is a credit to her work, as well as to the strong oversight of Norman O'Bryan and all of the Board.

It's a wonderful time to be involved with the Baker and I look forward to contributing to its great future.

A word from our patron

› Sir Laurence Muir

I HAVE been privileged to be associated with the Baker Heart Research Institute for over half its life. As we move into our 80th year it is timely to reflect on our rich partnerships – with The Alfred Hospital, with state and commonwealth governments, with corporations and charitable institutions, with the community and its generous volunteers. These partnerships have enabled us to employ 180 dedicated scientists and 40 support staff in 26 research laboratories, devoted to both clinical and basic research.

Thanks to the brilliance of our scientists and the outstanding leadership of Professor Garry Jennings, the Baker is a leading international cardiovascular research institute at the hub of a major medical research and creative centre of excellence on The Alfred campus.

Baker scientists today remain passionate about improving quality of life through their discoveries. Collaborating with the best researchers in the world and using innovative, cutting edge technology and research methods they continue to strive towards our one goal: the prevention, cure and treatment of heart disease.

As patron I congratulate the board and staff on all that has been achieved in 2005. It has been a year of expansion and of successes in the laboratories. I pay tribute to all of our partners and say a sincere thank you to Norman O'Bryan, our recently retired president who has been an inspirational leader.

Finally a warm welcome and sincere best wishes to our new president Robert Stewart.

The Board

Board members L–R:
Rob Stewart
David Lloyd
Professor Garry Jennings
Paula Dwyer
Anita Furnell (by invitation)
Lindsay Maxsted
Justin Arter
John Allen

Board Members absent:
Greg Hywood
Richard Smallwood
Peter Scott
Graeme Ryan
Edward Byrne

Robert Stewart
President

Rob Stewart was National Managing Partner of Minter Ellison, one of Australia's leading law firms, for 11 years, retiring in June 1999. He spent five years with Pacific Dunlop from 1976 to 1981 in a variety of general management positions within the Footwear Group.

He is Chairman of Melbourne IT Limited, an ecommerce infrastructure company providing key products and services such as domain names on the internet required by companies entering the digital economy; Chairman of Meditech Research Limited, a biotechnology company focused on developing and commercialising drugs that improve the health and quality of life of patients with cancer and other chronic diseases; deputy chairman of Emitch Limited, an online advertising and media placement company; chairman of C E Bartlett, one of the leading manufacturers in Australia of quality products in the fabrication of synthetic and canvas fabrics; and a director of QSR International Pty Ltd, which produces qualitative research software. He was also a non-executive director of Memtec Ltd, a high technology filtration company, from 1988 until 1997. Memtec listed on NASDAQ and then the New York Stock Exchange prior to being taken over by a US company in 1997.

He is also President of the Business/Higher Education Round Table, a member of the Council of Wesley College and a director of the Australasian Cardiac Surgery Research Institution Limited.

Paula Dwyer
Vice President

Paula Dwyer's background is in investment management and investment banking. In particular, Paula specialised in the provision of corporate financial advice to companies operating in regulated industries, including financial institutions and utilities. She provided corporate advice to major private and government sector clients in areas including the reform of public infrastructure, private sector investment in public infrastructure, mergers and acquisitions advisory and equity capital market raisings. She has extensive experience in the securities and investment industries.

Paula is presently a director of Tabcorp Holdings Limited, Promina Group Limited (Chairman of the Board Audit, Risk and Compliance Committee), David Jones Limited and Babcock and Brown Japan Property Management Limited.

Past appointments include serving as a director of RACV Ltd., as a member of the Victorian Casino and Gaming Authority and of the Victorian Gaming Commission, as a deputy director of Emergency Services Superannuation, VicSuper and Government Superannuation Office and as a committee member of Chartered Accountants in Business.

Lindsay Maxsted
Honorary Treasurer

Lindsay Maxsted is the Australian CEO and former managing partner of the Australian Corporate Recovery practice of the International Audit, Tax and Advisory firm of KPMG. He is a member of KPMG Australia's National Board and KPMG's ASPAC Regional Board.

His principal area of practice prior to his becoming CEO was in the Corporate Recovery field managing a number of Australia's largest insolvency/workout/turnaround engagements. Some of the assignments which he has handled include International Trucks Australia Ltd; companies associated with Abraham Goldberg including Linter Textiles Corporation Ltd, the shareholder company of businesses such as Speedo, King Gee, Hilton Hosiery etc. companies within The Bell Group Ltd, including the owner of West Australian Newspapers; the McEwans Hardware group of companies, and Brashs Pty Ltd.

At the request of the Victorian State Government, he joined the Board of the Public Transport Corporation ("PTC") in December 1995 and was appointed its chairman on 1 January 1997. As chairman he had the responsibility of guiding the Public Transport Corporation through the final stages of a significant reform process. The end process of that reform was the corporatisation and ultimate privatisation of the business units within the PTC.

He is also a Director of Racing Victoria Limited, Chairman of VicRacing Pty Ltd and Deputy President on the Board of Directors at Ruyton Girls' School.

John Allen

John Allen is Deputy Chair of Austral Credit Union, Director to Aust Photo Supply and Trustee of Kodak Superannuation Fund.

John concluded a 29 year career with Kodak at the end of 2004, where he had been chairman and CEO since 1999. His career covered a wide and diverse set of management skills including finance, consumer marketing, divisional and general management. John came to Australia in 1999 to assume the leadership of Kodak Australasia after managing Kodak NZ very successfully 1992–1998.

His particular forte is strategy and business development and he applying these skills to the companies and other interests he is currently involved with.

He has been chairman and CEO Kodak Australia, Director of HPA Pty Ltd and President of Photo Imaging Council Australia (PICA).

Justin Arter

Justin Arter is Managing Director Firmwide Strategy of Goldman Sachs JBWere, and a member of the firm's Board, Management Committee, Risk Committee, Commitments Committee, IT Steering Committee, Compliance Committee and Discretionary Portfolio Service Investment Committee.

Justin graduated from Melbourne University in 1984 with degrees in Law and Commerce. Soon after he completed his Articles of Clerkship and practised as a solicitor for a short time.

In 1986 he entered the stockbroking industry as a research analyst focusing on the food and household goods, entrepreneurs, transport and paper and packaging sectors.

He joined Goldman Sachs JBWere in 1991 as the research analyst responsible for the Transport sector as well as BTR Nylex, Foster's Brewing, Southcorp Holdings and the Telecommunications and Wine sectors. He was voted in numerous surveys as the top analyst in the Transport and Diversified Industrials sectors.

Following research, Justin worked in corporate finance for a short period, primarily on the Telstra 1 Float in both a corporate finance and equity capital markets capacity.

Appointed Head of Research and Strategist in 1998, he formulated equity market strategy. Throughout the time that Justin led this group, the strategy team rated as the number one team in many private and public surveys.

In 2001, he was appointed Joint Managing Director – Equities Products Group with institutional cash equities, derivatives and research reporting to him.

Professor Edward Byrne

Ed Byrne is Dean of Medicine, Nursing and Health Sciences at Monash University and has had an active career in clinical neurology and basic neurological research. Ed was the Founding Director of the Melbourne Neuromuscular Research Institute. He was the Founding Director of the Centre for Neuroscience and Professor of Experimental Neurology at the University of Melbourne. As Director of the Centre for Neuroscience, he played a major role in driving the establishment of Neurosciences Victoria and Neurosciences Australia. His research group has made significant contributions in muscular dystrophy and mitochondrial research.

He is a board member of Cochlear Pty Ltd, Neurosciences Australia and Neurosciences Victoria and immediate past Editor-in-Chief of the Internal Medicine Journal. He is a member of the Neuromuscular Steering Group of the World Federation of Neurology and was Secretary General and Chair of the program committee of the 9th International Neuromuscular Congress, governor of BHP Billiton Charitable Trustees and Board Member of Prince Henry's Institute, Burnet Centre for Medical Research, Monash Institute of Medical Research, and Southern Health. He has been awarded the Queen's Square prize for Neurological Research (1982), Bethlehem Griffiths Research Medal (2003) and Sir Louis Pyke Award for contribution to Multiple Sclerosis (2004).

Professor Garry Jennings
AM

Garry Jennings is director. He is an internationally recognised authority in cardiology. His background is both a clinical cardiologist and an academic with broad clinical experience and research ranging from community prevention to fundamental research on mechanisms and treatments of high blood pressure, atherosclerosis and heart failure. He has published well over 300 scientific papers in fields including exercise, cardiac and vascular hypertrophy, the neurobiology of cardiovascular disease and heart failure.

He is Cardiovascular and Respiratory Co-Director for Bayside Health, which includes the Alfred Hospital, and is a Professor of Medicine at Monash University. He heads a World Health Organisation Collaborating Centre for Research and Training in Cardiovascular Diseases and a National Health and Medical Research Council Centre of Clinical Research Excellence (the Alfred and Baker Medical Unit). Garry Chairs CVHAC, the peak committee overseeing the National Heart Foundation research and cardiovascular health programs. He represents the Cardiac Society on the National Heart, Stroke and Vascular Health Strategies Group and has been President of the High Blood Pressure Research Council of Australia. He is a Director of several biotechnology companies and has chaired Steering Committees of large multi-centre trials.

In 2005 he was awarded the honour 'Member in the Order of Australia'.

Greg Hywood

Gregory Hywood spent nearly 30 years in the newspaper industry. He joined the Australian Financial Review in 1976. He was variously Canberra Bureau Chief, European Correspondent and Washington Correspondent before becoming Editor in 1992 and then Publisher and Editor in Chief in 1996. In 1998 he was appointed Publisher and Editor in Chief of the Sydney Morning Herald and in 2000 Publisher and Editor in Chief of the Age and Group Publisher of Fairfax Magazines.

He is CEO of Tourism Victoria. He is a Board member of the Geelong Football Club, The State Library and the Baker Institute.

David Lloyd

David Lloyd is Chief Operating Officer of the Baker Heart Research Institute. He took up this position in August 2005 and joined the Baker Board in January 2006.

He holds a BA (Hons) in Philosophy from the University of Stirling and a Master of Public Administration from the University of Tasmania.

He began his career in the New Zealand Ministry of Foreign Affairs, then served in the New Zealand Trade Development Board from 1986 to 1990.

He moved into higher education administration in 1990, first in the New Zealand Polytechnic Sector and then as Director, International and Commercial Services at the University of Tasmania from 1993 to 1998.

In 1998 he was appointed CEO of Melbourne Enterprises International Ltd, the commercial arm of the University of Melbourne. When that company was merged with Melbourne University Private in 2001 he became CEO of MUP until his appointment to the Baker in 2005.

David is also a director of the Chifley Business School.

Professor Graeme Ryan
AC

Graeme Ryan is currently part-time director of Research Strategy at The Alfred Hospital. For more than 20 years, Graeme has had senior leadership and management roles in medical research, medical education and health care. These roles include a period of 10 years, from 1986 to 1995, as dean of Medicine at the University of Melbourne and then, from 1996 to 2000, as Chief of Clinical Services and board member, Inner and Eastern Health Care Network, Melbourne.

As well as his role at The Alfred since 2000, he is also currently chairman of the Board of Directors, Royal Victorian Eye and Ear Hospital, a Governor of the Ian Potter Foundation, chairman of the NHMRC Special Expert Committee on Transmissible Spongiform Encephalopathies, and a member of the Commonwealth Plasma Fractionation Review Committee.

Peter Scott

Peter Scott leads the Melbourne Investment Banking team of UBS and has more than 20 years experience in providing financial advice to large Australian companies and governments.

He has extensive experience in Mergers and Acquisitions (including public company takeovers), corporate financial restructuring, joint ventures, asset sales and purchases, public floats, equity and debt issues and privatisations. The sectors and industries in which he has worked with clients include health care, building materials, financial services, health care, manufacturing, media and telecommunications, public utilities, resources and transport.

Peter has been a member of the Takeovers Panel since 2002 and is also a director of UWC Limited.

Professor Richard Smallwood
AO

Richard Smallwood is an Emeritus Professor of Medicine, University of Melbourne.

As Professor of Medicine with the University of Melbourne, Richard was head of the Department of Medicine and Chairman of the Division of Medicine at the Austin and Repatriation Medical Centre. He was also Director of Gastroenterology at the centre, and has had over 30 years involvement in the teaching of undergraduates and postgraduates. He has published over 250 clinical and scientific papers, primarily in the field of the liver and its diseases. He was President of the Royal Australasian College of Physicians from 1996 to 1998.

In addition to his extensive Australian and international clinical and research experience, Richard had a long standing association with the National Health and Medical Research Council. He was chair of the council from 1994 to 1997 and has been member or chair of several committees. He was a member of the Australian Health Ministers Advisory Council from 1993 to 1997.

In November 1999 he was seconded to Canberra as Australia's Chief Medical Officer, a position he held until July 2003. He also provided consultation and advice on international aspects of health, and in 2000 was a Vice President of the World Health Assembly in Geneva.

Present appointments include chair of the National Blood Authority, Chair of the Ministerial Taskforce for Cancer in Victoria, chair of the Specialist Education Accreditation Committee of the Australian Medical Council and Member of the Board of VicHealth.

The early years – important people and some landmark papers

Celebrating
80
YEARS OF RESEARCH

THE Baker Heart Research Institute is Australia's largest heart research institute and one of this nation's most important resources in the fight against cardiovascular disease. Over the years our researchers have been responsible for many groundbreaking advances including:

- Establishing open heart surgery in Australia (in collaboration with The Alfred Hospital)
- Proving that exercise can lower blood pressure
- Improving preservation techniques for the long distance transport of donor hearts for transplantation
- Proving that mental stress and cigarette smoking both provide powerful, selective and potentially harmful stimulation of the nerves of the heart
- Developing techniques to assess stiffness of arteries, enabling the reliable early detection of atherosclerosis and hypertension
- Developing a method to repair heart valves without surgery
- Identifying key factors involved in clotting
- Defining the differences between the two forms of diabetes, type 1 and type 2.

› Director 1938–1949 Arthur Basil Corkill
› Director 1949–1974 Tom E.Lowe
Virologist Frank Fenner releases the myxoma virus, to control rabbits, in the Murray River Valley.
› Director 1926–1938 W.S. Penfold
› Charles Richter and Beno Gutenberg develop the Richter scale for measuring earthquakes.
› First assembly (and calculations) of a general purpose electronic computer, covering 1800 feet of floor space.
› US physician Jonas Salk develops the first polio vaccine
› February 6, first use of a mechanical heart in a human patient.
› Norman Watkins, 21, survives Australia's first organ transplant, a kidney graft operation at Royal Melbourne Hospital.
› US physician Jonas Salk develops the first polio vaccine
› February 6, first use of a mechanical heart in a human patient.
› First organ transplant Richard Herrick received a kidney from his twin brother Ronald at Boston's Peter Bent Brigham Hospital on December 23, 1954.
› April 18, death of Albert Einstein.
› April 12, Russian cosmonaut Yuri Gagarin becomes first human in space.

1926-48 | 1926 | 1932 | 1938 | 1949 | 1950 | 1951 | 1952 | 1953 | 1954 | 1955 | 1957 | 1961 | 1962 | 1963

April 1, 1926: The Baker Medical Research Institute is established.

When John F. Mackeddie, a clinical doctor and medical researcher, had the idea for improving the laboratory facilities of The Alfred Hospital, he wanted the hospital be able to keep up with the exciting new advances that were occurring overseas, especially in relation to the management of diabetes and other metabolic disorders. He was able to persuade his friend, the pharmacist and philanthropist Thomas Baker and his wife, Alice and sister-in-law, Eleanor Shaw, to assume financial responsibility for a medical institute. Together they decided that the institute should not only provide a better laboratory service for the hospital but should also have facilities for medical research. The Baker Medical Research Institute was born.

Research 1926 – 1948:

The institute's relationship with The Alfred Hospital from its very formation suggested it would evolve as a place of clinically relevant research. An overview of early research projects, before cardiovascular disease became the main focus in 1975, confirms this was the case. Early Baker research pursuits range from surgery to asthma and infectious diseases.

Important early projects ranged in focus from the central nervous system and pioneering work by Mackeddie and colleagues into better techniques for x-rays of the cerebrospinal fluid and studies of its cell content and chemistry in various diseases. Their work greatly improved the diagnostic ability for diseases of the central nervous system. From this base, Laurence Cox, between 1930 and 1938, was able to relate clinical observations with pathological findings in a large series of brain tumours. His research was reviewed in the American Journal of Pathology in 1933.

Work in infectious diseases by the Baker's first director, William J Penfold, led to a new technique for bacteriological research: "blood culture", by which organisms circulating in the bloodstream were grown in the laboratory.

Venous Occlusion Plethysmography: A critical study

Alfred J. Barnett
MD, FRACP, FRCP,

› Kimpton Research Scholar, Clinical Research Unit, Alfred Hospital, Melbourne and associate director of the Baker.
› Major contributions in peripheral arterial disease, hypertension and scleroderma.

Fluid Balance in Congestive Cardiac Failure two Mechanisms in Diuresis

T.E. Lowe,
MD, DSc Melb, FRACP, MRCP

› First director of the Clinical Research Unit (now known as ABMU), 1949.
› Director of the Baker 1949–1974.

An Anti-Insulin Factor in the Plasma of Diabetic Patients

Joseph Bornstein and Phyllis Trewhella

Professor Joseph Bornstein,
MD, DSc, FRACP

› At the Baker from 1948 –1952.
› Probably the first to recognise the distinction between Types 1 and 2 diabetes.

The Vectorelectrocardiogram in Bundle Branch Block

T.E. Lowe and J.M. Gardiner

Dr JM Gardiner, *MD, FRCP, FRACP, FACC*

› Dr Gardiner was a superb cardiologist who brought modern cardiology to Melbourne in the 1950s and established the Cardiovascular Diagnostic Service. A great teacher.

Gastric, Duodenal and Jejunal Motility in Man: Physiological studies by Balloon-Kymography

Roderick Andrew AO, MD, FRCP, FRACP

› Professor Andrew probably had the longest association with the Baker, from 1947 until his death in the mid-90s. An eminent gastroenterologist and first medical dean at Monash University. 1954 – The Mechanism of Arterial Hypertension: A Comparison of the Effects of Hexamethonium Bromide in Hypertensive and Normotensive Patients.

The Nature of the Pigmentary Disturbance in Addison's Disease

Bryan Hudson and Geoff Bentley

Professor Bryan Hudson,
DSc, MD, FRCP, FRACP

› A most distinguished endocrinologist with major findings on pituitary hormones and first Monash professor of medicine.

Associate professor Geoff Bentley, *PhD*

› Led pharmacology research from 1952–1955.

Total Body Perfusion

G.R. Stirling, K.N. Morris and F. Kincross

Dr George Stirling,
MBBS, FRACS, FACS (1955–1962)

› Dr Stirling pioneered research into the beginnings of modern cardiac surgery – heart-lung perfusion systems, myocardial preservation, and hyperthermia.

Dr. Ken Morris

› Performed the first open-heart operation in Australia in 1957.

Experimental Pancreatitis: Use of a new Antiproteolytic substance, Trasylol

A.D. McCutcheon,
MD, FRACP and D Race, MBBS

› Dr Doug McCutcheon worked at the Baker at various times from 1950 until 1961.

› January 11, US surgeon-general makes first announcement that smoking may be bad for health.
› July 20, First manned moon landing.
› US Department of Defence invents the internet.
› Director 1975–1989 Paul I. Korner
› Bill Gates and Paul Allen form company called Micro Soft.
› Immunologist Peter Doherty describes how the body recognises virus-infected cells.
› July 20, 1976: Viking 1 lands on mars, sends back first clear images of planet's surface.
› First vaccine for pneumonia.
› Director 1990–2000 John W. Funder
› US launches space shuttle Columbia.
› May, first report of the virus that causes AIDS.
› Space shuttle Challenger explodes, killing all seven on board.
› British computer programmer Tim Berners-Lee invents the world wide web.
› Scientists at Edinburgh's Roslin Institute clone first adult animal, Dolly the sheep.
› Director 2000 Garry Jennings
› Perth researchers Barry Marshall and Robin Warren win the Nobel Prize for Medicine for their discovery of a bacterium that causes gastritis and stomach ulcers.
› January 2, first successful human heart transplant.
› May 14, launch of the first US space station, Skylab.

1964 | 1968 | 1969 | 1973 | 1975-80 | 1976 | 1977 | 1980-90 | 1981 | 1983 | 1986 | 1989 | 1990-06 | 1996 | 2000 | 2004

A Structural Study of Abnormal Haemoglobins Occurring in New Guinea

C.C. Curtain

Dr Cyril Curtain,
PhD, DSc (1955–1966)

› Dr Curtain was a protein chemist and biochemist who conducted outstanding research on blood proteins in clinical disorders.

Myocardial Function during b-Adrenergic Blockade

Winifred G. Naylor

Professor Gwen Naylor,
DSc (1955–1972)

› Professor Naylor was one of the Institute's most prolific and innovative scientists and an international authority on myocardial metabolism, function and pharmacology. Her work contributed greatly to the introduction of calcium channel blockers, a keystone of treatment for high blood pressure and angina.

Some proud achievements 1975 to 1980

› Hypertension Evaluation Clinic was expanded
› Garry Jennings, Alex Bobik, Alf Burnett and Paul Korner introduced clinical pharmacological methods to optimise antihypertensive therapy.
› Paul Nestel recruited to take charge of atherosclerosis research.
› Lipid Clinic was established
› Exercise testing centre for detecting ischaemic heart disease was established.
› Heart Risk evaluation clinic was established (with the Victorian division of the National Heart Foundation)
› Commencement of collaborative studies between the Clinical Research Unit (now ABMU) and the Circulatory and Hypertension Experimental unit at the Baker Medical Research Institute. This collaboration leads to world leadership in aspects of hypertension research and treatment.
› First demonstration that it may be possible to normalise the structure of arteries disease when blood pressure is well controlled in hypertensive patients.
› Introduction of the ACE inhibitor enalapril to manage patients with essential hypertension resistant to standard therapies.
› Improvements in the clinical diagnosis and treatment of circulatory abnormalities associated with autonomic dysfunction.
› Epidemiological studies demonstrate that low HDL plasma levels are associated with significant risk of coronary heart disease.
› Establishment in humans that cholesterol leaving tissues is immediately and primarily transferred to HDL in plasma (study in obese subjects undergoing weight loss)
› Demonstration that moderate long-term exercise with apparent insulin resistance improved insulin resistance and lowered plasma triglycerides without affecting body weight.
› Studies focus on environmental factors that may play key roles in precipitating obesity and diabetes in humans.
› Dr Murray Esler demonstrates a neural defective noradrenaline uptake system in some hypertensive patients.
› New treatment is introduced to postural hypotension.
› Beta-adrenoceptors are found to be increased in patients with autonomic neuropathy, correlating with their greater response to beta-adrenergic stimulation.

Some proud achievements 1980 – 1990

› Development of radiotracer methodology to study sympathetic function in humans.
› Examination of the feasibility of using beta-adrenoceptor pro-drugs to prolong the duration of the beta-adrenoceptor blockade.
› Development of analytical methods for measuring noradrenaline metabolites.
› First ever measurements of regional sympathetic nerve activity in humans.
› Observation that the severity of coronary heart disease in men is more linked to cholesterol-rich lipoproteins, while in women it is more linked to triglyceride-rich fractions.
› Investigations into the usefulness of partial beta-adrenoceptor agonists for the treatment of heart failure.
› Enalapril is useful for the treatment of congestive heart failure.
› Demonstration of defective thermogenesis in obese people
› Marine polyenoic acids are potent triglyceride lowering agents.
› Fish oils lower plasma triglycerides.
› Demonstration that adrenoceptors (alpha and beta) are regulated in an inverse manner during chronic changes in sympathetic nerve activity.
› Increases in physical activity induce favourable reductions in cardiovascular risk.
› Evidence to suggest that cardiac sympathetic nervous activity contributes to arrhythmia development during ischaemia.
› Demonstration from noradrenaline spillover studies that, in congestive heart failure, clearance of noradrenaline is reduced and release from sympathetic nerves is increased.
› Demonstration that a new transport system- sodium hydrogen exchange- is the major sodium transport process responsible for sodium influx into vascular smooth muscle and cardiac cells.
› Sympathetic nervous activity increased in cirrhosis of the liver.
› Demonstration that most people with high blood pressure have some structural and functional cardiac abnormality.
› Exercise may modify renal sympathetic function which is important for control of vascular resistance
› Exercise is recognised as one of the most reliable life-style methods for lowering blood pressure in sedentary people
› The opening up of new blood vessels is found to account for falls in blood pressure that occur in training individuals. Later reductions in sympathetic nerve activity also contribute.
› Demonstration that exercise lowers blood pressure in hypertensives without demonstrable changes in the structure or compliance of the heart.
› Demonstration in animals with genetic hypertension that early prevention of cardiac and vascular hypertrophy results in markedly attenuated hypertension later in life.
› Echo-Doppler methods introduced to study aortic distensibility.
› Impairments in vascular function (contraction and relaxation) identified in patients with heart failure.
› Transforming growth factor-beta is identified as a key factor which contributes to vascular hypertrophy and collagen deposition in arteries of hypertensives.
› First demonstration that sodium-hydrogen exchange is a major intracellular pH regulatory pathway in cardiac and vascular smooth muscle cells.
› First ever measurement of noradrenaline release from brain in human subjects.

Some proud achievements 1990 – 2006

› Defining the genetic basis of pseudohypoaldosteronism
› Pets associated with lower cardiovascular risk factors
› Enzyme actions provide a novel mechanism of selectivity of action of steroids.
› 11BHSD cloned for the first time
› The hypertension of renal artery narrowing defined
› Leptin shown to be produced in the human brain
› Hypertension has several causes in many patients proven by unique new methods of studying human brain release of amines

Research Partners

THE Baker is a member of the Alfred Medical Research and Education Precinct (AMREP) and has advanced relationships with other AMREP tenants – The Burnet Institute, The Alfred Hospital, Monash University, The Australian Centre for Blood Diseases, Nucleus Network (a wholly owned Baker subsidiary offering phase 1–4 clinical trials), the Centre for Health Care Innovation and The National Trauma Research Institute – as well as other academic and research institutions outside of AMREP. These alliances are critical to the Baker's success: good science does not thrive in isolation and these mutually beneficial relationships are key to our standing as the nation's premier cardiovascular research institute.

The Baker is a member of the Alfred Medical Research and Education Precinct (AMREP) and has advanced relationships with other AMREP tenants

The Alfred Hospital

The Baker and The Alfred have been integrally linked for 80 years, particularly since the establishment of the Clinical Research Unit in 1948 (which became the Alfred Baker Medical Unit in 1989). Much of the research profile of the Baker has depended on access to clinical practice, patient data and human tissue provided by The Alfred; and The Alfred's service reputation as a hospital has been built in large measure around the research strengths of the Baker, including catheter laboratories, heart and lung transplants, vascular medicine, biochemistry, endinocrinology and clinical pharmacology.

The Burnet Institute /the Austin

The highly regarded Burnet Institute has merged with the Austin Research Institute, and this merger is bringing the Austin to the AMREP site. This brings with it opportunities for greater collaboration, and makes it necessary also for the Baker to respond to the greater call that will now be made on jointly funded core services.

Monash University

The substance of the Baker's collaboration with Monash is with the components of the university based on AMREP – the Inner and Eastern Medical School and the Australian Centre for Blood Diseases. At an institutional level, the Baker's formal affiliation with Monash is managed out of its Clayton campus. Just over half of the PhD students being supervised at the Baker are enrolled with Monash, and the university provides access to academic status for Baker research staff.

The University of Melbourne

The Baker benefits from the university's willingness to support the institute in its research activity through student enrolment, credentialing of staff, the provision of core services (such as proteomics through Bio21) and research collaboration in general.

Atherosclerosis Research Trust

This UK Trust has supported the work of Professor David Kaye since 2001 under the Wynn Department. The grant honours a distinguished Melbourne-born clinician-scientist, Professor Victor Wynn. Since its establishment, the department has conducted research into various aspects of heart failure prevention and cure.

State and Federal Governments

Locally, we receive strong support from the Victorian Government Department of Infrastructure, Industry and Regional Development (DIIRD) in the form of vital infrastructure funding to support the Baker's research profile. At a federal level, the National Health and Medical Research Council provides substantial funding that is crucial to the continuing work of our scientists.

National Heart Foundation (NHF)

The work of the National Heart Foundation intersects with that of the Baker at a number of levels; as a provider of research funds, as a collaborator on certain projects, and as a co-contributor to national awareness of risk factors of cardiovascular disease and preventive health measures.

World Health Organisation

The Baker is a World Health Organisation Centre for Cardiovascular Research and Training – recognition of its role at the forefront of heart disease research, and of its focus on prevention and cure.

The Juvenile Diabetes Research Foundation

The philanthropic, US-based JDRF is a major supporter of research at the Baker, recognised in the JDRF Diabetes and Metabolism division of the institute, led by Professor Mark Cooper. JDRF grants in 2005 exceeded $4 million.

Research

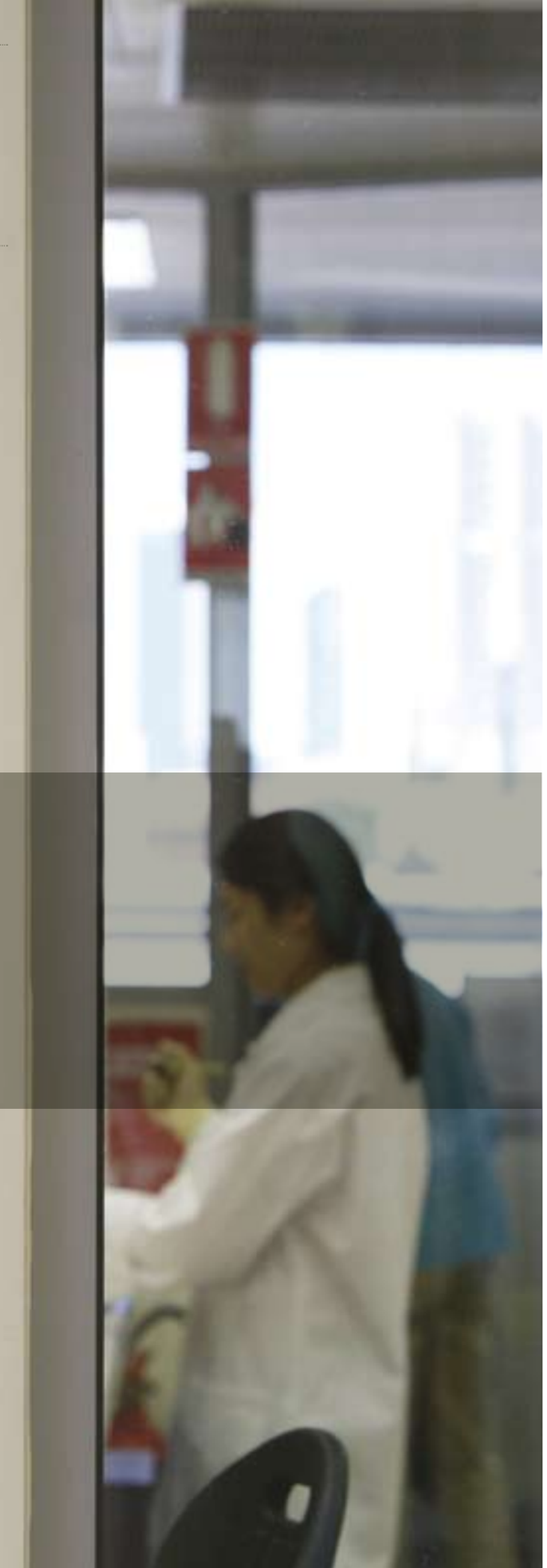
THE Baker leads the fight against heart disease. Cardiovascular disease is Australia's most serious health problem. Over the last decade the prevalence of cardiovascular disease rose by close to 20 per cent and at a cost of more than $7 billion a year, it demands 11 per cent of the nation's total health care expenditure.

The major areas of research at the Baker are:

- The risk factors and prevention of heart disease
- Coronary heart disease, heart attack and sudden coronary death
- Heart failure
- Diabetes and its complications
- Cardiovascular disease and the brain

We are recognised as one of the world's leading medical research centres. Four divisions: Experimental Cardiology and Heart Failure, Atherothrombosis and Vascular, JDRF and Metabolism and Cardiovascular Neurosciences oversee the work of 26 labs. Their work is dedicated to the prevention and cure of heart disease by concentration on the themes outlined above. The work of these labs and our talented scientists is crucially supported by a series of core services that each play an important part in the translation of our research from bench top to bedside.

4 Divisions, 26 Labs – dedicated to the prevention and cure of heart disease. In addition, Baker Clinical weaves together the institute's research pursuits with our clinical goals, many of which are realised through our collaboration with The Alfred Hospital.

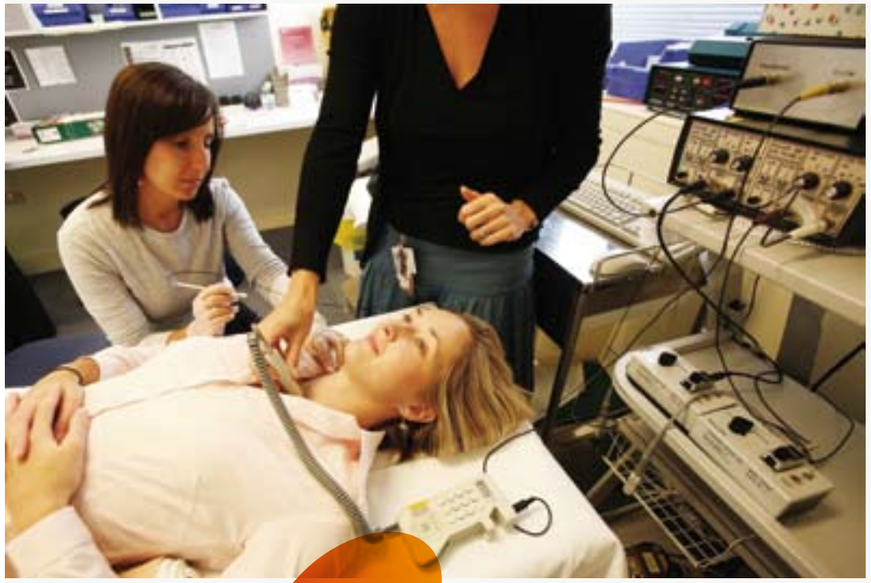


Baker Clinical

The pioneering work of Tony and his team of researchers from the Baker has added significantly to the way cardiovascular disease risk is assessed and how disease is treated.

ASSOCIATE director of Baker Clinical and head of Cardiovascular Medicine at The Alfred Hospital, Professor Anthony Dart oversees clinical research across all divisions of the Baker. As both a clinical cardiologist and distinguished researcher, Tony also works in collaboration with the Baker's Experimental Cardiology lab, run by Xiao-Jun Du.

As the head of Baker Clinical, Tony oversees the direction and function of the Alfred & Baker Medical Unit, the hub of collaborative studies between The Alfred and the Baker; the Cardiovascular Disease Prevention Unit (CVDPU) and the Risk Clinic and Gene Bank.



Clinical studies in the past have been strongly focused in large arteries and systolic hypertension in endothelial function – the lining of blood vessels and how they affect blood vessel function and the regulation of blood pressure. More recently clinical studies have been moved more prominently into the area of atherosclerosis, the development of plaques in coronary blood vessels.

Alfred-Baker collaborative clinical studies in large arteries have made a major contribution to the fight against cardiovascular disease. The study of large arteries was far from mainstream when it became Tony's area of research focus some 15 years ago. The pioneering work of Tony and his team of researchers from the Baker has added significantly to the way cardiovascular disease risk is assessed and how disease is treated.

In recent years clinical and experimental research has focused more on acute coronary syndromes – the causes of acute heart attacks. As time goes on, this body of work is contributing to our understanding of such coronary events in a number of ways. These include establishing a methodology for studying acute coronary disease by obtaining blood samples from the coronary circulation in patients, and relating findings to the structure of disease plaque. There have also been novel findings both in substances released by coronary plaques and in the structural changes that plaques undergo.

Ongoing research projects include an investigation of the triggers of symptomatic coronary atherosclerosis while another major area of investigation is related to understanding the causes of heart rupture, a deadly complication of heart attack. These projects, running across different labs at the Baker with a different clinical and experimental focus in each, all aim to determine how such complications can be predicted and prevented.

The Alfred & Baker Medical Unit (ABMU)

THE Alfred and Baker Medical Unit (ABMU), established in 1949, represents decades of rewarding collaboration between the Baker Heart Research Institute and The Alfred Hospital. This partnership, unique in Australian medical research, plays an important part in securing the Baker's position as a world leader in cardiovascular research.

Positioned in The Alfred Hospital's third floor Heart Centre, the ABMU is the hub of joint research and clinical activity between the two institutions. The Alfred is renowned for its treatment and care of heart disease patients. In turn, the Baker's scientists are leaders in cardiovascular disease research. Their combined force ensures that Baker research remains directly relevant – both to disease as it is experienced by those who are sick and to community needs and priorities.

The vast database of patient clinical information held by The Alfred is available, with the consent that almost all patients give, to Baker researchers daily. This network of information allows broad and up-to-date profiles of patients and disease as well as the effectiveness of treatments. It is also a resource that allows scientists to identify suitable candidates for participation in research – from the effect of exercise on blood sugar levels to the relationship between depression and cardiovascular disease risk.

The ABMU also fulfils a health promotion and risk assessment role for the Baker, through the Risk Reduction Clinic and the Cardiovascular Disease Prevention Unit.

The Risk Reduction Clinic focuses on the prevention of cardiovascular disease and identifies links between nutrition, exercise and heart disease. Staff at the Risk Reduction Clinic run heart disease risk assessments for members of the community and are involved in research studies. With consent, information gathered in this clinic is added to samples collected for The Alfred and Baker Gene Bank, an invaluable store of genetic samples that can provide researchers with a genetic "snapshot" of health and disease over time.

Inpatients and outpatients at The Alfred's Heart Centre are invited to participate in ABMU research. Many take up this option, which gives Baker scientists access to the most clinically relevant groups for their studies. State-of-the-art facilities and equipment at the Heart Centre are used for clinical treatment and for clinical research equally.

This partnership, unique in Australian medical research, plays an important part in securing the Baker's position as a world leader in cardiovascular research.

Experimental Cardiology and Heart Failure Division

Professor David Kaye is an associate director of the Baker and head of the Experimental Cardiology and Heart Failure Division.

RESEARCH across this division aims to find ways of stopping the deterioration of heart failure patients through a range of means – from better understanding the cellular mechanisms involved in the process of heart failure itself to developing therapeutic devices to improve the health of those living with the condition.

Heart failure is a debilitating, progressive condition that can begin as a response to injury of the heart muscle, for example after heart attack. Heart failure has devastating consequences for patients, representing a host of secondary conditions that result from the failing heart's inability to adequately pump blood around the body. It is the third largest cause of death among the various forms of cardiovascular disease in Australia, and the major cause of disability in the elderly.

The broad work of David's team is centred on understanding the processes of heart failure in order to identify those who might be at risk of the condition and to halt its progression in those already suffering. In extreme cases, heart failure patients require heart transplants if they are to have any chance of survival. The cardiac surgery laboratory works on ways of improving the health of people who must undergo surgery for heart failure and other cardiac disease.

The research of this team ranges from work on the cellular, molecular and genetic underpinnings of the progression from initial heart muscle damage to heart failure, to large animal studies with immediate clinical relevance and the development of therapeutic devices to improve the lives of those living with the condition. Our labs are studying the mechanics of the heart and heart muscle across a range of disciplines.

Projects underway include studies of the enlarged heart (cardiac hypertrophy) – why it is beneficial to athletes but a harmful development in heart failure; the effects of diabetes on the muscle of the heart; the effects of the hormone relaxin on fibrotic heart tissue and the investigation of better cardiac surgical techniques.

The following pages will give some details on the work of the individual labs within this division, and the way their research fits into the work of the Baker as a whole.

Wynn Department of Cardiology

› David Kaye

HEART failure – a debilitating, progressive condition in which the heart muscle deteriorates and fails to adequately pump blood around the body – can occur in people who have suffered some damage to the heart, commonly after a heart attack. As more people survive heart attack, heart failure is becoming more common. The quality of life of heart failure patients is dramatically reduced and in many cases it leads to death. It is currently estimated to affect 300,000 Australians and up to 30,000 new cases develop each year.

David Kaye's own research concentrates on the investigation of the development and progression of congestive heart failure, with an emphasis on designing therapies that are of direct use in the treatment of this condition. In addition, by exploring what can be done to regenerate hearts that have failed, and specifically how the heart muscle can be rebuilt to make it function better, David and his team hope to find a way to cure heart failure, not just treat it.

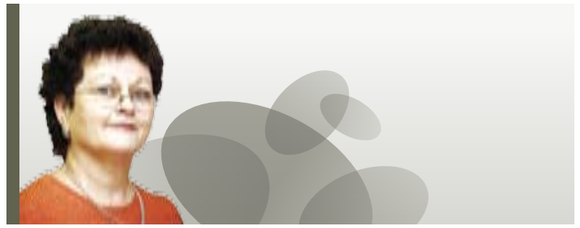
In association with the Baker's John Power, David has developed a non-surgical method for mitral valve repair: For many patients with advanced heart failure, secondary failure of the mitral valve to function normally results in a considerable worsening of the disease because of the effect of mitral regurgitation. When this circumstance arises, the risk of death, hospitalisation and disabling symptoms increases. Unfortunately for these patients, the risk of reparative cardiac surgery is too high.

Having recognised this significant clinical problem, with an unmet need, David and his team developed a novel technique for mitral valve repair which could be performed via catheter, removing the need for open heart surgery. The first patient implant was successfully conducted in 2004 and the device is now under trial internationally. This development was nominated as one of '10 of the best' Australian medical research developments by the federal Government and the National Health and Medical Research Council in 2005.

Professor David Kaye is an associate director of the Baker and heads the institute's Experimental Cardiology and Heart Failure division. He is also head of the institute's Wynn Department of Metabolic Cardiology, a laboratory within the division, and works as a cardiologist at The Alfred.

Cellular Biochemistry

› Elizabeth Woodcock



Associate professor Elizabeth Woodcock is a principal fellow of the National Health and Medical Research Council and heads the institute's Cellular Biochemistry laboratory.

ASSOCIATE Professor Elizabeth Woodcock is a Principal Research Fellow of the National Health and Medical Research Council and heads the institute's Cellular Biochemistry laboratory.

Liz is known primarily for studies of mechanisms where the heart responds to stimulation, and how these processes contribute to heart disease. In particular this laboratory studies mechanisms associated with the regulation of intracellular calcium and the maintenance of ion channels. The laboratory is best known for defining a new cause of arrhythmogenesis, leading to sudden cardiac death. Their research concentrates on pinpointing the exact mechanisms involved in atrial and ventricular fibrillation, where the heart muscle cells beat out of synchrony and thus the heart is unable to pump blood effectively.

The long term aim is to develop treatments for sudden cardiac death that are well tolerated. Liz's laboratory is also investigating novel mechanisms to increase the strength of the heart beat. This will improve quality of life for heart failure patients. They are also hoping to identify factors that may reduce damage to the heart during a heart attack. Reduction in damage to the heart will reduce the incidence of heart failure in the longer term.

Experimental Cardiology

› Xiao-Jun Du

DU's research group at the Baker was established in 1995, when, in a first for Australia, he shifted his research focus from classical models to genetically modified mouse models: animals which have been genetically altered, allowing the close examination of the effects of specific genes in heart disease. Du's research is pivotal to the work at the Baker: application and discovery in vivo is critical to understanding genetic and molecular mechanisms.

The contribution of these new classes of genetically modified mice to cardiovascular disease research cannot be overstated. Eliminating or over expressing a gene in a mouse and then inducing a range of conditions from diabetes to heart attack in the animal allows detailed study of the behaviours of that gene and the mechanisms affected by it. Crossing these animals would also allow for research on gene–gene interactions.

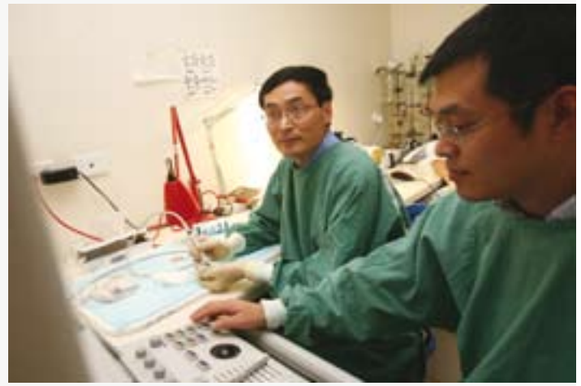
Du's stamp on this field has been the development of intricate research techniques on these animals. The heart of a mouse is roughly the size of a soybean and weighs about 0.1 gram. Microsurgery, open chest surgery and other sophisticated procedures such as heart catheterisation and echocardiography, the estimation of the size and shape of the heart, are infinitely complicated by the very tininess of the organ. Performing these procedures is an exacting technical process and one that Du has pioneered. His is the only group in Australia capable of performing this surgery and one of only a few in the world with such expertise. Du is regularly called upon to train other scientists and internationally his skills are in high demand.

The importance of mice to cardiovascular disease research was also highlighted with the discovery in 1997 by Du's team that the mouse was the only animal model to develop one of the most serious complications known in heart attack: rupture of the ventricular wall. This event almost always leads to sudden death and accounts for 5~25% of total deaths during the acute phase. While many other areas of heart disease have seen great improvements, this, one of the most malignant complications, has been out of reach of researchers because none of the other species used in heart research develop ruptures after heart attack is induced.

This significant discovery has led to ongoing research by Du and his lab into ways of eliminating the risk of this complication – understanding why ruptures occur in the first place and which drug treatments might stop them occurring.

Another key research area for Du is on the peptide hormone relaxin, a study that is continuing and expanding in its collaboration with the Howard Florey Institute in Melbourne. While it has long been associated with reproduction, its increase in the female body in pregnancy allowing the enlargement of the uterus and the safe delivery of a baby, it appears that relaxin, which breaks down collagen in the reproductive system, may also help prevent heart disease.

Until now however, the function of this hormone had only been investigated in relation to the reproductive system. Developing a model of mouse without the relaxin gene, Du discovered its absence causes a build up of scar tissue in the heart, a condition known as fibrosis and the hallmark of heart disease in humans. Fibrosis is one of the body's most basic responses to heart disease and greatly contributes to the decline of heart function. The importance of reducing fibrosis is well documented but as yet there is no effective drug treatment. Most recent research has found that treating animals with relaxin for a period as short as two weeks significantly reduced their fibrosis. Plans are now underway for a clinical trial.



Xiao-Jun Du is a medical doctor by training and switched his focus from the clinic to the laboratory early in his career, when he was still living in China.

Cardiac Hypertrophy

› Julie McMullen

Julie McMullen trained at the University of NSW and completed a postdoctoral research fellowship in the US at Harvard before joining the Baker early in 2005.

THIS lab focuses on understanding heart enlargement, cardiac hypertrophy, through comparisons between models of health and disease: examining the enlarged athletic heart in comparison to heart enlargement associated with disease.

It is well understood that the hearts of athletes grow: the super fit have a heart size greater than the average person. This enlargement is of benefit to them in their training and works to enable them to continue their level of exercise and fitness. When they stop training that healthy heart growth stops and the heart returns to a normal size. Conversely, heart failure patients commonly experience heart growth but this change is devastating. It wreaks havoc and is usually impossible to reverse.

From this observation, Julie's research has focused on understanding the changes in the athlete's heart that might benefit people with heart disease, whose heart growth might be caused by hypertension and/or heart failure.

Julie's studies demonstrate there are changes in genes that occur in people with cardiac hypertrophy associated with heart failure that do not occur in the athlete's heart. She has established that even though there are comparable increases in heart size, there are clear molecular and histological changes between the two.

Julie is working to identify genes causing heart enlargement that are good for the heart, as opposed to those genes causing heart enlargement with detrimental effects. In doing so she hopes to reproduce the work of the "good genes" in the failing heart.

Her research is novel in its suggestion that it is possible to promote and activate "good" genes in the heart as opposed to just inhibiting "bad" genes that cause the growth of the diseased heart.

Her research involves genetically modified mouse models of heart failure. By over expressing a gene involved in the growth of the athlete's heart in a mouse model with heart failure, Julie hopes to understand whether this gene might be of use to patients with heart disease, and whether its promotion and growth can negate the effects of the "bad" growth genes.

In understanding what is making the heart pump well in the athlete's case, Julie's research is going a long way towards trying to find a cure for the failing heart. Current therapeutics are largely treating heart failure–her aim is to help find a cure.

Cardiac Surgery

› Salvatore Pepe

THIS research unit is devoted to improving the condition of patients before, during and after heart surgery by better understanding the biology and metabolism of both the diseased and the healthy heart.

Based at the Baker, the lab is closely tied to its clinical research unit, headed by Professor Franklin Rosenfeldt, a surgeon in the Department of Cardiothoracic Surgery at The Alfred Hospital. Although heart surgery is often undergone in an emergency after a sudden heart attack, or in chronic conditions such as heart failure when other medical approaches have been exhausted, elective surgery occurs far more frequently when the patient has stabilised and involves coronary artery bypass grafting, heart valve repair or replacement. By its nature the cardiac surgery patient's profile is one where surgery is a risk and health is compromised by other symptoms of heart disease or by the advanced age of the patient, with most being over 60 years old.

Salvatore's lab is investigating the molecular deficiencies of the human heart that can give rise to the metabolic dysfunction that occurs in ischaemic heart disease, heart failure and atrial fibrillation. Atrial fibrillation, where the heart beats irregularly and ineffectively, is one debilitating and expensive complication of surgery being investigated by this research unit. About 30 per cent of patients suffer this complication after surgery. Atrial fibrillation can be treated but the drugs used have potent side effects, are used after the condition arises, and can often be ineffective. Consequently, in-hospital recovery and care is usually greatly extended and more expensive. Although atrial fibrillation is itself not fatal, left untreated it leads to blood clot formation, substantially increasing the risk of serious complications such as stroke and heart failure.

Salvatore Pepe, a scientist by training, heads the Cardiac Surgery laboratory.

This research group is taking a new approach to tackle post-operative atrial fibrillation by targeting before surgery the factors that make atrial fibrillation more likely to occur. The lab's previous work established that the ageing process creates a deficiency in the capacity of human heart muscle to recover from the metabolic stress of heart disease and of surgery itself. This is mainly due to deficiencies in the heart's natural antioxidants and related enzymes. The group recently demonstrated in a clinical trial of Coenzyme Q10 that it afforded elective cardiac surgery patients improved metabolic benefits and greater tolerance of stresses imposed by heart surgery.

Salvatore has been recently funded by the National Health and Medical Research Council, starting in 2006, to conduct a three year clinical trial to test whether omega-3 fatty acid pre-treatment of elective cardiac surgery patients can reduce the incidence of post-operative atrial fibrillation, reduce the length of hospital stay and other related clinical and molecular complications. Positive results from this trial will provide an inexpensive, drug free approach to minimising a major complication of heart surgery.

Applied Cardiovascular Research

› John Power

John Power trained as a vet and worked in rural private practice for 17 years before returning to the city and undertaking a PhD at The Alfred Hospital. He has worked in heart failure for his entire research career.

JOHN's focus is on the development of novel devices to treat and manage the failing heart and problems associated with it. He runs a large animal facility at Werribee and conducts studies that are immediately clinically applicable.

John's work translates directly into human disease. His research focuses on therapeutic devices to treat and manage heart failure. Heart failure, where a weak heart is unable to pump effectively, creates a syndrome of debilitating conditions, ranging from arrhythmia to muscle wastage and weight loss.

Most of the work conducted in John's lab goes on to testing in humans. He is the co-founder, with the Baker's David Kaye, of two start-up companies with therapies now in, and close to, clinical trial. V-Kardia Pty Ltd has patented a revolutionary system that allows the delivery of drugs directly to the heart, with little systemic circulation of that drug. By isolating the coronary circulation from the general circulation, toxic effects and dangers to other organs of the spread of a drug intended for the heart are substantially reduced. V-Kardia has established a US subsidiary, V-Kardia Inc, to develop close relationships with world-leading researchers in the area of gene therapy for heart failure, and this company is expanding its collaborations with groups specialising in gene therapy for other major organs.

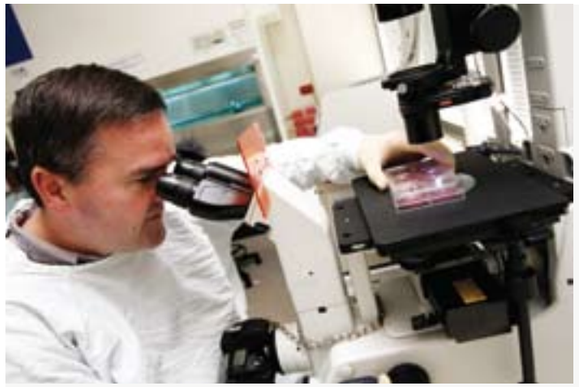
Cardiac Dimensions Inc represents another significant discovery for John and David. For many patients with advanced heart failure, secondary failure of the mitral valve compounds their illness and decline. Mitral valve failure, where a valve does not close properly, causes blood to leak during each heartbeat, putting greater pressure on the failing heart and further increasing the risk of heart attack.

John and David's research uses a small device to reduce the size of the valve. The device is inserted through the jugular vein under local anaesthetic, avoiding the need for major surgery in patients with this condition, most of whom are elderly and for whom general anaesthesia presents a great risk. Human trials continue at The Alfred Hospital and it is hoped the procedure will become available to the general community within a few years.

This lab regularly conducts research for overseas companies who come to John for his large animal expertise and use of his facility at Werribee where he has developed many models of heart failure, mostly in sheep. Research directions in this lab are now focused on the rapidly expanding areas of gene and cell therapy, and on a holistic approach to heart failure using these new technologies. There is a strong drive to understand better the causes of the various devastating symptoms heart failure, such as fluid retention, or cardiac cachexia, where fat is retained but vital muscle is lost. By focusing research on the underlying hormonal mechanisms responsible for symptoms, John hopes that the lack of knowledge about heart failure can begin to be addressed.

Molecular Endocrinology

› Walter Thomas



Walter Thomas did his PhD in Queensland and postdoctoral training in the US. His research focuses on the renin angiotensin system.

WALTER has worked at the Baker since his return to Australia from the US in 1996. His team of molecular and cell biologists work exclusively on the G-protein coupled family of receptors, specifically, on the renin angiotensin system.

Angiotensin is a vital hormone in the body, but an excess of it can lead to high blood pressure and heart attack. Research is focused on better understanding how angiotensin works, so treatments can be found that retain the benefits of angiotensin while limiting its production – not blocking it entirely.

The Molecular Endocrinology team at the Baker study the regulation of blood pressure by studying the mechanisms of the renin angiotensin system. This is an acute system, triggered by the kidneys, that recognises a sudden drop in blood pressure – due to injury or disease - and adjusts the body's functions to compensate for it. It does this by releasing into the blood vast amounts of a protein called renin. The renin attaches itself to a precursor protein in the blood, angiotensinogen, and effectively cuts a bit off it. This protein is not usually active but it is converted into an active hormone – angiotensin - by coming into contact with renin under these extreme conditions. This newly activated hormone circulates through the blood at very high levels, constricting the blood vessels to slow down blood loss and at the same time inducing an extreme thirst and a craving for salt. In so doing, it is trying to get the body to correct the salt and fluid loss caused by the dramatic loss of blood.

The hormone angiotensin, like hundreds of other hormones in our body, cannot work without interacting with its own receptor, or "lock". It is this protein receptor that is the main focus of research for Walter and his team, as a means of understanding the relationship between other G-protein coupled receptors in the body, of which angiotensin is just one.

It is known that people with high blood pressure overproduce angiotensin, but drug treatments currently work by blocking the angiotensin receptor and inhibiting production of the hormone. Because it is known that the renin angiotensin system is an important one, Walter's team is finding out all they can about this system. For example, by regulating blood pressure and constricting blood vessels, angiotensin causes heart growth in the longer term. While that has some benefits, it is detrimental over time. By studying what it is about angiotensin that causes heart growth, Walter's team discovered that the hormone didn't itself directly cause this growth, but did so by taking over another receptor, called the epidermal growth factor receptor, a hormone indicated in 25 per cent of breast cancer cases.

Understanding the mechanism behind how two different families of receptors can communicate is the subject of the next phase of research for this lab, which has recently secured an NHMRC grant to investigate this link further.

Walter and his team hope that better understanding the mechanisms of the renin angiotensin system will lead to the development of better targeted treatments that would allow blood pressure regulation but inhibit heart growth or vice versa. This would allow heart growth - which is necessary after heart attack – but stop the excessive production of renin angiotensisn that leads to hypertension.

Molecular Pharmacology

› Rebecca Ritchie

SCIENTIST Rebecca Ritchie heads the Molecular Pharmacology lab, pursuing three main areas of research: the cellular mechanisms responsible for cardiac hypertrophy, or heart growth associated with disease; heart complications related to diabetes, and addressing reperfusion injury, the damage caused to the heart after a heart attack.

Work is building on their discovery that elevated levels of a small heart cell chemical called cyclic GMP, a natriuretic peptide, will prevent abnormal heart growth. They also have evidence that other such hormones also increase in response to this heart growth or cardiac hypertrophy, and work to stop it from worsening or progressing to heart failure.

Rebecca's work in cardiac hypertrophy has focused on identifying elements within the heart muscle cells themselves that might prevent this unwanted growth. Her most recent research showed that a different chemical form of nitric oxide, gas released by the innermost layer of the blood vessel wall, prevents hypertrophy by elevating levels of the cyclic GMP chemical within the cells. Continuing research will look at whether this gas has other effects not related to cyclic GMP which nonetheless protects against heart failure. It is well known that one of the contributing factors to hypertrophy and heart failure is oxidative stress, where the metabolic balance of a cell is disrupted and there is an increase in the body of harmful free radicals. The powerful antioxidant action of this gas, occurring naturally where there is injury to the heart, will be the focus of further study and has implications for the development of drugs that promote the production and release of these natriuretic peptide hormones.

Scientist Rebecca Ritchie heads the Molecular Pharmacology lab pursuing three main areas of research

The damage to the heart caused by diabetes is often characterised by hypertrophy, myocardial fibrosis (stiffening) and impaired pumping. Furthermore, diabetics with heart complications fare worse than non-diabetics with comparable cardiovascular disease. Work conducted in this lab suggests that free radicals play an important role and their presence has implications for the most appropriate way to treat heart disease specifically in diabetes. The changes in structure and function occurring in the hearts of rats with diabetes have been characterised and their research has shown that both the levels of free radicals and the enzymes that generate them are increased in rats and mice with both type 1 and type 2 diabetes. Studies are now focusing on whether boosting the genes thought to reduce the production and numbers of free radicals in the body will improve the health of diabetics with these complications.

Reperfusion injury can occur after a heart attack. Reduced blood supply to the heart, known as myocardial ischaemia, can lead to heart attack during which cells can die. But the damage does not always stop with a return of blood flow: in fact the death of cells can create its own havoc, releasing their own "nasties", and restoring blood flow – reperfusion – can cause additional damage.

Rebecca's hypothesis is that a naturally occurring, anti-inflammatory protein called annexin-1 improves how the heart recovers from a heart attack. She believes that it may reduce the accumulation of inflammatory white blood cells and also maintain the viability and pumping action of the heart muscle following the event. Her research involves administering annexin-1 to mice and rats in which heart attack has been induced. Mouse models lacking annexin-1 are also studied for comparison, and in an effort to isolate its function. Understanding the protective role played by annexin-1 opens exciting new possibilities for reducing long-term damage from human heart attack.

Atherothrombosis and Vascular Division

Professor Karlheinz Peter oversees the research of seven labs in his role as an associate director of the Baker and head of the Atherothrombosis and Vascular division.

HEART attack is a sudden catastrophic event in the lives of many people in our community. The direct cost of coronary heart disease in Australia is the largest of any single cardiovascular condition, at $1.76 billion, or 28.6 per cent, of all costs associated with heart disease. Stroke is the second largest at $1.08 billion, or 16.5 per cent. It is the single most common cause of death in Australia and is most commonly manifest as angina, heart attack or sudden death. For a growing number of elderly Australians, atherosclerosis, the development of plaques, fatty deposits in blood vessel walls, and its complications – such as coronary heart disease and stroke – will be the major health care problem in terms of mortality, reduction in quality of life, and cost to the public health system.

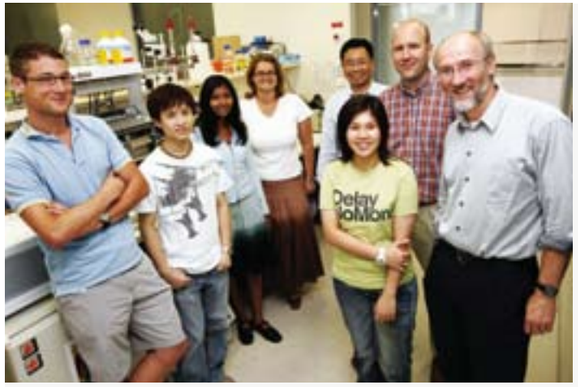
The Atherothrombosis and Vascular division comprises a diverse range of labs with research interests that are addressing these problems in a range of ways: from the investigation of those cells that play an important role in plaque development to the study of nutritional approaches that might prevent atherosclerosis and even the prevention and reversal of cholesterol accumulation in blood vessels.

This division hopes to address these public health concerns from a number of angles, including working towards the design of a new class of "intelligent " drugs. These will prevent clotting, or dissolve clots that have caused a heart attack or stroke without the excessive bleeding complications that are a feature of currently available drugs. The division is also working towards the identification of biomarkers (such as elevated levels of certain proteins in the blood) which, when added to existing knowledge of family history and lifestyle risk, help predict coronary plaque rupture.

Karlheinz's division, like all divisions of the Baker, is highly collaborative. The overall aim of prevention and cure of cardiovascular disease is realised by overlapping research that is molecular, cellular, physiological and highly translational – research that has a strong clinical focus. The following pages give more detail on the research focus of labs within this division.

Thrombosis & Myocardial Infarction

› Karlheinz Peter



THE development of "intelligent drugs", drugs that can target and dissolve blood clots but do not carry the devastating side effect of uncontrolled bleeding is a major research focus.

The work of Karlheinz and his team of researchers can be broadly divided into two areas: thrombosis – the blood clots that are a cause of heart attack and stroke, and inflammation.

Professor Karlheinz Peter, an associate director of the Baker and head of the Atherothrombosis and Vascular division, leads research in the Thrombosis and Myocardial Infarction laboratory. He is a practising internationally recognised cardiologist familiar with both molecular research and acute clinical cardiology practice.

Using basic molecular biology techniques, Karlheinz's lab is studying how platelets responsible for blood clots that lead to heart attack and stroke can be inhibited without causing the potentially fatal side effect of excessive bleeding. Current therapies used for treatment in myocardial infarction (heart attack) and stroke are very aggressive and are themselves responsible for disability and even death. One group of drugs now in use prevent the coagulation function of platelets so they cannot form a network – a clot – by stopping them from binding to certain plasma molecules. It is this binding function that creates the network. Activated platelets attach to fibrinogen, a plasma protein, causing a blockage that leads to heart attack and stroke. This relationship forms the basic architecture of a blood clot and treatment inhibits the binding function of the fibrinogen molecule, inactivating the coagulation function of platelets. But in so doing the treatment blocks every available platelet, of which there are hundreds of billions in the blood of a single patient, causing the excessive bleeding that is itself a complication.

Karlheinz's studies are working on the development of "intelligent drugs"; drugs that will block only activated platelets – the ones involved in clot formation. Laboratory research conducted to date shows a reduction in overall bleeding time while clot formation at the site of injury is allowed to occur. Another research avenue being investigated is concentrating on techniques that will make use of activated platelets by allowing them to enrich the action of drugs at the site of the blood clot. The lab has developed an antibody molecule that recognises only activated platelets and can be fused to different products, for example a clot-dissolving drug, so its action is enriched at the site and does not circulate through the blood.

The lab's other main area of research looks into inflammation mechanisms. Inflammation is recognised as a major driving force of atherosclerosis, the accumulation of fatty deposits, plaques, in blood vessels. Rupture of these plaques can cause heart attack and stroke and it is understood that inflammation is the process that drives this rupture. Inflammatory cells in the blood such as neutrophils and monocytes are being investigated for clues that might lead to a better understanding of their role in plaque rupture. The ability to inhibit inflammation in these plaques offers an opportunity to prevent heart attack. Peter's team is looking into how these inflammatory cells are activated. They have developed an antibody that recognises this monocyte activation and this is now being used as a tool to understand inflammatory stimuli and how these might regulate the activation of cells such as monocytes.

The long term goal of this lab is to develop an anti-inflammatory drug better than ones currently available, for example those used to treat rheumatoid arthritis, as they have been linked to an increased risk of heart attack.

Cell Biology

› Alex Bobik

THIS lab pursues two main areas of research: (1) cellular and molecular mechanisms that promote atherosclerosis (inflamed fatty lesions that develop in blood vessels and cause strokes and heart attacks), and (2) mechanisms that lead to development of cardiac fibrosis (where excessive collagen stiffens the heart muscle and impedes electrical conduction leading frequently to sudden death) and (3) understanding how bone marrow-derived stem cells can be used to repair the heart after damage from a heart attack.

During 2005 Alex was able to show that a specific cell type of the immune system called a regulatory T cell is important in controlling the development of atherosclerosis. These cells, which can be identified by the expression of specific markers on their cell surface called CD4 and CD25, were shown to reduce the development of atherosclerosis in genetically modified mice. When these cells are removed mice develop more severe atherosclerosis. These studies have important implications for the treatment of atherosclerosis and have the potential to be used in conjunction with other therapies to prevent development of severe lesions. This is currently being studied.

Other cell types are also being studied, in particular cells that cause inflammation and promote the development of atherosclerotic lesions that are rich in fat and low in collagen. These lesions are weak and highly susceptible to rupture, which can cause a blood clot and lead to strokes and heart attacks. These include immune cells called natural killer T cells (NKT) cells. Alex and his team have shown that a specific type of NKT cell, which can be identified by expression of the marker CD4, promotes development of these lesions. Research is continuing into how they do this. Other studies on atherosclerosis focus on proteins that are secreted by macrophages, cells in the body's circulation that accumulate in lesions and take up fats. One such protein called high mobility group box protein-1 appears to be a potent stimulator of atherosclerosis.

Studies on cardiac fibrosis have led to the identification of unexpected mechanisms that promote fibrosis. When the heart has to pump against high pressure, such as in hypertension, the heart muscle produces proteins that attract specific bone marrow derived cells from the circulation. Alex and his team have identified two such proteins called secondary lymphoid chemokine and monocyte chemotactic protein-1. These attract several circulating cell types into regions of developing fibrosis including lymphocytes that express the marker CD4, macrophages, and an as yet unidentified cell that produces large amounts of collagen. Current studies are focused on depleting these cell types in mice and examining how this affects the development of fibrosis and proteins that regulate collagen production, in particular transforming growth factor-beta and interleukin-10.

Studies on the role of bone marrow derived cells in healing the heart after a heart attack have shown that a substance which Alex's lab has shown improves healing, called granulocyte-colony stimulating factor (G-CSF), increases the number of blood vessels in the damaged region. It does this by stimulating the production of growth factor systems that promote the development and growth of new blood vessels. These include vascular endothelial cell growth factor-A, placental growth factor and thymidine phosphorylase. This lab is currently studying bone marrow-derived cells that invade the damaged region and their contribution to development of new blood vessels are producing these.

Another area of study is the possibility of using genetically modified bone marrow stem cells to attract heart stem cells into damaged regions of the heart to further improve cardiac repair.

Professor Alex Bobik heads the Cell Biology Laboratory in the Baker's Atherothrombosis and Vascular division.

Clinical Physiology

› Bronwyn Kingwell

RESEARCH in this lab is focused on two main areas: coronary plaque stability (in collaboration with Dr Stephen Duffy and Professor Anthony Dart) and diabetes. Work is largely driven by the goals of better management of existing disease and the development of better predictive tools against it.

The formation of plaques, known as atherosclerosis, inside the heart's blood vessels is a major contributor to heart attack. Plaques, essentially small fatty deposits, are characterised by a thick, fibrous layer, like a scab, containing a soft, semi-liquid core.

It is understood that most people have plaques in these arteries by a certain age, but in roughly half of that group the plaques don't cause any problems – they are stable. For the other half though, those with unstable disease, plaques rupture, exposing the soft substance within it to the blood flowing through the artery. Once there, this substance forms a clot, also known as a thrombus. That clot can block off the whole blood vessel, causing a heart attack by stopping blood supply to some of the heart muscle. Some plaques, however, grow outside of the blood vessel. While this type of plaque doesn't obstruct blood flow it is prone to rupture causing a sudden heart attack.

A physiologist by training, associate professor Bronwyn Kingwell is head of the Baker's clinical physiology lab. In 2005 she was president of the Australian Society of Medical Research, spearheading advocacy for research support nationally.

The difficulty with this type of plaque growth is that standard diagnostic techniques – the use of an angiogram, where dye is released into the middle of an artery to identify problems – are not effective because the artery looks clear. The introduction of intravascular ultrasound has made diagnosis of this type of plaque possible by examining the blood vessel wall and it's a technique used in the research conducted in this lab.

Predicting the stability of coronary plaques is a major research interest of Bronwyn's team. Understanding why some people have unstable plaques and others do not will go a long way towards preventing heart attacks. Looking at what the plaque releases into the blood might hold clues as to why some plaques rupture.

Using intravascular ultrasound techniques, researchers have identified plaques in patients and collected blood samples from either side of the deposit. A recently completed three-year study, collecting blood samples from about 200 patients, has shown that people with a particular genetic version of an enzyme in the blood seem to be more susceptible to plaque rupture. In a recently submitted paper, Bronwyn and her research team argue this enzyme is associated with positive remodelling – where the plaque grows outside the blood vessel wall – and increases the patient's susceptibility to unstable disease, or sudden heart attack. This finding will significantly contribute to heart attack risk prediction.

Another significant research study has focused on patients with peripheral vascular disease (PVD). This group suffers from the formation of these plaques – atherosclerosis – in the top of their legs. A symptom of this disease is great pain on walking, essentially angina of the leg. Drug treatments, such as anti-platelet therapy to stop the blood clotting, are available but not very effective. One of the best treatments is exercise but getting this group to exercise is difficult because of the pain associated with physical activity. This lab tested the effects of an Angiotensin-Converting Enzyme (ACE) inhibitor drug on patients with PVD. This group of drugs is commonly used to treat other forms of heart disease, but has never before been examined in relation to symptoms of this leg disease. Results in this relatively small but groundbreaking study have been startling: 20 patients in the study taking the ACE inhibitor increased their walking distance by as much as 200 per cent over 24 weeks: this group doubled their treadmill walking time, from 300 to 600 seconds. The 20 patients in the other half of the study took the placebo drug and no change was evident in the distance they could walk without pain. This study has major implications for the treatment of patients with PVD and by providing them with a treatment that makes it easier for them to exercise, their own ability to manage their disease is dramatically improved. This work was recently published in the high impact medical journal, Annals of Internal Medicine.

Exercise is also a key factor in the prevention and management of diabetes; another of this group's major research interests. Bronwyn's team has been trying to understand what it is about exercise that helps to prevent diabetes and why exercise is critical to managing the illness. Understanding that exercise serves the same function as insulin – that is, to move glucose from the bloodstream into the muscles that need it – was the platform for the identification of some of the molecules in muscle that, activated by exercise, coax the glucose from the blood to that muscle. This team is continuing its important work on identifying the exact effects of exercise on the body because doing so will enable the development of drugs that can activate the molecules stimulated by physical activity and replicate their beneficial effects in people who can't, or won't exercise.

Vascular Pharmacology

› Jaye Chin-Dusting

JAYE Chin-Dusting came to the Baker as a postdoctoral scholar in 1990. Since then, the Vascular Pharmacology lab conducts experimental drug studies in animal models of disease and translates them directly into work in human blood vessels, tissue and cells.

They study the relationship between blood vessels and cardiovascular disease, in particular the innermost layer of blood vessels, known as the endothelium.

Jaye and her team of researchers have significantly built on the discovery more than 25 years ago that the endothelium – the innermost layer of the blood vessels, separating the blood from the muscle – was not a passive barrier as it had been assumed but in fact a very active structure in its own right. The discovery that nitric oxide was released by the endothelium, expanding blood vessels, during activity was significant. During exercise the heart needs more oxygen and pumps harder. As a result the blood flows harder and the sheer stress of movement along the endothelium triggers this release of nitric oxide. This release of nitric oxide expands the muscles allowing more oxygen to go to the heart as is needed. When there is disease, however – hypertension, diabetes, heart failure – there is impairment of the endothelium and the release of nitric oxide is impaired. Without its release there is not the necessary dilation and sometimes there is a restriction of the vessel, causing angina. The lack of nitric oxide can limit the carriage of oxygen to the heart, resulting in heart damage.

From this starting point, the Vascular Pharmacology team have investigated cellular mechanisms in a range of cardiovascular diseases. It was the work of this lab that established a new form of treatment for people with cirrhosis, or scarring, of the liver. The observation that cirrhotic patients have exactly the opposite physiological profile to patients with CVD, for example low blood pressure as opposed to high was taken further by Jaye and her team. While this opposite profile had been noted, Jaye's lab was the first to look at the role of nitric oxide in these two patient groups, and whether there was an over-production of nitric oxide in the cirrhotic patients responsible for the low blood pressure and other complications.

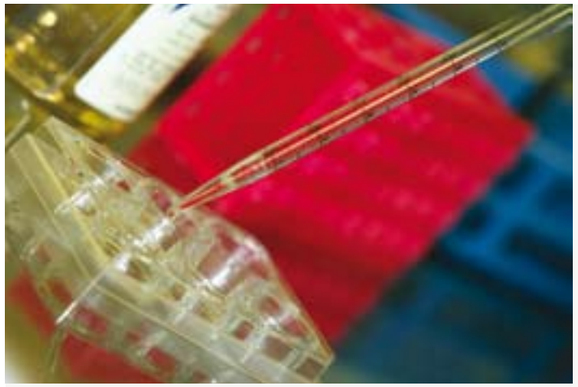
They hypothesised that the scarring of the liver in cirrhotic patients interfered with the process of blood cleansing that occurs in the portal system, where blood is transferred from the gut to the liver. Cirrhosis congested this flow and new blood vessels formed to compensate, allowing the transfer of blood from the gut directly into the systemic circulation, bypassing an important cleansing process. In patients with alcohol-induced cirrhosis, diet is often poor, resulting in an increase in bacteria levels in the gut that in turn compounds the effects of liver dysfunction. The Vascular Pharmacology team surmised that the high level of endotoxins in this group – toxins released from cells – was responsible for the copious release of nitric oxide, as these toxins switched on an enzyme triggering the inappropriate production of this gas in cirrhotic patients. To test their hypothesis, they recruited a group of cirrhotic patients and treated them with an antibiotic, to great effect. The successful outcomes for liver patients with a treatment model developed at a cardiovascular institute is a prime example of how the work of Baker researchers feeds into the improvement of health in the community on many different levels.

Postdoctoral researcher Kevin Woollard has been working with the lab on the effect of the endothelium on the blood, a new direction for Jaye's team. While previously work has been focused on the influence of the endothelium on muscle constrictions and dilations, research is now turning to the release of nitric oxide into the blood. When the endothelium is damaged blood cells start to stick together forming plaques. Kevin's research is looking at the production of "sticky" proteins during endothelial cell damage. These proteins, only expressed in cell injury, are of interest because their presence in the blood at high levels is understood to be a marker of disease. Kevin and the Vascular Pharmacology lab are particularly interested in the protein selectin, and research is focusing on the discovery that selectin is not merely an inactive biomarker but a significant contributor to disease in its own right and as such, drug treatments for disease indicated by its presence can focus on switching off the effects of this protein.

Jaye came to the Baker as a postdoctoral scholar in 1990. Since then, the Vascular Pharmacology lab has conducted experimental drug studies in animal models of disease and translates them directly into work in human blood vessels, tissue and cells.

Cell Biology & Diabetes

› Peter Little



Professor Peter Little is head of the Cell Biology and Diabetes laboratory in the Atherosclerosis and Vascular division. He is also president of Diabetes Australia

RESEARCH in this lab is focused on better understanding the causes of atherosclerosis, the build up of fatty plaques in blood vessels, particularly in people with diabetes. Little's lab is working towards the development of a drug that can prevent the formation of atherosclerotic plaques by preventing changes in proteoglycans, protein molecules that exist in the blood vessel wall.

The major cause of premature death in people in Western and now developing societies is the formation of atherosclerotic plaques in blood vessels. The rupture of those plaques causes a heart attack if they are in the heart or a stroke if the rupture is in the brain. Commonly prescribed drugs to prevent this process lower blood pressure or lower cholesterol levels, but research has shown that these drugs are not entirely effective and a significant amount of disease occurs despite the use of medication.

The development of atherosclerosis is accelerated in people with diabetes, who often suffer from high blood pressure and other complications as well as high glucose levels. As the incidence of diabetes continues its alarming rise, complications such as cardiovascular disease are becoming more commonplace.

The Cell Biology and Diabetes laboratory focuses on basic research into the causes of atherosclerosis, and is contributing to existing hypotheses for how this process occurs. One theory most relevant to Peter's work is called response to retention, and suggests that while lipoproteins – balls of fat in the blood also known as lipids – would usually pass straight through a healthy blood vessel wall, under some circumstances the blood vessels become sticky and that lipid gets stuck. Molecules called proteoglycans are responsible for the stickiness. These molecules contain long sugar chains that are negatively charged, while the lipid is positively charged, and as a result they stick together. Research in Peter's lab has added to growing evidence that the stickiness of blood vessels is caused by changes in proteoglycans and is the initiating step in atherosclerosis.

Work in 2005 continued on understanding the synthesis and structure of proteoglycans, studying the factors that make these molecules stickier and the processes by which they might be able to be prevented from becoming sticky at all – with a view to stopping atherosclerosis.

So far Peter and his team have discovered a new area of signalling molecules and last year completed a study in atherosclerotic mice, giving them a specially designed drug which stopped changes occurring in proteoglycans. They found a statistically significant reduction in the degree of atherosclerosis in those animals. Patents are in place and research is continuing on the development of this drug.

Lipoproteins & Atherosclerosis

› Dmitri Sviridov

Dr Dmitri Sviridov trained as a doctor in Russia and now heads one of the longest established research areas at the Baker, the Lipoproteins and Atherosclerosis laboratory.

LIPOPROTEINS are responsible for the accumulation of cholesterol in blood. This accumulation causes fatty deposits in the blood vessel wall, known as atherosclerotic plaques. This lab investigates the metabolism of cholesterol and the mechanisms responsible for its accumulation.

Lipoproteins and atherosclerosis form the basis of one of the oldest research areas at the Baker. For the last four years Dmitri has led this research. Atherosclerosis, the development of fatty plaques in the blood vessel wall is the direct cause of about half of all cardiovascular diseases and as such is probably the major single cause of death in humans.

The key element of the formation of an atherosclerotic block is change in the metabolism of cholesterol, which is the main area of investigation for this laboratory.

Cholesterol is moved around in the blood with lipoproteins. An imbalance of elements in the blood inhibits the transfer of cholesterol through the blood vessel wall to the liver, the only part of the body with the ability to break down cholesterol.

Statins are possibly the most successful drug in the history of medicine. They have been a very effective therapy in the reduction of blood cholesterol levels and are generally prescribed to people with high cholesterol levels that put them at risk of heart attack. They are also prescribed to people who have suffered a heart attack, as a way of preventing a second event. The combination of this drug and better diet has greatly improved life expectancy in developed nations, and decreased the incidence of heart disease by as much as 40 per cent. But for the 60 per cent whose lives are not saved by statins and dietary modification, the work by Dmitri and his team is crucial.

The Lipoproteins and Atherosclerosis lab is focusing on the pathway within the body responsible for removing cholesterol from the blood vessel wall, known as reverse cholesterol transport. Research is focused on the balance between the delivery of cholesterol to blood and its removal. Dmitri's work aims to combine current therapies with the manipulation of this cholesterol delivery pathway: allowing less cholesterol to pass through the liver while boosting its removal. Reverse cholesterol transport depends on two processes, both of which are examined by this lab: the ability of cells to remove cholesterol from themselves, and the tendency of plasma to accept cholesterol from the cells. The balance between these two mechanisms is what essentially determines healthy or unhealthy blood cholesterol.

One of the lab's most significant ongoing projects is concerned with the development of atherosclerosis in HIV patients. While people with HIV are living longer with better drug treatments, heart disease is a major complication. Other research has established that they have anywhere from three to 100 times greater risk of cardiovascular disease than the rest of the community.

Dmitri's group has discovered that in HIV patients there is a severe disregulation of the pathways that remove cholesterol. His pioneering work has found that it is most likely HIV itself, and not its treatment, that is responsible for this imbalance. When combined with HIV drugs which increase the delivery of cholesterol and impair the mechanism in the body that removes it, the development of atherosclerosis is dangerously accelerated. Work is continuing to establish the independent roles of both HIV and its treatments in this process with the aim of developing drugs that can compensate for these effects.

Human Vascular Biology

› Stephen Duffy

Stephen Duffy heads the Human Vascular Biology research unit at the Baker. He divides his time between cardiovascular disease research and seeing patients at The Alfred, where he works as a clinical cardiologist.

ONE area of focus for Stephen's lab is the better prediction of unstable coronary disease – the rupture of coronary plaques, a major cause of heart attack and stroke. Plaques, essentially fatty deposits in the coronary arteries, can be stable and as such not cause problems but their rupture can cause blood clots. This can lead to heart attack and stroke.

Traditionally, risk is predicted by family history, lifestyle and whether there are other known risk factors present. These include diabetes, high cholesterol and high blood pressure; but the process of assessing the stability of plaques themselves is very invasive and expensive and not an option on a broader community scale.

This group is working on the vital and rapidly expanding area of biomarkers, identifying measurable and reliable physiological changes that can predict plaque rupture. They are investigating new markers of unstable disease by studying protein molecules that are released by plaques into the blood. To date increased levels of MMP-3 and MMP-9 have been associated with unstable disease. MMPs are of broad interest because they are known to have the ability to break down the blood vessel wall and might be a mechanism by which the fibrous cap of the plaque is broken down. But they are only one example of investigation into biomarkers. It is believed there are dozens of other proteins in the blood, the elevated levels of which might even be masked by the presence of other proteins. Advancing techniques to isolate these proteins is another area of interest to the lab, as they could hold a significant contribution to the better prediction of disease.

Stephen's position as a cardiologist gives the research conducted in this lab a significant edge. Access to heart disease patients at The Alfred ensures a wide and clinically relevant range of blood samples are collected, studied and compared.

A controversial area, of interest to Stephen's team, is the effect of iron in blood vessels. Iron is a vital component of blood and it has been noted that the iron stores of people at risk of heart disease are higher than average.

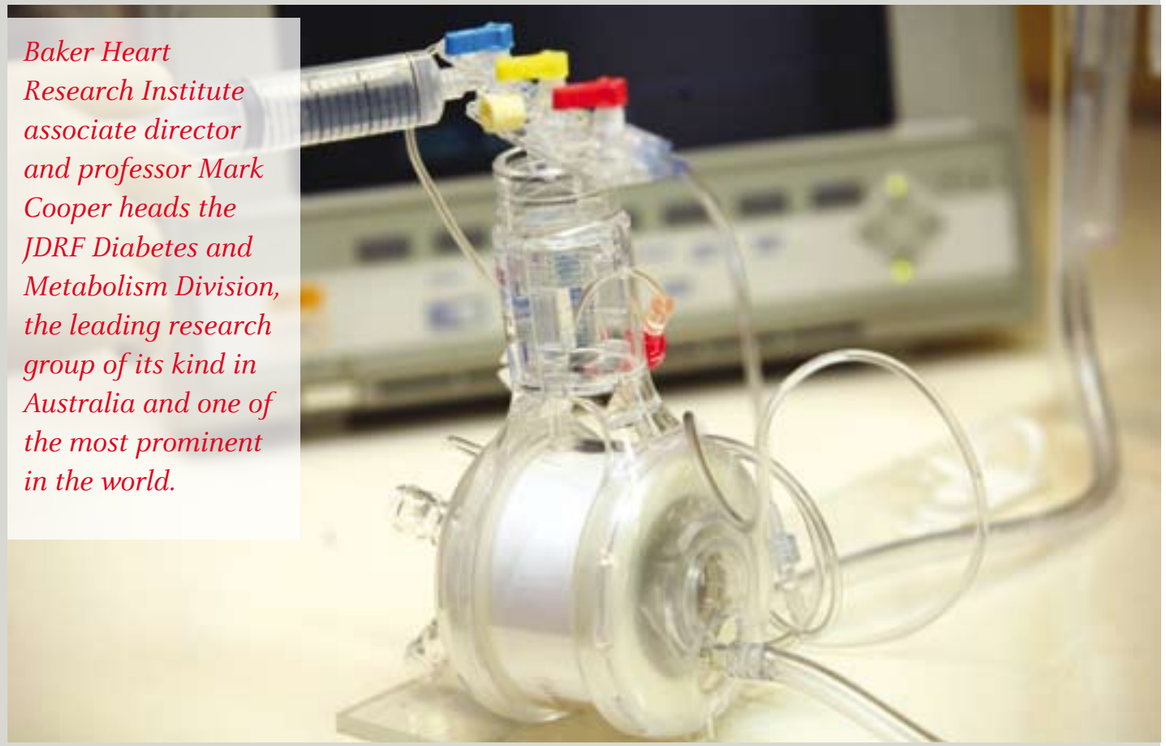
It is thought high iron levels might be implicated in heart disease because of iron's ability to increase oxidative stress and free radical production. Oxidative stress is in turn linked to atherosclerosis.

This lab hopes to investigate the role iron stores play in the development of heart disease and whether decreasing iron levels in certain patient groups could reduce their risk of heart disease.

Stephen is also involved in a long-term collaborative project looking at cardiac patient health after successful intervention and discharge from hospital. At present there are very few long-term follow up studies on patient health after a coronary event. Stephen's work as part of the Melbourne Intervention Group, a collaboration between 12 hospitals in the Victorian public and private health systems, will go towards establishing a large clinical database that will be able to track the efficacy of existing and new cardiovascular procedures by monitoring the health of patients after discharge. So far the registry contains more than 3000 patients eligible for follow-up.

JDRF Diabetes and Metabolism Division

Baker Heart Research Institute associate director and professor Mark Cooper heads the JDRF Diabetes and Metabolism Division, the leading research group of its kind in Australia and one of the most prominent in the world.



DIABETES is a serious public health issue and the dramatic rise of diabetes in the community is a major concern. The complications of diabetes include kidney disease, eye disease and vascular disease. Diabetes is a major factor in cardiovascular disease and the most common cause of kidney failure in the western world.

The main aim of this division is to understand why people develop complications from diabetes, a high blood glucose level, and the mechanisms responsible for those complications. Research feeds directly into the development of new treatments to target and prevent the development of diabetes-related disease. Mark's group has recently secured a multi-million dollar grant from the prestigious US-based National Institutes for Health to explore the causes of glycation – a biochemical process brought on by an excess of sugar – and atherosclerosis in Type 1 diabetes.

The current focus of this division is the development of new techniques for early diagnosis of complications, primarily gene and proteomic approaches to diagnosis.

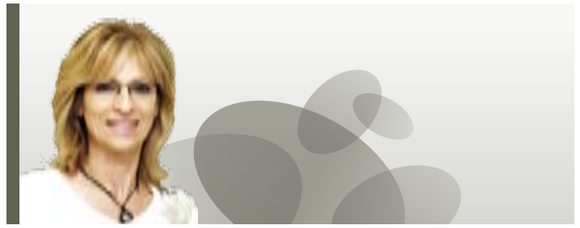
Mark himself has received many awards and is an eminent researcher in the field of diabetes and its complications. His work has profoundly improved our understanding of this disease and has been of direct benefit to millions of sufferers around the world. His distinguished body of research has led to new treatments for sufferers of diabetes that are today considered standard. He was involved in very early studies using Angiotensin-Converting Enzyme (ACE) inhibitors in diabetic complications, now a routine treatment, and was also involved in the original description of microalbuminuria, now used as a tool in predicting diabetic complications.

His work on the combination of ACE inhibitors and A2 antagonists for use in the treatment of diabetic kidney disease has seen this therapy become widespread and is reducing the risk of end-stage renal failure.

Mark's group derives funding from the New York-based Juvenile Diabetes Research Foundation as well as from NHMRC grants.

Oxidative Stress

› Judy de Haan



Judy de Haan, an expert in the harmful effects of oxidative stress on the body, originally trained in South Africa and then completed her PhD at Monash University. She has been with the Baker since 2003.

OXIDATIVE stress has been linked to atherosclerosis, the accumulation of fatty deposits in the lining of blood vessels. This group is investigating the genetic component of oxidative stress in atherosclerosis and in diabetes. They are working on the development of dietary interventions or drug compounds to increase the activity of antioxidant enzymes, reducing the effects of atherosclerosis.

Judy started her research in the area of oxidative stress and Down Syndrome. Oxidative stress describes a state characterised by an excess of unstable elements, known as free radicals, in the body. Free radicals can be overproduced as a result of exposure to some environmental toxins and are believed to be involved in the premature ageing of organs and in cellular damage.

Beginning her studies by examining the presence of certain enzymes in the normal ageing process, Judy's research team developed a mouse model lacking an important antioxidant enzyme, one that is usually present to remove an excess of free radicals. Experiments showed that these mice could function quite normally until they were stressed in some way. From there studies moved on to trying to better understand the link between oxidative stress, injury and disease.

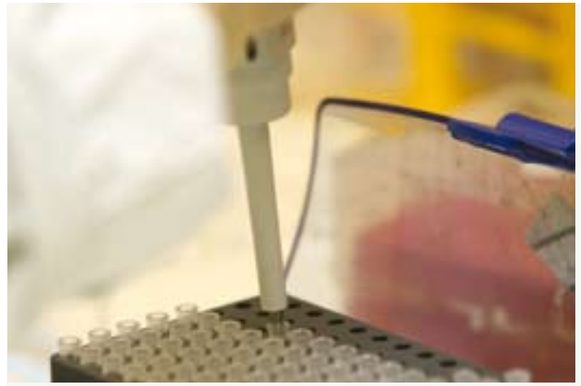
For the last five years Judy has focused exclusively on atherosclerosis, both within and outside the setting of diabetes, and the role that oxidative stress plays in the development of atherosclerotic disease. Oxidative stress is understood to play an important role in atherosclerosis.

Increased glucose levels in diabetic patients predispose them to oxidative stress and diabetics are at a far greater risk of developing atherosclerosis. Judy's work is now focused on the relationship between the two, using the mouse models already developed. Studying atherosclerotic diabetic mice that are missing the antioxidant enzyme, which would otherwise mop up the free radicals, this lab is investigating whether there are increased components of atherosclerosis in these animals, increased lesions, for example.

This study has established the framework for the next important phase of Judy's research: the effects in mice carrying an over expression of the antioxidant enzyme – more than would normally be present – and whether that reduces the effects of diabetic atherosclerosis. From there, this lab will look into the development of drugs that can mimic the effects of these antioxidants, as well as dietary supplements that can boost their presence thereby reducing atherosclerosis.

Human Epigenetics

› Assam El-Osta



Assam El-Osta is head of the Human Epigenetics laboratory within the JDRF Diabetes and Metabolism division.

THIS lab is working hard to understand the behaviour and "misbehaviour" of genes in disease, with a particular focus on diabetes, cancer and chromosomal disorders such as Fragile X syndrome.

Epigenetics is the study of reversible changes in gene function, changes that occur without any mutation in the sequence of the DNA itself. Epigenetics concerns itself with trying to understand how information that regulates gene behaviour but that is not expressed in DNA sequences can be passed on from one generation to the next. Most of the diseases we seek to prevent and cure at the Baker have both genetic and environmental causes. Understanding their interaction is a key step in developing our research.

Sam and his team focus on understanding why genes are "switched on" or "switched off" in certain diseases. His research in this area began with looking at what happens to genes in cancer, particularly the behaviour of genes in people who suffer from drug resistance. Resistance to chemotherapy drugs, which is often part of a multi-drug resistance, is a serious problem for cancer patients. Understanding the way genes act in this condition may help researchers find a way of developing treatments and therapies that are more effective. But more than that, the findings can lead to a better understanding of gene behaviour in other diseases.

In 2005 Sam and his team generated a great deal of interest among the international scientific community with their discovery, which was highlighted on the cover of the prestigious scientific journal Nature Genetics, of a master regulator, a class of molecules that control the "switching on" or "switching off" of genes. His discovery has significantly increased our understanding of the way that genes are controlled and may represent. This may be a critical link between the environment and whether a cell faithfully produces the proteins programmed by its genes. By uncovering how genes are manipulated in this way, researchers have a better chance of preventing genetic diseases or, when they haven't been prevented, designing better treatments.

Sam's research has uncovered very distinct patterns in the way these genes "misbehave", regardless of the disease being studied. He has focused his work on the need to understand why the gene is switched off. By understanding the modus operandi of, for example, the Fragile X gene "silencing", or "switch off" mechanism, in the future we may be able to interrupt that mechanism and reactivate that gene, and genes in other devastating diseases.

Biochemistry of Diabetic Complications

› Merlin Thomas

Associate professor Merlin Thomas heads the Biochemistry of Diabetic Complications lab.

THE growing epidemic of diabetes already affects over 1.3 million Australians and twice that number again is at risk of developing diabetes in the next 5–10 years. Despite the clear and present danger of diabetes, the role of high sugars in causing blindness, kidney failure and heart disease is poorly understood. Merlin is working on breaking the links between sugar and the damage it causes.

His research has concentrated on Advanced Glycation End-products (AGEs), formed when sugars bind to protein, making it sticky, sweet and brown. In food like chocolate and caramel, this reaction is appetizing. But when sugar accumulates in diabetes, this same process contributes to blindness, kidney failure and heart disease. Merlin's research has shown that this reaction leads to changes in the shape and function of AGE-modified proteins. In the same way that lamb is more tender than mutton, AGE-modified proteins tend to be inelastic. This means that AGEs gradually build up in tissues, making them in turn more stiff; literally 'hardening' the arteries. Where the sugar concentration is high, AGEs accumulate much more quickly. This is one reason why strong sugar control is so important in diabetes.

For Merlin, the best way of reducing the impact of diabetes is to break the link between high sugar levels and the damage they cause because even with the best treatment, patients can suffer from kidney failure, amputations and blindness from their diabetes. AGEs are one of those links. For the millions with diabetes who struggle to control their sugars every day, an understanding of this pathway will provide an important advance to their care.

Another key focus of the Biochemistry of Diabetic Complications lab is the renin angiotensin system (RAS), a pivotal element of vascular function in both health and disease. Many patients with diabetes are already taking drugs that block the RAS, in an attempt to prevent some of the complications of diabetes. However, these agents are only partly effective. Merlin and his team are working to define novel regulators of the RAS, using unique methods to disrupt the RAS, with the aim of making current interventions for diabetes even more effective.

This group is also coordinating the NEFRON study, the largest study of patients with type 2 diabetes across Australia. NEFRON is a collaborative effort of the Baker Heart Research Institute, Kidney Health Australia and Servier Australia, that aims to define the prevalence and severity of complications of diabetes in Australian general practice. Already this study has been able to show that every second individual with type 2 diabetes in Australian currently has chronic kidney disease, with clear potential to influence their health and well being, as well as contribute to premature mortality.

Kidney Disease in Diabetic Complications

› Karin Jandeleit-Dahm

Dr Karin Jandeleit-Dahm is a nephrologist, currently working with patients at The Alfred Hospital. As a researcher she heads the Kidney Disease in Diabetic Complications laboratory.

KARIN's lab primarily focuses on the link between kidney and cardiovascular disease, particularly in people with diabetes. Research extends to the relationship between diabetes, kidney disease and atherosclerosis, and finding ways to predict the development of these diseases in those at risk.

People with kidney disease have a higher risk of cardiovascular disease, and kidney disease is a major risk factor of diabetes. The kidney is a very vascular organ and findings in disease there translate into cardiovascular disease. In this way the work of Karin and her team is of benefit both to understanding kidney disease but also more broadly to the prevention and cure of cardiovascular disease.

Advanced glycation end products (AGEs) are formed in diabetes at a very high rate and are believed to be responsible for irreversible damage to the kidney and to the cardiovascular system. Karin's lab has studied these substances and found that they play an important role in the development of atherosclerosis as well as the development of kidney disease.

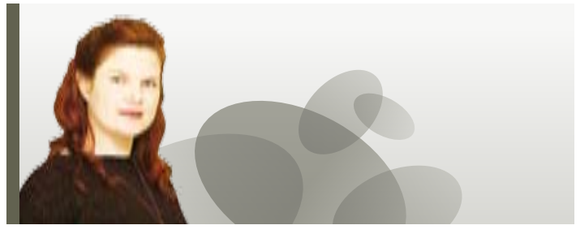
Work in 2005 focused on measuring AGEs and markers of inflammation and oxidative stress in diabetic patients and comparing those levels to control subjects (people who do not have diabetes) to see if AGE levels or other markers can be used as a predictor or marker of cardiovascular disease in diabetic patients. So far, about 150 diabetic patients have been screened.

By using drugs to inhibit AGEs, kidney damage and atherosclerosis might be controlled. The Kidney Disease in Diabetic Complications lab is investigating the effectiveness of existing and novel drugs to investigate the cardio-renal protection of these interventions.

Another area of this research is focusing on why some people with diabetes are more likely to develop complications than others. Using the same screening process and group of patients, attempts are being made to understand what genetic or other factors in the blood might protect against diabetic complications. Identifying markers of resistance to disease in those at risk will allow early, preventative treatment. This is a major driver of research, which aims to ward off disease altogether by stopping the accumulation of AGEs or halt its progression before damage is irreversible.

Advanced Glycation in Diabetic Complications

› Josephine Forbes



Josephine Forbes did her PhD in kidney disease at the Royal Children's Hospital in Melbourne and heads the Advanced Glycation in Diabetes Complications lab at the Baker.

RESEARCH in this lab focuses on kidney disease in diabetes, specifically, the effects of advanced glycation on the diabetic kidney. Kidney disease is one of the most important risk factors for heart attack.

Advanced glycation is a biochemical process brought on by an excess of sugar – we see it in the browning of fruit and the process is also apparent in the ageing of collagen, resulting in the gradual formation of wrinkles and lines on our skin as we grow older. Glycation is a major problem in diabetes, and these molecules resulting from an excess circulating blood sugar have the capacity to do major damage to the organs of a diabetic person over several decades. Essentially, it speeds up the ageing process, and can lead to a "caramelisation" of major organs such as the kidney. Kidney disease is an important risk factor for heart attack. It is estimated that as many as 70 per cent of people with diabetes die from heart attack or stroke.

One of the major functions of the kidney is to regulate blood pressure, and blood pressure is directly related to heart attack and stroke. The kidneys also regulate fluid volume, important in determining how hard the heart pumps and serve as the body's waste filter, removing toxins from the blood stream before they reach the heart. Poor kidney function has devastating effects on health, particularly on the heart, and advanced glycation irreversibly harms kidney function.

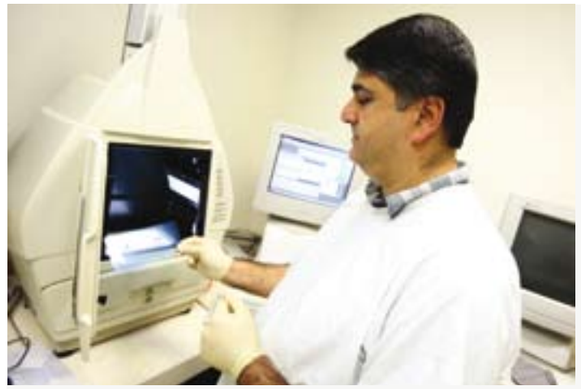
One of the major research interests of this group is to better understand how advanced glycation occurs and the very process by which sugar attaches itself to proteins in the blood. They are trying to find out if they can inhibit the process once it has begun and crucially, whether it can be reversed. One of the main difficulties in this area is that many people who present with kidney problems have been suffering from diabetes for many years but have not known it. As a result, their kidney dysfunction has not been addressed and is at an advanced stage. The challenge taken up by Josephine's team is to find some way of undoing the damage in these patients.

A significant research area for this group is the development of a new drug, expected to enter clinical trials in 2007, known as "the scissors". This compound has the ability to go to the protein and literally break off the sugar. In so doing, it has the capacity to renew the protein and return it to its normal state, reversing the detrimental effects of advanced glycation. The drug alagebrium is currently in clinical trials in other diseases but this will be its first application in kidney disease.

Josephine's team is also looking at ways to predict who in the community might be at risk of developing diabetic complications. The main complications involve the eyes, heart, kidneys and nerves. By investigating genetic risk factors in people with diabetes who are as yet not suffering from any related health problems but have a diabetic relative with eye, kidney or heart disease, they hope to help prevent the progress of this disease in a new generation of sufferers.

Genomics of Diabetic Complications

› Phillip Kantharidis



Dr Phillip Kantharidis has a PhD in molecular virology and joined the Baker four years ago. He heads the Genomics of Diabetic Complications lab.

RESEARCH for this lab focuses on genes that regulate cell growth and differentiation in response to diabetic disease, with a particular focus on kidney disease.

The lab is primarily concerned with the investigation of genes and their products that are altered as a consequence of diabetes, with particular interest in genes that regulate the activity and expression of factors that result in kidney fibrosis, where the tissue becomes scarred and hardened.

Many small and large molecules in our bodies undergo modifications in the context of diabetic disease. DNA is often damaged as a result of oxidative stress in diabetes, resulting in the activation of a number of proteins. One of these proteins, PARP, is known to modify other proteins in the nucleus of the cell in response to DNA damage. While some of the effects of these modifications are known, many are not. Better understanding of these modifications and the protein targets may help to contain diabetic kidney disease and eventually prevent it.

Another project of this group focuses on the response of cells to the diabetic environment. Of particular interest is the activation of key regulatory molecules called transcriptional repressors that control cell differentiation through a process called epithelial to mesenchymal transition (EMT). The lab has demonstrated that this process can occur as a result of high glucose and exposure to advanced glycation end products, influencing the cell phenotype in the kidney and potentially contributing to fibrotic kidney disease. Focusing on the kidney, this team is investigating when these cells change from their original state and start producing things that make the kidney harden and eventually fail. The group hopes eventually to prevent the progression of disease caused by diabetic complications and also prevent the worsening of disease in those already suffering.

The third major interest of the group is the study of proteins called histones, which may be affected by advanced glycation. These proteins form the scaffolding on which DNA is tethered in the nucleus, playing an intricate and extremely important role in regulating which genes are active and which genes get switched off. The focus of this project is to investigate whether modification of histones in the context of diabetes affects their normal nuclear function and hence contributes to diabetic disease.

Proliferation & Fibrosis in Diabetic Complications

› Zhonglin Chai

Zhonglin Chai trained as a vet in China and in Australia completed a PhD in molecular biology with CSIRO before going on to postdoctoral studies at Monash University.

CHAI is currently building on his earlier, groundbreaking work where he identified a new molecule, CDA1. CDA1 is understood to have an anti-proliferation function: increasing the level of this protein in a cell stops cell division. CDA1 is present in elevated levels at sites in the body, particularly blood vessels and the kidneys, where there is damage caused by diabetes. Chai aims to understand the biological function of CDA1, how it works and its role in disease.

Building on earlier work that both identified this molecule, and recognised its anti-proliferation properties, Chai and his team are currently investigating CDA1 and its role in diabetic complications. The team has established that CDA1 interferes with TGF (transforming growth factor)-beta signalling. TGF-beta is known as a pro-fibrotic factor: it stimulates extra cellular matrix proteins, thereby promoting fibrosis, or tissue scarring. Chai and his team believe that far from being purely the result of diabetic injury, CDA1 actively promotes damage where it is present in raised levels. Research is centred on understanding the biological function of this molecule and its relationship with other proteins and pathways within the body.

By better understanding how CDA1 works, and understanding its exact molecular mechanisms, Chai and his team will come a step closer to targeting it for the treatment and prevention of disease, slow down the injury or prevent it altogether. His previous research has indicated that CDA1 levels are related to the severity of disease and therefore may play a role in mediating its development.

Atherosclerosis in Diabetic Complications

› Terri Allen

Dr Terri Allen heads the Atherosclerosis in Diabetes lab in the JDRF Diabetes and Metabolism division of the Baker. Terri has a PhD in diabetic kidney disease and has been working in the area of atherosclerosis since 2000. Terri is also chair of the AMREP Animal Ethics Committee.

TERRI's lab focuses exclusively on atherosclerosis, the accumulation of fatty deposits in the heart's blood vessels, in diabetes. Heart disease is a major complication of diabetes, and its greatest cause of death in people with the disease. People with diabetes generally have an abnormal cholesterol level, known as a lipid profile. So even though, compared to the rest of the population, diabetics have higher cholesterol levels, they run a greater risk of going on to have a heart attack than a person with a higher cholesterol reading but who does not have diabetes. The presence of diabetes is a risk factor for heart disease as great as family history, high cholesterol and even having had a heart attack previously.

Terri's lab, which works in collaboration with many other Baker labs on projects, investigates the effectiveness of drug treatments in diabetic atherosclerosis, as well as the effectiveness of dietary interventions. Using a genetically modified mouse model with diabetes and high cholesterol, Terri's group monitors the effects of diet and drugs on the development of atherosclerosis and also studies what has taken place at a cellular and molecular level. This approach gives insight into why a particular intervention may or may not have proved effective and does so in a condensed space of time: in humans diabetic complications such as atherosclerosis can take 15–20 years to develop.

Ongoing research projects, many conducted in collaboration with pharmaceutical companies, include the study of a new application of the hormone endothelin, which constricts blood vessels, in diabetic kidney disease and atherosclerosis.

In conjunction with the Baker's Paul Nestel, Terri's lab has conducted research into the controversial notion of reducing cholesterol and the incidence of atherosclerosis by boosting cow's milk with a specific oil. Their finding, that the effects on disease were unremarkable, will add to the body of information on this topic.

Research now underway, conducted in collaboration with the Australian Centre for Blood Diseases, will look at the relationship between changes in platelets, manufactured in the bone marrow and associated with the blood's ability to clot, and atherosclerosis.

Cardiovascular Neurosciences Division

› Murray Esler

As an associate director of the Baker and head of the Cardiovascular Neurosciences Division, Professor Murray Esler leads the institute's extraordinary research into the relationship between the brain and heart health.

A CLINICAL cardiologist practising at The Alfred, Murray also has a PhD in neuroscience.

Research is conducted in humans and in animals and focuses on the importance of psychological mechanisms and mental stress in heart disease and high blood pressure.

The brain-heart link in cardiovascular disease has come into the medical research mainstream in the last 10 – 15 years, but only after many years of being relegated to the sidelines: stress and psychological illness as causes of heart disease have long been accepted by the public but the body of science supporting this folk wisdom is relatively new.

Data that has come to light during earthquakes, though, has gradually silenced sceptics. Multiple international studies have shown that the incidence of sudden cardiac death is increased manifold, up to seven times, on the day of a major quake. Earthquake data is compelling in that some people seem to thrive on forms of stress that may have a harmful effect on others but during an earthquake it is accepted that people are stressed and frightened without exception, and the increased rate of heart attack and sudden death during such natural phenomena has been apparent since the 1960s.

In collaboration with the Human Neurotransmitters lab, led by the Baker's Gavin Lambert, Murray oversees an active research program on depressive illness. Major depression is known to be a major cause of heart attacks and sudden death. As an isolated risk factor it is equally high to the risk posed by high blood pressure or high cholesterol. Investigations by Murray and Gavin, in association with psychiatrist and PhD candidate David Barton, have measured the brain transmitters in people newly diagnosed with depressive illness and found that in about 40 per cent of this group the sympathetic nervous system – our "flight or flight' response – is permanently switched on, placing the heart under unrelieved pressure.

Previous groundbreaking work by Murray on heart failure patients, which showed their sympathetic nervous system was active without relief, led to the lifesaving use of beta-blockers in this group patients. It was this previous discovery that led Murray to look into whether the sympathetic nervous system has a role in the increased risk of heart attack in patients with depressive illness. The findings, that there is abnormal activity in 40 per cent of sufferers, have direct implications for future treatment of sufferers of depression and this anomaly in their risk of heart attack may hold clues about different types of depression.

Neuropharmacology

› Geoff Head

Associate Professor Geoff Head leads research at the Baker's Neuropharmacology lab in the Cardiovascular Neurosciences division.

THE influence of the central nervous system on long-term blood pressure levels and the relationship between blood pressure and stress pathways in the brain is a major focus of Geoff's studies.

Research in this lab centres on cardiovascular neuroscience and fills a niche between the clinic and basic research. Work is carried out to understand the mechanisms that trigger cardiovascular diseases through environmental factors. Stress is a main area of investigation, and research is also being conducted on the effects on the central nervous system and control of the cardiovascular system of obesity and other metabolic disorders.

Geoff hopes that better understanding circadian patterns, the day/night oscillations of blood pressure, will shed light on why people are two to three times more likely to have a stroke or other cardiovascular event in the early part of the day. Geoff and his team have developed the first mathematical model used to estimate the rate of blood pressure rise in the morning. While this morning surge has been previously documented, Geoff's work, which involves a relatively simple but robust mathematical program, will go towards proving the relationship between these natural elevations in blood pressure and the incidence of cardiovascular events. By analysing ambulatory blood pressure in patients against his mathematical model the underlying mechanisms that trigger heart attack and stroke can be better understood. Research in this area is focusing on the role played by hormones and the nervous system on this phenomenon and whether arteries stiffened by atherosclerosis lead to a greater surge in morning blood pressure.

Geoff's computer program allows analysis of the impact of everyday life on the blood pressure of a large number of patients. Continuing research has shown that in people with hypertension, the morning rise in blood pressure is steeper than usual at first, and then plateaus more slowly.

Another research focus of Geoff's lab is looking into a better treatment for congestive heart failure. People with heart failure –a serious, progressive disease – have as little as a 50 per cent five-year survival rate. ElaCor Pty Ltd is a company established in 2005 to further develop research conducted in collaboration with IMBCom at the University of Queensland. The Elacor technology is based on the discovery of a group of natriuretic peptides – part of the body's natural response to heart failure – isolated from the venom of the Taipan snake. The lead compound is showing great promise as a treatment for congestive heart failure and has outperformed human natriuretic peptides in early studies.

Translational Proteomics Ramaciotti Centre

› Greg Rice

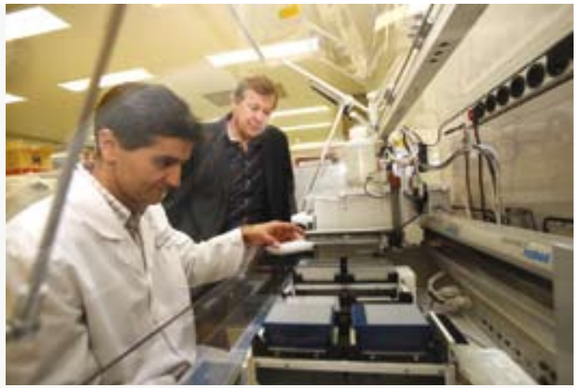
GREG'S work in the rapidly expanding discipline of proteomics is not confined to one disease setting. Although much of his research and background is in the development of new diagnostic tools for use in female reproductive health and in gynaecological cancers, his appointment to the Baker will see his research expand into cardiovascular disease.

One of the strengths of proteomics is to allow the measurement and comparison of a wide range of different biomarkers in one sample. Research into the features of proteins in health and in disease as well as their changes, both over time and in the presence of different stages of disease, will give rise to the development of new and better predictive and diagnostic tests.

In collaboration with the Mercy Perinatal Research Centre at the Mercy Hospital for Women, Greg has developed a new screening method for the early detection of complications in pregnancy. Major complications of pregnancy include miscarriage; pre-eclampsia; preterm labour; premature rupture of membranes; intra-uterine growth restriction, gestational diabetes and stillbirth. Despite many other advances in pregnancy healthcare, the incidence of these complications has not changed and most cannot be diagnosed until late in the pregnancy. Greg's team has identified 10 different substances present in the blood of pregnant women that could be used develop a new test for pregnant women who might be at risk of later complications. Such a test would be used at the first antenatal visit.

In 2005 Greg's team completed a small Phase 1 trial of a series of biomarkers. That trial established that more 90 per cent of the women in the study who were going to develop a complication of their pregnancy could be identified.

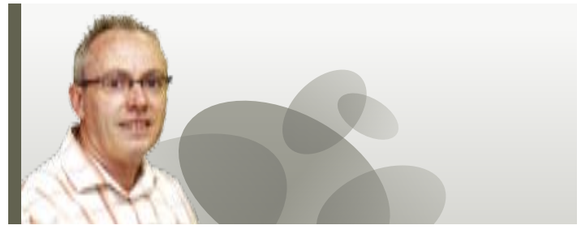
By establishing risk of complication early in a pregnancy, a woman has the best chance to tailor care to her needs and minimise the effect of the complication – or avoid it altogether.



Associate professor Greg Rice is a new recruit to the Baker. With his appointment in 2005 as head of the institute's Translational Proteomics Ramaciotti Centre, he brings to the Baker an expertise in the area of proteomics, the study and identification of proteins and their functions.

Human Neurotransmitters

› Gavin Lambert



RESEARCH in Gavin's lab focuses on the link between factors such as different forms of stress and heart disease.

In addition to the groundbreaking work on depression and heart disease, conducted with Professor Murray Esler, Gavin's lab is investigating the way that obesity contributes to raised blood pressure. While it is well known that an excess of body fat distributed around the abdomen increases the risk of heart disease, the precise reasons for this are not yet understood. High cholesterol, high blood pressure and high blood sugar levels are all commonly found in overweight and obese people and this cluster of symptoms, referred to as "metabolic syndrome", significantly increases the risk of heart attack and the development of diabetes.

Research conducted by Gavin's team suggests that an important link between heart disease and body fat might be due to an overactive sympathetic nervous system. The sympathetic nervous system is associated with the body's response to stress and in an active state the stress hormone noradrenaline is released, which raises blood pressure. Studies conducted on overweight and obese volunteers and published in 2005 have shown that weight loss and exercise not only improved every symptom of metabolic syndrome but an average weight loss of 6.5 kg in 22 volunteers led to an average reduction in the release of noradrenaline of 43 per cent. Research is continuing into whether the process of weight loss or a stable lower weight is more important in modifying sympathetic nervous system activity.

Another area of study examines the link between panic disorder and cardiovascular disease. It is believed that the risk of heart disease is increased in people suffering from panic disorder and is due to an over stimulation of their sympathetic nervous system. Gavin's lab has shown that during a panic attack, patients display some symptoms similar to those experienced when somebody is experiencing a myocardial infarction or heart attack. Gavin's team is studying the effects on heart risk of two different types of treatment: cognitive behavioural therapy and selective serotonin reuptake inhibitor medication

Dr Gavin Lambert is head of the Baker's Human Neurotransmitters laboratory.

Commercialisation

The Baker exists to reduce death and disability from cardiovascular disease, and technology transfer – the transfer of laboratory findings to the community – is vital in realising its mission.

Commercialisation

THE commercialisation of research activities is one of the most effective ways we have of ensuring that knowledge and ideas developed by scientists at the Baker Heart Research Institute improve the lives of people living with, and at risk of, cardiovascular disease. The Baker exists to reduce death and disability from cardiovascular disease. To do this successfully the Baker needs to ensure that laboratory findings are translated into good results for patients.

A hierarchy of principles informs the way the Baker enters into technology transfer initiatives and these are considered in every commercialisation venture. They include:

- The attraction of commercial funding to support basic R&D at the Baker.
- Seeing the generation of new ideas applied and taken up in the commercial world in a way which ensures they are used to improve health;
- The mitigation of risk associated with commercialisation pursuits.
- Profit from the commercialisation of technology developed at the Baker directly returned to support future research.
- Providing an appropriate level of personal reward and incentive to individual researchers involved in the development of new technologies.

2005 marked a boost in our involvement in research contracts, which will continue throughout 2006. The commercial partnerships we develop through such contracts provide us with an opportunity to interact with scientists and research in the commercial sector.

This is one useful indicator of the currency of our own research, and an important source of funding for our research activity. It also ensures our scientific work is connected with and informed by the best science underway in the commercial sector – this kind of work ensures we are connected with the commercial scientific mainstream.

The appointment in December 2005 of Dr Chris Nave as the Baker's commercialisation director put the institute at the forefront of the biotechnology sector in Victoria. Chris has international experience in the pharmaceutical/biotechnology industries, with particular focus in the areas of business development and commercialisation of new technology. Most recently he was the biotechnology manager at Melbourne Ventures, the commercialisation arm of the University of Melbourne and one of the state's most respected biotechnology development agencies. He has been co-founder, director and business development manager of various start-up biotechnology companies and has worked for Leiras Pharmaceuticals (Finland), a fully owned subsidiary of Schering AG (Germany). He is currently the director of three biotechnology companies and plays an active role in their business development and management, and has previously worked as a professional scientific consultant for government organisations and private corporations.

His appointment supports a broader strategy for the Baker that encompasses technology transfers and associated intellectual property issues, contract research and commercial research. A strong and experienced team, also newly recruited to the Baker, will support Chris in his new role.

Commercialisation manager Bev Thomas has both academic and industrial pharmaceutical development experience and has worked on industry funded projects as a research fellow in preclinical pharmacokinetics and disposition before working for the drug delivery start-up company Acrux.

Chris and Bev are also joined in 2006 by Elise Needham, who has taken on the position of commercial contracts manager and Zoe Kristall, business development associate. Elise, who has a PhD in medical research from the University of Melbourne, has previously worked as a clinical trial coordinator at the Royal Melbourne Hospital and as a research project manager at the Royal Australian and New Zealand College of Psychiatrists.

Zoe holds an honours degree in chemical engineering and an MBA in Entrepreneurship and Innovation. She previously worked in IP commercialisation for QPSX/ Offspring Ventures and has held technical, operational and sales roles in the mining industry.

Under Chris's guidance, the Baker's newly revitalised commercialisation team is offering an unparalleled support service to the institute's scientific community. Their job is to ensure that our most exciting bench top research is transformed into viable treatments and therapies for people living with, and at risk of, cardiovascular disease. Their combined experience offers business development expertise, access to research development funds and superior project management skills. The establishment of this high level of support to the Baker's scientific community in 2005 is an indication of the Institute's commitment to encouraging an atmosphere in which commercialisation is well understood, and in which success is celebrated for the benefits it brings to the community and researchers.

2005 marked a boost in our involvement in research contracts, which will continue throughout 2006. The commercial partnerships we develop through such contracts provide us with an opportunity to interact with scientists and research in the commercial sector.

L–R. Bev Thomas, Paul Howie, Chris Nave, Zoe Kristall and Elise Needham

V-Kardia Pty Ltd & V-Kardia Inc

V-KARDIA Pty Ltd and its sister US operation V-Kardia Inc, a fully owned Baker subsidiary, are medical device companies dedicated to the development of V-FocusTM, a new, minimally invasive, percutaneous (delivered through the skin) system for the selective administration of genetic, cellular or pharmaceutical agents to targeted organs without systemic leakage. V-Kardia overcomes a major problem with heart disease therapies: it allows drugs to be delivered directly to the heart, with little leakage around the rest of the body. By isolating the coronary circulation from general circulation, the toxic effects and dangers to other organs of drugs intended for the heart are substantially reduced. This catheter-based system allows the circulation of the heart to be isolated from the systemic circulation. V-Kardia's first therapeutic target is the treatment of heart failure, a disease of epidemic proportions. The system may also be used to deliver drugs to other organs.

Drug delivery has become an integral part of drug development strategies. Some of the most promising new therapeutic agents are gene-based and when successfully delivered to the patient can restore the function of the failing organ. But because these drugs can have dangerous side effects when delivery is systemic, localised delivery is the key to their effectiveness. Both new drugs and existing drugs that are known to be effective but that have toxic side effects when they circulate through the body will benefit from the development of this technology, which is the work of Baker scientists David Kaye and John Power.

The first disease targeted for V-Kardia is heart failure. This progressive disease, there the heart cannot pump blood to meet the requirements of the body, can be a consequence of all forms of serious cardiac disease but coronary heart disease and cardiomyopathy are the most common underlying conditions. Patients with heart failure have impaired quality of life, with median survival of only 1.7 years in men and 3.2 years in women. Heart failure is a growing problem around the world: in the US, it costs the US health care system $40 billion a year. There is no cure for heart failure short of heart transplant and treatment that can improve heart function carries the serious challenge of systemic leakage, which David and John's technology has been developed to overcome. While clinical trials are planned for use of the device in delivering drugs to the heart, studies to develop its effectiveness in use with other organs are continuing.

ElaCor Pty Ltd

ELACOR Pty Ltd is a spin-off company established to further develop work from the Baker Heart Research Institute's Geoff Head working in collaboration with the Institute for Molecular Bioscience at the University of Queensland. ElaCor is focused on developing a novel and effective therapy for congestive heart failure, (CHF).

CHF is an often fatal condition in which the heart muscle becomes weakened and lacks the strength to adequately pump blood around the body. It is usually a chronic disease – a long-term condition that gradually becomes worse. Conversely, acute CHF has a sudden and severe onset and requires immediate hospitalisation. It is drastically increasing in prevalence all over the world and now causes more than 10,000 deaths per year in Australia and more than 260,000 in the US. It is a condition that causes long term disability and requires ongoing treatment.

Natriuretic peptides (NPs) are part of the body's natural response to heart failure and as such they have been adopted as treatment for the disease. However they have a number of inadequacies as drugs, including a short life span in the body, which restrict their usefulness. There is a demonstrated need for new NP therapies and the ElaCor technology is based on the discovery of a new group of NPs isolated from the venom of the Taipan snake. The lead compound is showing great promise for drug development.

ElaCor is a spin-off company established to further develop work from the Baker Heart Research Institute's Geoff Head working in collaboration with the Institute for Molecular Bioscience at the University of Queensland.

Nucleus Network

› A wholly owned Baker subsidiary offering phase 1-4 clinical trials

Australia in total has only 0.25% of the global early phase clinical trial market. We have a strong belief that Australia can significantly increase its share of this international market. Working closely with Australian industry, Nucleus Network is promoting Australia as a destination for clinical studies.

Nucleus Network

NUCLEUS Network is a wholly owned Baker subsidiary, offering phase 1–4 clinical trials and has evolved significantly in the last 18 months. It is a tribute to the dedication and talent of the staff and to the goodwill and support shown by the founding members of both the Centre for Clinical Studies (CCS) and Clinical Trials Victoria (CTV).

Clinical Trials Victoria and Centre for Clinical Studies were conceived by clinicians and researchers to provide a framework for world-class clinical research services for the Australian and International Pharmaceutical and Biotechnology industries. This was a platform was created to help clinicians and researchers market Australia's capabilities in clinical research to domestic and international industry.

Nucleus Network is now a fully self supporting business without any reliance on government grant funding. It remains a commercially operating not-for-profit company, and reinvests earnings in developing the business itself and supporting research and industry initiatives on the AMREP site, in Victoria and nationally.

The business is active in industry building activities including international promotion, participation in the Pharmaceutical Industry Action Agenda (PIAA), and establishing the Australian chapter of ACRP. Nucleus Network also established a marketing and business development presence in San Francisco.

In July 2004 the Centre for Clinical Studies, at that time a joint venture between The Alfred, Monash and the Baker moved into a newly built, world class, 24 bed clinical trial facility in the Burnet Tower at AMREP. At the same time Clinical Trials Victoria Limited moved in to share the office space. Clinical Trials Victoria was then a business to build clinical trials capability within Victoria. The founding members on CTVL were Melbourne Health, Cancer Trials Australia (CTA), Neurosciences Victoria and Centre for Clinical Studies. CTVL initially administered seed funding from the Victorian Government that provided some capital investment to establish important technologies including PET scanning facilities at Callan Institute, Peter Mac for oncology research, an analytic laboratory at the Royal Melbourne Hospital and the CCS clinical trial unit. The majority of this funding was for capital equipment and fit-out with significant staff resource contributions in-kind from the founding members of CTVL and CCS.

2004 and early 2005 was a time when the business was becoming established and beginning to undertake significant business development activity to bring clinical research investments to Victoria. In 2004 it ran an Australian Clinical Trials Symposium in San Francisco, an event that is running again in April 2006. We have also joined the Victorian delegation to BIO2004, BIO2005 and BIO2006, the world's largest biotechnology congress. In 2005 we joined with the state government and BioMelbourne in a biotech road show to China. We also established relationships with over forty alliance partners within Australia to deliver a full range of drug development services.

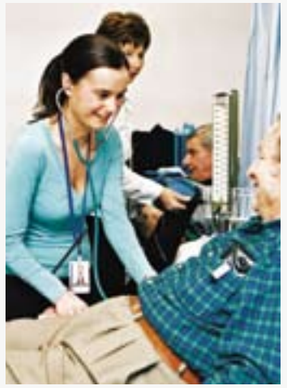
In early 2005, CTVL was facing expiration of initial grant funding. In March three of the founding members; Monash, Neurosciences Victoria and Melbourne Health withdrew from membership and the Baker Heart Research Institute took control. In order to grow both CCS and CTVL it was agreed by the partners of CCS that it should merge with CTV. CTV had also by this time established a successful clinical development consulting business, Clinical Trials Consulting and a fledgling training business in Good Clinical Practice Education.

The formal merge of CCS Ltd and CTV Ltd occurred on 1st July 2005, the entity continued as CTVL. In August 2005, The Hon. John Brumby, Minister for Innovation, re-launched the business under a new trading name of Nucleus Network.

This re-launch was a significant event for Nucleus Network as it marked the clear establishment of Nucleus as a member of the Baker family.

Since August Nucleus Network has shown impressive growth in clinical study numbers. There has also been good growth in both the consulting business and the eduction business. A three-year growth plan that will see Nucleus Network grow to conduct over 30 studies per year.

Australia in total has only 0.25% of the global early phase clinical trial market. Australia can significantly increase its share of this international market. This belief is a driving force for all Nucleus Network staff.



A platform was created to help market Australia's capabilities in clinical research.

Nucleus Network

The unit has shown rapid growth in both in-patient and outpatient studies and is attracting a significant flow of work internationally. Over 70% of revenue has come from overseas investment.

SIGNIFICANT achievements and events within each line of business include:

Nucleus Network Education:
Nucleus Network has established an exclusive arrangement with the Association of Clinical and Research Professionals (ACRP), which is the leading global industry association with over 20,000 members. Nucleus Network Education offers an Australian adaptation of the ACRP course in Good Clinical Practice (GCP). GCP is the standard by which all research involving humans is required to be undertaken. Australia has a strong international reputation for the quality of its medical and clinical research, however many staff have not received formal training in GCP.

The focus of these programs is to train investigational site staff in GCP and then encourage them to undertake certification by examination. Developing the number of GCP qualified researchers in Australia will increase Australian competitiveness in the international market place.

In 2005 a licensing arrangement was established to deliver the ACRP GCP course in Queensland and plans are underway for a similar arrangement in NSW. Modules on GCP within the University of Melbourne graduate programs in clinical research are offered.

Centre for Clinical Studies:
The unit has shown rapid growth in both in-patient and outpatient studies. CCS is attracting a significant flow of work internationally, over 70% of revenues have come from overseas investment. CCS has strong relationships with two top 10 global pharmaceutical companies, each of them placing multiple studies with the unit. CCS also has relationships with and is conducting studies for some of the largest global biotech companies as well as many Australian biotechs. The unit has grown from around 10 staff in 2004 to a regular staff of over 40, comprising permanent and sessional staff.

The unit is now supported by full-time medical and nursing staff, dedicated subject recruitment staff, project coordinators, full-time technical laboratory and quality management staff.

The unit also benefits from a close and supportive relationship with Monash and The Alfred hospital. The Alfred provides medical services including emergency support, pathology laboratory, medical imaging and biomedical engineering.

The Alfred's patients also benefit as many of our studies provide access to new treatments that would otherwise be unavailable. Nucleus Network enjoys strong support from the Baker Heart Research Institute particularly in strategy, specialist analytics, business development and contract resources. Monash Department of Epidemiology and Preventive Medicine and Clinical Pharmacology are also close collaborators.

Clinical Trials Consulting:
The CTC business has grown from strength to strength and has become a core part of business. It is also key to one of the original goals of building a platform to support clinical research and development for Australian companies. This consulting business focuses on the transition from bench research to clinical research in human subjects. One element of this is combining an understanding of pre-clinical, trials, stock manufacture and regulatory strategy. Many small Australian biotech companies do not have sufficient experience in these areas to efficiently enter human clinical development. We have assembled a team of highly experienced consultants who have significant experience in regulatory, pre-clinical, clinical and manufacturing scale up strategy. We also have a great deal of experience in later phase studies and are able to offer advisory services to create a full clinical development plan and regulatory filings for international agencies such as FDA and EMEA.

The consulting business also creates a significant flow of work for the CCS business through establishing trusted relationships at the very early stage of drug developments. It will eventually provide these services to discoveries and new treatments arising from discoveries made by the Baker Heart Research Institute. An additional aspect of the consulting business combines experience in managing trial sites and business management. Staff are engaged in a number of projects that support development of the clinical research industry as a whole. These projects include infrastructure developments as well as helping additional trials sites to become established and operate to international standards.

Finally the consulting business also provides commercial sponsorship services to off-shore companies who do not have an established entity in Australia. These services can range from simple sponsorship through to full project and site management.

Across all consulting work, the business is engaging with additional Australian clinical research service providers to offer a full spectrum of services. This provides good spin-off benefits to Australian industry, particularly in terms of manufacturing, bioanalytic services, pharmacogenomics, site management and monitoring and general laboratory services.

CTC has have provided consultancy services to over 20 Australian companies and have acted as international sponsor for five companies.

Core Facilities

DNA sequencing.
THE Baker's DNA sequencing service has been integrated with that of the commercially run IDI facility, and is involved in a broad range of collaborations with the laboratories of the institute and elsewhere. As well as providing an essential support to the Baker's laboratories it has been the source of several successful publications in its own right.

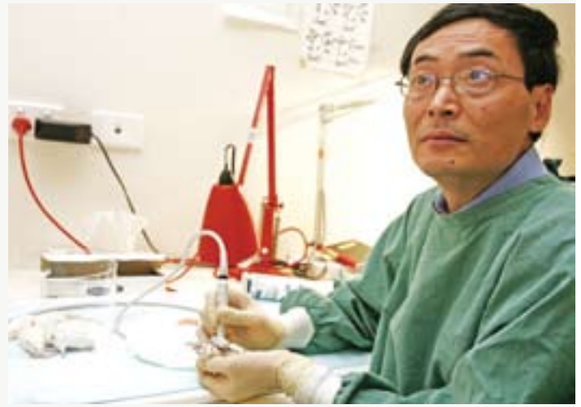
Adenovirus facility.
The institute's virus facility, run by the Baker's Walter Thomas, head of the Molecular Endocrinology lab, has been developed to produce medically modified adeno-associated viruses and lenitvirus capabilities that crucially support Baker research. The work of this core facility has become increasingly important as several Baker labs are now exploring more specific targeting of gene therapies which can use the viruses created to carry the therapies into the circulation.

Confocal imaging.
New graphics software was purchased for the Baker's confocal imaging equipment in 2004 and more recently a consortium of AMREP partners has been established to bring together imaging equipment under a new imaging joint secretariat. This has greatly enhanced access to high level imaging capabilities across the precinct.

Proteomics
Proteomics, the study and identification of proteins, is a critical service for Baker scientists and underpins much of their research. The Clive and Vera Ramaciotti Proteomics Centre was expanded in 2005 with the recruitment of associate professor Greg Rice from the University of Melbourne. In 2005 we purchased new Bruker Daltonics Mass Spectroscopy equipment. This has enabled the proteomics core facility to develop more precise and wide-ranging predictive tests, and has supported the identification of new biomarkers of cardiovascular disease and diabetes. Distinguished proteomics expert Dr Gert Talbo heads the institute's proteomics centre and provides crucial support that enables scientists to better understand their lab findings.

Mouse Surgery/Cardiology
The Mouse Cardiology Core Facility provides collaborative support to other groups at the Baker Institute in conducting cardiovascular research using mice. The selective use of genetically manipulated animals allows Baker scientists to determine the role of significant genes and proteins in cardiovascular physiology and disease. Because mice are the most common choice of species for this type of research, determining mouse heart and vascular function and reproducing cardiovascular diseases in small animals have become vital. A range of functional and microsurgical methodologies has been developed which are now available to other laboratories. Dr Xiao-Jun Du, head of the institute's Experimental Cardiology lab and a world leader in mouse cardiology, runs this core facility.

Precinct Animal Centre (PAC).
The Animal Centre plays a vital role in research at the AMREP precinct, conducting scientific research and breeding animals for research. There are approximately 350 users of the facility, all part of the process of delivering science from the "bench top to the bedside." Managed by the Baker under the guidance of Debra Ramsey, PAC serves the animal needs of all partners of AMREP. Each piece of research involving animals requires approval by the National Health and Medical Research Council and the precinct's own animal ethics committee. Some examples of procedures that were researched by the facility include cardio myoplasty procedures used by surgeons today and bypass surgery, which has evolved to a point where the procedure is carried out by keyhole surgery.



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BA, Dphil, BMBCh, FRCP
Professor David Kaye –
MBBS, PhD, FRACP, FACC
Professor Karlheinz Peter
Professor Mark Cooper –
MBBS, FRACP, PhD, FAHA, FASN
Professor Murray Esler –
BmediSci, MBBS, PhD

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Senior Principal Research Fellows
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Professor Mark Cooper –
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Professor Murray Esler –
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Associate Professor
Zygmunt Krozowski –
BSc (Hons), PhD
Associate Professor
Elizabeth Woodcock –
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Professor Murray Esler –
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Associate Professor Geoff Head –
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Head Of Laboratory
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Sonia Dougherty

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› Continued

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BmediSci, MBBS, PhD

Administration
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Human Neurotransmitter

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Associate Professor
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Karen Oliva – *DipAppSci*

Biological Media Preparation

Professional & Technical Staff
Willissa D'Souza

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David Lloyd

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Executive Assistant
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Scientific Projects Officer
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Receptionist
Barbara Spaccatore –
Receptionist

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Bcomm, ACA
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BBS, CA, MIMS
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Bec (Acc), CPA, DipOD
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Accounts Payable/rec Officer
Dale Hince –
Accounts Clerk
Lisa Skigopoulos –
Payroll Officer

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Information Systems Manager

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OHeS Chemical Project Officer
Tracey Oakes – *OHeS Project Officer*

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Brian Motz
Meg Kaegi

Monthly Baker Science Awards

Monthly Baker Research Prize Winners for 2005

Month	Winner	Article
Dec-04	Alex Bobik	Kalinina N, Agrotis A, Antropova Y, DiVitto G, Kanellakis P, Kostolias G, Ilyinskaya O, Tararak E, Bobik A. Increased expression of the DNA-binding cytokine HMGB1 in human atherosclerotic lesions: role of activated macrophages and cytokines. Arterioscler Thromb Vasc Biol. 2004 Dec;24(12):2320-5.
Jan-05	David Kaye (1) Murray Esler (2)	(1) Schlaich MP, Parnell MM, Ahlers BA, Finch S, Marshall T, Zhang WZ, Kaye DM. Impaired L-arginine transport and endothelial function in hypertensive and genetically predisposed normotensive subjects. Circulation. 2004 Dec 14;110(24):3680-6. (2) Campbell DJ, Krum H, Esler MD. Losartan increases bradykinin levels in hypertensive humans. Circulation. 2005 Jan 25;111(3):315-20.
Feb-05	Karin Jandeleit-Dahm	Lassila M, Jandeleit-Dahm K, Seah KK, Smith CM, Calkin AC, Allen TJ, Cooper ME. Imatinib attenuates diabetic nephropathy in apolipoprotein e-knockout mice. J Am Soc Nephrol. 2005 Feb;16(2):363-73.
Mar-05	Sam El-Osta	Harikrishnan KN, Chow MZ, Baker EK, Pal S, Bassal S, Brasacchio D, Wang L, Craig JM, Jones PL, Sif S, El-Osta A. Brahma links the SWI/SNF chromatin-remodeling complex with MeCP2-dependent transcriptional silencing. Nat Genet. 2005 Mar;37(3):254-64.
Apr-05	No entries	
May-05	Dmitry Mayorov	Mayorov DN. Selective sensitization by nitric oxide of sympathetic baroreflex in rostral ventrolateral medulla of conscious rabbits. Hypertension. 2005 May;45(5):901-6.
Jun-05	Anna Ahimastos	Ahimastos AA, Natoli AK, Lawler A, Blombery PA, Kingwell BA. Ramipril reduces large-artery stiffness in peripheral arterial disease and promotes elastogenic remodeling in cell culture. Hypertension. 2005 Jun;45(6):1194-9.
Jul-05	No entries	
Aug-05	Josephine Forbes	Forbes JM, Thorpe SR, Thallas-Bonke V, Pete J, Thomas MC, Deemer ER, Bassal S, El-Osta A, Long DM, Panagiotopoulos S, Jerums G, Osicka TM, Cooper ME. Modulation of soluble receptor for advanced glycation end products by Angiotensin-converting enzyme-1 inhibition in diabetic nephropathy. J Am Soc Nephrol. 2005 Aug;16(8):2363-72.
Sep-05	Anna Calkin	Calkin AC, Forbes JM, Smith CM, Lassila M, Cooper ME, Jandeleit-Dahm KA, Allen TJ. Rosiglitazone attenuates atherosclerosis in a model of insulin insufficiency independent of its metabolic effects. Arterioscler Thromb Vasc Biol. 2005 Sep;25(9):1903-9.
Oct-05	Merlin Thomas	Thomas MC, Tikellis C, Burns WM, Bialkowski K, Cao Z, Coughlan MT, Jandeleit-Dahm K, Cooper ME, Forbes JM. Interactions between renin angiotensin system and advanced glycation in the kidney. J Am Soc Nephrol. 2005 Oct;16(10):2976-84.
Nov-05	Bronwyn Kingwell (1) Jeremy Jowett (2)	(1) Natoli AK, Medley TL, Ahimastos AA, Drew BG, Thearle DJ, Dilley RJ, Kingwell BA. Sex steroids modulate human aortic smooth muscle cell matrix protein deposition and matrix metalloproteinase expression. Hypertension. 2005 Nov;46(5):1129-34. (2) Curran JE, Jowett JB, Elliott KS, Gao Y, Gluschenko K, Wang J, Azim DM, Cai G, Mahaney MC, Comuzzie AG, Dyer TD, Walder KR, Zimmet P, Maccluer JW, Collier GR, Kissebah AH, Blangero J. Genetic variation in selenoprotein S influences inflammatory response. Nat Genet. 2005 Nov;37(11):1234-41.
Dec-05	Emma Baker	Baker EK, Johnstone RW, Zalcberg JR, El-Osta A. Epigenetic changes to the MDR1 locus in response to chemotherapeutic drugs. Oncogene. 2005 Dec 1;24(54):8061-75.

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The Institute is grateful for major contributions from:
- Atherosclerosis Research Trust of the UK
- Australian Rotary Health Research Fund
- The Baker Foundation
- Diabetes Australia
- Juvenile Diabetes Research Foundation
- National Heart Foundation
- National Health & Medical Research Council
- National Institutes of Health (USA)
- Victorian Government

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- William Angliss (Vic.) Charitable Fund
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- Henry Cooper Fellowship
- The Cybec Foundation Scholarships
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- Mrs J E Watkins
- Dr W G Wicks
- Mrs Gwen Williams
- Mr Kenneth Woolfe

Development

THE Baker could not do what it does to combat cardiovascular disease without the support of its many donors and benefactors. The many generous donations, bequests and contributions of time and support we receive through the year are vital, and the job of the Development team is to ensure that those who provide this support to the Institute are themselves supported in the partnership they have chosen to establish with our scientific community.

In 2005, the department was involved in a broad range of activities geared to increasing awareness of the valuable and innovative research being undertaken at the Baker, and raising funds to support that research. The contribution of donors was substantial, and as we progress we will build on the achievements to ensure a sustainable funding and support base.

Integral to our success is, of course, our loyal supporter base. We have approximately 60 volunteers assisting in wide ranging tasks. We have established 'Friends of Baker'. This enthusiastic, lively group are committed to organising events for us that will expose our organisation to a broader audience and provide much needed funds.

Financial and resource support comes from a number of sectors, including individuals, trusts, foundations, the business community and from people who have kindly remembered us in their wills.

The Baker's Wine Lovers' Dinner has become a popular event on the Melbourne social calendar. The 2005 event was once again a huge success and we thank Ian Loftus for sourcing the magnificent wines from the following generous wine makers –:

- Casella Estate
- Delatite Winery
- Majella Wines Pty Ltd
- Morris Wines
- Peter Lehmann Wines
- Plunkett's Winery
- Taltarni Vineyards
- Tuck's Ridge
- Westend 3 Bridges Estate & the Milawa Cheese Company for their award winning cheeses.

Also on our event calendar was the Great Debate – "Does a healthy lifestyle really mean a a longer life?", hosted by Mark Mitchell. The creative idea behind this event was for guests to come and learn interesting facts about their health in an entertaining way. The tone of the debate was informative yet light-hearted. We did not realise the talent for comedy our scientific researchers possess. This made for an inspiring learning experience as well as a most entertaining evening.

Keverne Pearson had a near fatal heart attack and underwent heart surgery in 2004. Kev's Relay Ride for Life was his inspirational way to say thank you to the team that saved him – a state-wide relay bike ride, with six participants. Over six weeks the team rode around Victoria, holding approximately 30 seminars in regional towns. The seminars presented information on Cardiovascular disease and the innovative work of the Baker.

Once again we were indebted to Maestro Vladimir Vais, legendary conductor of the Bolshoi Theatre, Moscow, for arranging an evening soirée with opera's rising stars Emily Wang, Lynlee Williams, Cosimo Ciccone and Matthew Davine. The acoustics of Christ Church South Yarra ensured a memorable evening of arias from our favourite classics.

Although it gives a level of satisfaction to review the past year, we are always excited and eager to look to the future. This office was previously known as the Foundation, but in 2005 we decided that it should be called the Development Department. We believe this better reflects the work that we undertake. Foundations are often defined as philanthropic organisations that distribute funds. We see our role as raising funds and resources for the Baker, by building relationships and promoting the science to a broad audience. Development is associated with an act of improving, by expanding or enlarging or refining – characteristics that we closely identify with our efforts.

The Development department serves to support the scientific and clinical mission of the Baker. Our activities are designed to align with the direction of the organisation to ensure our efforts assist the Institute in achieving its goals.

In reflecting on the attributes of the Baker, there is much that is unique and much that we can promote to the broader community. The organisation is extremely successful in the arena of prevention, treatment and cure of cardiovascular disease. Less obvious perhaps, is the exceptional skills and culture within, that makes the organisation a great success. Our capacity to mentor and nurture students and early career scientists provides a wealth of scientific 'stars' for our own facility workforce, and those of international and national organisations. We are fortunate that in this particular area, we are well supported by donors who specifically contribute to our scholars' program. This program enhances our ability to attract 'the best of the best'.

A talent for creative thought and a mindset of continuous improvement throughout the Baker results in constant progression and innovation in our research. Diversity of skills, specialisation and cultures provides the basis for robust, multi-disciplinary teams who collaborate to explore ideas and methods to ensure unique and valuable research findings. These findings will ultimately save lives and improve the quality of life for many. Our donors play a major role in this process. By supporting innovation donors provide us with the flexibility to build on our successes and attract research 'stars'.

We sincerely thank all those who have contributed to the Baker in 2005, particularly our loyal base of volunteers who worked over 1000 hours this year – a huge saving in man-hours, and a truly delightful group of people we have come to know very well. We look forward to continuing these rewarding relationships, as well as new ones into the future.

Friends of Baker Comittee
Mrs Bernadette Brodribb
Ms Catherine Collier
Mr Stephen Cook
Mrs Miriam Greenfield
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Mrs Margaret Ross
Mr & Mrs Eric & June Ross
Mr Philip Ross
Mr Michael Stillwell

The Development team serves to support the scientific and clinical mission of the Baker. Our activities are designed to align with the direction of the organisation to ensure our efforts assist the Institute in achieving its goals.

L-R: Bobbie Renard, Elizabeth Veal, Margherita Boemo, Lyn Brodie

Baker Medical Research Institute

› Income Statement for the year ended 31 December 2005

	Consolidated		Parent	
	2005	2004	2005	2004
	$	$	$	$
Revenue from ordinary activities	29,920,164	22,301,699	25,795,069	22,301,699
Expenses for building works	-	(1,895,018)	-	(1,895,018)
Employee benefits expense	(15,608,148)	(12,474,984)	(13,714,482)	(12,474,984)
Laboratory consumables	(5,322,948)	(3,380,071)	(4,314,372)	(3,380,071)
Depreciation and amortisation expenses	(1,280,559)	(1,148,452)	(1,227,237)	(1,148,452)
Share of loss in associate	(93,040)	-	(93,040)	-
Fixed assets written off	(664,062)	-	(502,178)	-
Building overheads	(431,101)	(360,950)	(372,029)	(360,950)
Borrowing costs expense	(114)	(35,552)	-	(35,552)
Laboratory support expenses	(2,528,279)	(1,313,078)	(1,795,787)	(1,313,078)
Research and development	(211,982)	-	-	-
Other expenses from ordinary activities	(1,229,063)	(1,612,781)	(1,194,448)	(1,612,781)
Surplus from ordinary activities before income tax expense	2,550,868	80,813	2,581,496	80,813
Income tax expense	(70,877)	-	-	-
Surplus from ordinary activities after income tax expense	2,479,991	80,813	2,581,496	80,813
TOTAL CHANGE IN FUNDS	**2,479,991**	**80,813**	**2,581,496**	**80,813**

Baker Medical Research Institute

› Balance Sheet as at 31 December 2005

	Consolidated		Parent	
	2005	2004	2005	2004
	$	$	$	$
ASSETS				
Current assets				
Cash assets	4,888,886	2,746,574	3,200,150	2,746,574
Trade and other receivables	2,372,365	3,367,728	1,471,801	3,367,728
Intercompany loan	-	-	226,463	-
Available-for-sale financial assets	13,306,474	6,901,515	13,306,484	6,901,515
Investment in associate	21,961	-	21,961	-
Other	107,464	90,754	67,057	90,754
Total current assets	**20,697,150**	**13,106,571**	**18,293,916**	**13,106,571**
Non-current assets				
Plant & equipment	4,453,638	4,538,053	4,216,899	4,538,053
Intangible assets	65,140	45,338	65,140	45,338
Total non-current assets	**4,518,778**	**4,583,391**	**4,282,039**	**4,583,391**
TOTAL ASSETS	**25,215,928**	**17,689,962**	**22,575,955**	**17,689,962**
LIABILITIES				
Current liabilities				
Trade and other payables	3,892,621	4,369,671	2,824,497	4,369,671
Prepaid income	1,663,136	-	179,441	-
Provisions	2,246,750	1,733,477	2,134,188	1,733,477
Income tax payable	70,877	-	-	-
Total current liabilities	**7,873,384**	**6,103,148**	**5,138,126**	**6,103,148**
Non-current liabilities				
Provisions	133,831	241,123	133,831	241,123
Other	6,220	-	-	-
Total non-current liabilities	**140,051**	**241,123**	**133,831**	**241,123**
TOTAL LIABILITIES	**8,013,435**	**6,344,271**	**5,271,957**	**6,344,271**
NET ASSETS	**17,202,493**	**11,345,691**	**17,303,998**	**11,345,691**
FUNDS				
Accumulated funds				
Operating fund	(7,372,845)	(7,329,085)	(7,271,340)	(7,329,085)
Capital fund	19,326,017	18,138,457	19,326,017	18,138,457
Specific purpose fund	1,872,510	536,319	1,872,510	536,319
Fair value reserve	3,376,811	-	3,376,811	-
TOTAL FUNDS	**17,202,493**	**11,345,691**	**17,303,998**	**11,345,691**

Baker Medical Research Institute

› Cash Flow Statement for the year ended 31 December 2005

	Consolidated		Parent	
	2005	2004	2005	2004
	$	$	$	$
CASH FLOWS FROM ORDINARY ACTIVITIES				
Receipts from granting bodies	12,279,185	9,947,993	12,147,321	9,947,993
Donations and bequests	4,141,020	3,193,181	4,141,020	3,193,181
Receipts for building works	-	450,000	-	450,000
Payments to suppliers & employees	(22,965,869)	(19,808,796)	(20,715,924)	(19,808,796)
Dividends received	696,885	288,629	696,885	288,629
Interest received	197,244	191,645	186,178	191,645
Rent received – Baker and Burnet buildings	1,260,148	1,003,311	1,260,148	1,003,311
Commercial Income	9,676,405	6,578,703	5,930,932	6,578,703
General income	454,156	407,471	454,156	407,471
NET CASH INFLOW FROM ORDINARY ACTIVITIES	5,739,174	2,252,137	4,100,716	2,252,137
CASH FLOWS FROM INVESTING ACTIVITIES				
Payment for available-for-sale financial assets	(6,654,451)	(5,856,551)	(6,654,381)	(5,856,551)
Proceeds from sale of available-for-sale financial assets	4,100,035	2,575,918	4,100,035	2,575,918
Payment for plant & equipment	(1,297,875)	(1,258,376)	(1,092,724)	(1,258,376)
Proceeds from related party loan	226,463	-	-	-
Cash transfer from subsidiary	29,036	-	-	-
NET CASH OUTFLOW FROM INVESTING ACTIVITIES	(3,596,792)	(4,539,009)	(3,647,070)	(4,539,009)
NET CASH INCREASE IN CASH HELD				
Cash at beginning of the financial year	2,746,574	4,998,710	2,746,574	4,998,710
Effects of exchange rate changes on cash held in foreign currencies	(70)	34,736	(70)	34,736
CASH AT THE END OF THE FINANCIAL YEAR	**4,888,886**	**2,746,574**	**3,200,150**	**2,746,574**

The summary financial information provided above and in the preceding two pages, being an income statement, balance sheet and cash flow statement, has been extracted from the audited special purpose financial statements of the Baker Medical Research Institute and its controlled entities. The summary financial information does not include all the information and notes normally included in a statutory set of financial statements. A full set of audited special purpose financial statements can be obtained from our website at http://www.baker.edu.au

The statutory financial statements (from which the summary financial information has been extracted) have been prepared with Australian Accounting Standards, which include Australian equivalents to International Financial Reporting Standard ('AIFRS'). The statutory financial statements were qualified by the auditors Ernst & Young Australia in respect to the Institute's policy to expense capital works undertaken on the buildings, which the Institute utilises. Full details of the audit qualification are contained within the audit opinion in the statutory financial statements.

Journal Articles 2005

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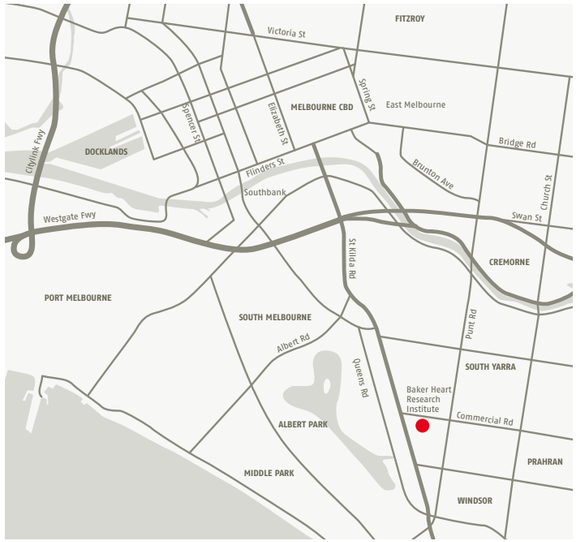

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