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Research Update 2007





The Baker Heart Research Institute leads the nation's research fight against cardiovascular disease, its causes and complications.

All our research efforts are aimed at reducing the incidence of, and providing better treatments and cures for, these conditions:

- **Diabetes and Obesity**
- **Acute coronary syndromes**
- **Heart failure**

The following pages provide an overview of these health problems and our team's various molecular, cellular, physiological and clinical research efforts towards solving them.

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Foreword

By Garry Jennings AM, Director

The deadly trio of obesity, diabetes and cardiovascular disease is our most serious impending health burden. Premature death and disability from these conditions continues to rise and the international community is being crippled, both socially and economically, by this ugly phenomenon. So great is the cost, and so widespread the problem, that obesity and diabetes are now discussed and considered at the highest levels of government by politicians and health policy-makers. Tragically most of the chronic disease brought on by these conditions is preventable. Lifestyle interventions and community-based awareness and risk reduction programs are in place, but new approaches are needed, and their effectiveness needs careful and regular evaluation.

The Baker is the nation's leading cardiovascular research institute and we are evolving to keep pace with these growing challenges to public health. Reflecting the relentless rise of diabetes in the community, diabetes research makes up some 30 per cent of the institute's research efforts and we also have boosted our studies into the causes and effects of obesity. Cardiovascular disease is the main complication of diabetes, and obesity is a major precursor to both. We cannot afford to have our research efforts conducted in silos and so we constantly recognise, reinforce and investigate the interplay between these conditions. Supporting the work of our basic scientists is the recently revamped Preventative Cardiology Unit (PCU). This unit is devoted to reducing rates of heart disease in the community by increasing



Murray Esler won the prestigious Shaikh Hamdan Award

awareness of, and encouraging the reduction of, cardiovascular disease risk factors.

Part of the Baker, but based in Alice Springs, is the newly created Centre for Indigenous Vascular and Diabetes Research. Headed by Alex Brown, this satellite unit is part of our boosted commitment to improving the cardiovascular health of indigenous Australians – because that's where the greatest disparity in our community occurs, in terms of cardiovascular disease. Mortality rates are three times the rate of the rest of the population, life expectancy is 20 years less and the median age of death is just a little over 50 years. Only 2-6 per cent of aboriginal people are aged over 65, so the elders can not lead their communities because so many of them have passed away. Cardiovascular disease strikes early in Aboriginal people. Those aged 25-54 are 12 times more likely to suffer cardiovascular disease than the rest of us. Behind that is diabetes which is at least four times more common but much more lethal in this group. We have much to be proud of in Australia, and in heart health we have led the world, but this is an area where we have been lagging, and we have not really come up with the solutions. We are striving now to become part of the solution to the nation's indigenous health crisis.

In 2006 the Baker celebrated its 80th anniversary, a significant milestone and one of which we are all proud. Far from resting on our laurels, however, I am delighted to report that 2006 was also one of our most productive scientific years, 239 peer-reviewed scientific publications and many of our staff achieving important national and international recognition for their research. One example of a major finding for the institute last year came from the work of Assam (Sam) El-Osta in the area of epigenetics. Sam's work has identified a unique master molecular controller which is responsible for turning genes that "misbehave" and cause disease "on and off". This master switch underpins cancer, cardiac disease and a form of intellectual disability known as Fragile X syndrome. The



Paul Nestel was recognised by the International Atherosclerosis Society

research was published in the prestigious journal Nature Genetics and last year earned him the Amgen Medical Research Award.

Other research highlights included a study led by Merlin Thomas which showed that one in three type 2 diabetic patients visiting their GPs carried with them symptomless, early stage kidney disease.

From the PCU came new research showing that one third of people receiving treatment for high cholesterol remain at unnecessary risk of heart disease. This is due to their ignorance of their own cholesterol levels and the lifestyle changes that could save their lives. Both of these studies reflect the Baker's focus on community as well as laboratory research.

In another highlight we'd like to congratulate Paul Nestel, an internationally-renowned long-serving Baker scientist and member of our senior faculty. Paul was recognised last year as a Distinguished Fellow by the International Atherosclerosis Society, for his professional achievements as an outstanding specialist in atherosclerosis and related diseases. Paul was the only Australian to earn this distinction, a sign of the esteem in which he is held in the international scientific community.

Murray Esler, an associate director of the Baker and head of the Cardiovascular Neuroscience division, last year won the prestigious Shaikh Hamdan bin Rashid Al Maktoum Award for Medical Sciences in the field of Pathogenesis of Hypertension. Murray was also



Peter Kistler specialises in atrial fibrillation

recognised locally in January of this year when he was awarded Member of the Order of Australia, for his services to medical science through research in human cardiovascular neuroscience, development of health policy and treatment policies.

I am pleased to report newer Baker recruits and early career scientists also continue to earn accolades for their tremendous research efforts. Among last year's highlights was that Enzo Porrello, then a 2nd year PhD student in the Molecular Endocrinology lab, won the Young Investigator Award at the prestigious Angiotensin Gordon Conference held in France. Locally, the Australian Diabetes Society presented its two main Diabetes Australia Research Trust Awards to Baker scientists. The Millennium Type 1 diabetes award went to Josephine Forbes and Melinda Coughlin and the new Millennium Type 2 diabetes award to Barbora de Courten, while the Young Investigator Award went to Anna Calkin. At the Keystone Conference on Metabolic Disease in Colorado, Graeme Lancaster from the Cellular & Molecular Metabolism Laboratory was awarded a scholarship to present his work on fatty acid-induced macrophage inflammation. Graeme was one of only four people awarded this prize and the only Australian. Tony White, from the Clinical Physiology lab also won the prestigious Clinical Young Investigator Award at the World Congress of Cardiology in Barcelona. His work establishes a plausible mechanistic link between a common genetic variant in a matrix protease (MMP-3) and unstable coronary syndromes.

Last year we introduced a new suite of awards to Baker scientists, designed to foster exciting new ideas and new multidisciplinary collaborations. These include internal competitive research grants as well as grants to support early career scientists and two stipends for PhD students. Congratulations to lab heads Sam El-Osta, Mark Febbraio, Stephen Duffy and Bronwyn Kingwell for receiving the major Baker grant under this new initiative. Their collaborative work will be the study "Does a high-fat diet initiate an epigenetic program for diabetes?" Awardees of the first round of early career scientist grants were James Armitage, Michelle de Silva and Vance Matthews.

While supporting our existing scientists in new ways, we also recognise the importance of continuing to invest in new scientific talent. Boosting our pool of researchers in 2006 were some of the nation's finest cardiovascular disease scientists, and I would like to welcome them here: Peter Kistler, a Neil Hamilton Fairley Fellow recently returned from post doctoral studies at Barts in London, brings to the Baker welcome research skills in clinical electrophysiology and the emerging field of ablation therapy for cure of atrial fibrillation. Simon Stewart has started as the new head of the PCU. Simon joins us from a conjoint appointment at the University of South Australia, where he was chair of cardiovascular nursing and the University of Queensland, where he was professor of health research. Mark Febbraio joined us as head of the cellular and molecular metabolism laboratory. Mark's team will continue to pursue his



Markus Schlaich is a hypertension specialist

internationally recognised research into the metabolic changes that lead to diabetes.

Another new recruit is Markus Schlaich, a nephrologist and hypertension specialist, investigating the link between the sympathetic nervous system, the kidneys and high blood pressure.

A major scientific conference was held in October to mark our 80th anniversary. Baker 80 – Facing the Future of Cardiovascular Disease was a two-day symposium which attracted an outstanding faculty of local and international speakers to take stock of the latest advances in cardiovascular disease. Ralph Kelly and Albert Schomig were just two of our international guest speakers who joined our own researchers for the stunningly successful two-day event.

In November I took over the presidency of the Australian Association of Medical Research Institutes, an organisation representing 36 independent medical research institutes across Australia, following on from the ever-capable Suzanne Cory from the Walter and Eliza Hall Institute of Medical Research. Suzanne did an outstanding job when she held the post for the two preceding years, and is a hard act to follow.

On the commercialisation front this has also been an outstanding year. Nucleus Network has established itself at the forefront of clinical trials activity for Australia and the region. Other newly established subsidiaries are developing exciting new treatments for cardiovascular disease.

It is an exciting and busy time for the Baker, and its team of scientific and support staff has never been stronger. It is a great pleasure to work with such a team, supported by an outstanding Board of Management and our tireless patron Sir Laurence Muir. Add to this the efforts of so many community stakeholders including sponsors, volunteers, collaborators, government and industry, without whom none of our important work can be achieved.

Organisational Chart





The Baker and IDI are striving to improve the health of the nation

A New Force in Heart and Diabetes Research



Obesity rates in Australia are expected to double by 2025 which will represent 29 per cent of the population, or 7.2 million obese people. In turn, diabetes rates will double and the most detrimental effect of these projections will be on cardiovascular disease, already the major cause of death and disability worldwide.

Obesity, diabetes and cardiovascular disease are enormous public health problems. In order to tackle them effectively now and improve the nation's dire public health projections, research forces must be combined and the best minds brought together. It no longer makes sense to work in isolation from our best and brightest colleagues.

This is the rationale behind the announcement we are combining forces with another world-renowned research organisation, the International Diabetes Institute, to create a new **national and international heart and diabetes institute**. Under this merger we will combine our strengths, our staff and our research capabilities – and indeed significantly add to them – to better fight obesity and its cardiovascular and diabetic complications. This landmark, \$29 million venture will serve as a model for medical research collaboration here and overseas. Our vision has been supported with a \$14 million commitment from the federal Government and \$5 million grant to IDI from the Victorian Government. We are in the process of raising another \$15 million to see our plans through to fruition by 2009. Stage one of the merger, including a physical relocation of some IDI staff to the Baker site, will be

“While medical technology, procedures and pharmaceuticals continue to improve, a growing number of Australians are developing diseases and suffering premature death because of avoidable lifestyle risk factors.”

Federal Health Minister Tony Abbott, 2007

complete by the end of 2007, as will the consolidation of some administrative resources.

Health, environmental and social issues all have an effect on obesity, starting in utero and continuing right through until old age. The complexity of this problem requires a comprehensive range of research expertise, from basic biology to population health. Together the Baker and IDI will build on existing expertise to create an organisation that will improve the health of Australians now and help protect the health of future generations. Although this project is the merger of two outstanding organisations, we have been careful to plan in such a way that the very separate histories, characters and cultures of the Baker and IDI will be preserved and indeed enhanced. Far from becoming a blended and indistinguishable new group, the two institutes will retain some distinct pursuits and projects. But with strategic collaboration, IDI and the Baker are effectively giving us a third force in the fight against obesity – a world first national heart and diabetes institute.

As a combined force against obesity, diabetes and cardiovascular disease, the merged entity will expand to:

- Develop and evaluate lifestyle intervention strategies such as nutrition and exercise, as well as develop the best ways to educate families, schools and communities about the need to make lifestyle improvements
- Identify individuals (including children and indigenous Australians) at greatest risk of becoming obese, as well as identify those obese individuals at greatest risk of the cardiovascular complications of obesity
- Study new experimental models of obesity and Type 2 diabetes to improve our understanding of these complex diseases
- Develop and evaluate effective drug therapies for obesity, Type 2 diabetes and cardiovascular disease for when lifestyle interventions fail
- Extend preventative programs for aboriginal Australians through our Centre for Indigenous Vascular and Diabetes Research in Alice Springs
- Identify the mechanisms and new treatments for the cardiovascular and other complications of diabetes and obesity

Diabetes



Mark Cooper leads the Baker's diabetes research

In 2005, 3.2 million Australians were obese. Obesity is a serious and complex health problem, with type 2 diabetes and cardiovascular disease its major complications. In 2005 there were 379,000 new cases of cardiovascular disease and 102,000 new cases of type 2 diabetes caused by obesity. The health and economic burden for Australia is alarming: the total financial cost of obesity was estimated at \$3.7 billion in 2005.

Adding to this existing burden are projections that obesity rates in Australia will double by 2025 – translating to 7.2 million obese Australians. The effect of this will see diabetes rates double, and the greatest pressure of these two rises will be on cardiovascular disease, which is already the major cause of death and disability worldwide. Conservatively, between 2025 and 2050, obesity will alone contribute to:

- 900,000 preventable hospitalisations for cardiovascular disease (\$2.2 billion in hospital costs alone)
- 240,000 mainly premature deaths

The complications of diabetes include kidney disease, eye disease and vascular disease. It is a major factor in cardiovascular disease and the most common cause of kidney failure in the western world.

The only way to reduce the current disease burden of obesity and ensure that these projections are not realised is to understand it as a complex disease while investigating its molecular, cellular and physiological precursors and implications. The development too of sound preventative strategies informed and evaluated by research are imperative. If we can help reduce the development of new cases of obesity and diabetes we will dramatically improve the rate of death and disability, especially from cardiovascular disease now and in the future.

Reflecting this need, investigations into diabetes and metabolic conditions makes up about 30 per cent of our research effort.

Across the institute, scientists at the Baker are striving to understand why people develop complications from diabetes and, importantly, understand the mechanisms responsible for those complications. Research is directed at the development of new treatments to target the pathways within the body responsible for the development of diabetes and obesity-related disease. The current focus of research is on the development of new techniques for early diagnosis of complications, including gene and proteomic approaches; lifestyle interventions, and the development of drug therapies for use in cases where exercise and diet are not a simple answer.



A research-led effort will improve diabetes projections

Our aim is to dramatically reduce the incidence of obesity and diabetes, two largely preventable causes of death and disability and an increasing strain on health budgets around the world. A research-led effort, with the development of sound community awareness, education and intervention programs will improve the health of those suffering, and those at risk of, these conditions. In this way, our work will have direct effect on future projections of diabetes and obesity and in turn reduce the burden of cardiovascular disease, their major complication.

Some research projects underway include:

- The development of drugs to increase the activity of antioxidant enzymes to reduce the effects of diabetes
- The identification of a master molecular controller, responsible for turning genes "on" and "off", and how this master switch underpins diabetic and metabolic disease
- How health and disease in one generation modifies genes and affects the next, predisposing infants to diabetes and obesity
- Community-based research understanding the incidence of symptomless kidney disease in type 2 diabetes patients
- The comparison of advanced glycation end products (known as AGEs, these are formed when sugars in the blood attach to proteins in the body) measurements and markers of inflammation and oxidative stress in diabetic patients to predict the development of cardiovascular disease

- The development of a new drug with the ability to reverse the detrimental effects of AGEs in the body, responsible for many of the diseases caused by diabetes
- The way key regulatory molecules that control cell differentiation are activated: research is showing that this damaging process can occur as a result of high glucose levels
- The identification of a new protein molecule, CDA1, has uncovered its anti-proliferation properties. Increasing the level of this protein in a cell stops cell division. The role of this protein in diabetic complications is being further investigated
- The effectiveness of drug treatments in diabetic atherosclerosis, or a hardening of the arteries caused by the damaging effects of diabetes, as well as the effectiveness of dietary interventions in the prevention of this condition
- The complexity of the metabolic changes that precede diabetes and the development of medication to mimic the effects of exercise in the body
- Understanding that the “stickiness” of blood vessels that are diseased can be caused by molecules called proteoglycans, and this may be the initiating step in atherosclerosis
- Identifying genetic or other factors in the blood that might protect against diabetic complications. Understanding the markers of resistance to disease will allow early, preventative treatment
- Investigation of genes and their products that are altered as a consequence of diabetes, and how the body is altered, on a molecular level, by diabetic disease



Acute Coronary Syndrome



Karlheinz Peter is working on new therapies for blood clotting

Acute coronary syndrome, commonly known as heart attack, is an umbrella term referring to a set of signs and symptoms that suggest a reduced blood supply to the heart. The most common cause of this is the development of atherosclerosis, the accumulation of fatty deposits, known as plaques, in the blood vessels. It is the rupture or erosion of these plaques that can lead to heart attack and stroke and sudden death. Atherosclerosis is the underlying cause of most cardiovascular disease and understanding the development and nature of these plaques, and who is at greatest risk of their rupture, is a major research concern across the institute. Advances in this area will have a profound effect on reducing the death and disability caused by cardiovascular disease. At present we have no way of detecting which plaques will cause heart attack (and, or death) and which will not.

The direct cost of coronary heart disease in Australia is the largest of any single cardiovascular condition, costing more than \$1.7 billion and representing nearly 30 per cent of all costs associated with heart disease. Stroke is the second largest, at more than \$1 billion. Coronary heart disease is also the single most common cause of death in Australia and is generally manifest as angina (chest pain caused by a reduced flow of blood to the heart) heart attack or sudden death.

Our work in this area of great community need focuses on the investigation of those cells that play an important role in plaque development,

the study of nutritional approaches that might prevent atherosclerosis and even the prevention and reversal of cholesterol accumulation in blood vessels. This area of research pursuit at the Baker is addressing these problems in a range of ways, including the design of a new class of "intelligent" drugs. These will prevent clotting, or dissolve clots that have caused a heart attack or stroke but do so without the excessive bleeding complications that are a feature of currently available drugs. We are also working towards the identification of biomarkers (such as levels of certain proteins in the blood) which, when added to existing knowledge of family history and lifestyle risk, will help predict coronary plaque rupture.

Another major research focus within the institute investigates the effects of stress and psychological illness on heart disease. An active research program is underway on the link between depressive illness and coronary heart disease. Depression is known to be a major cause of heart disease and sudden death, and as an isolated risk factor it is equal to the risk posed by high blood pressure or high cholesterol. Our team has 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 is permanently switched on, placing the heart under unrelieved pressure. These findings have direct implications for future treatment of sufferers of depression, a major cause of disability. This anomaly in their risk of heart attack may hold clues about different types of depression.

For a growing number of older Australians, atherosclerosis and its complications, including 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. Depression is also a major health problem, across all demographics and we know this increases the risk of heart disease.

For many, the first indication of a cardiac problem is sudden heart attack or death.

Through understanding the mechanisms involved in the development of these conditions, we are developing new tests and new treatments to prevent these events and address some major barriers to their prevention, detection and treatment. Our research in this area is highly focused on providing direct benefits to the many people living with heart disease and their families. Importantly, we are also striving to prevent sudden death and chronic disease in those millions of people who are currently symptomless, but for whom coronary heart disease, stroke and heart attack are on the horizon

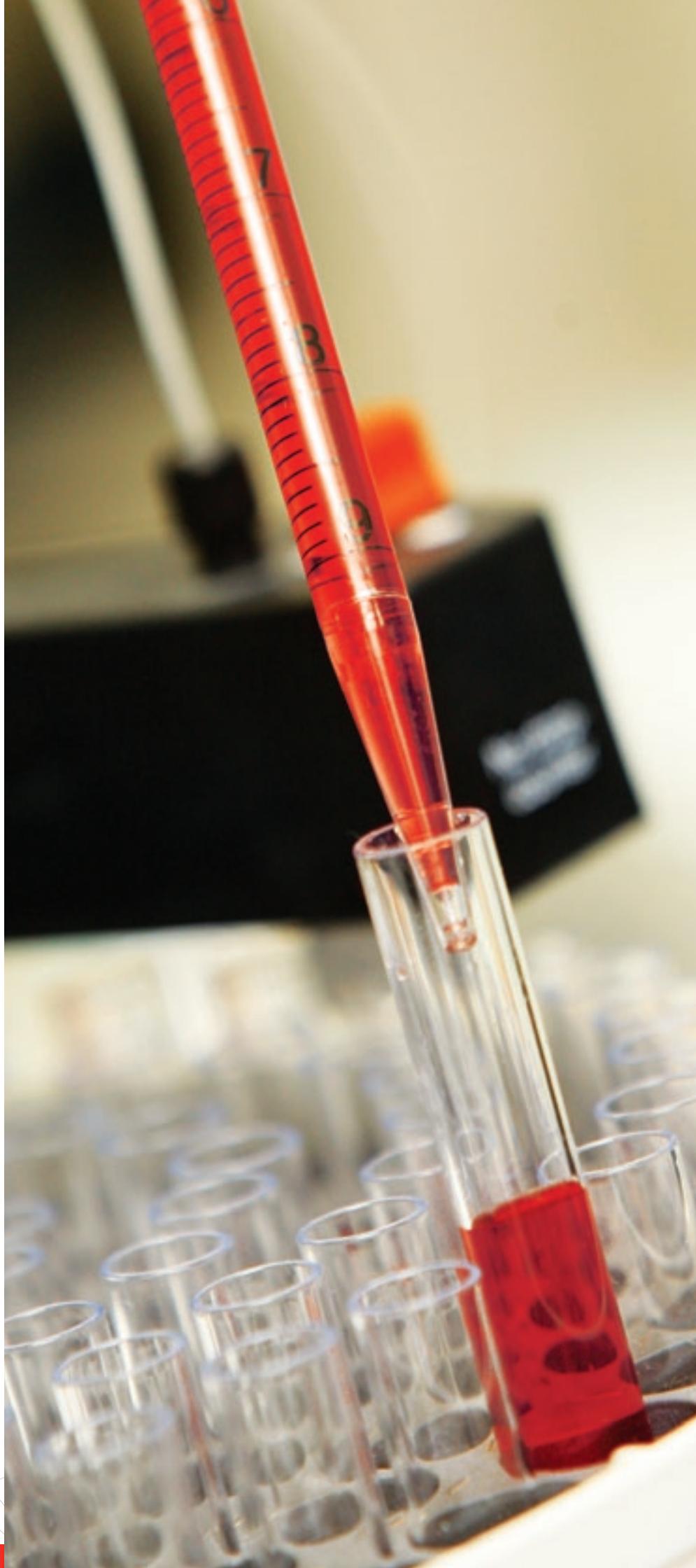


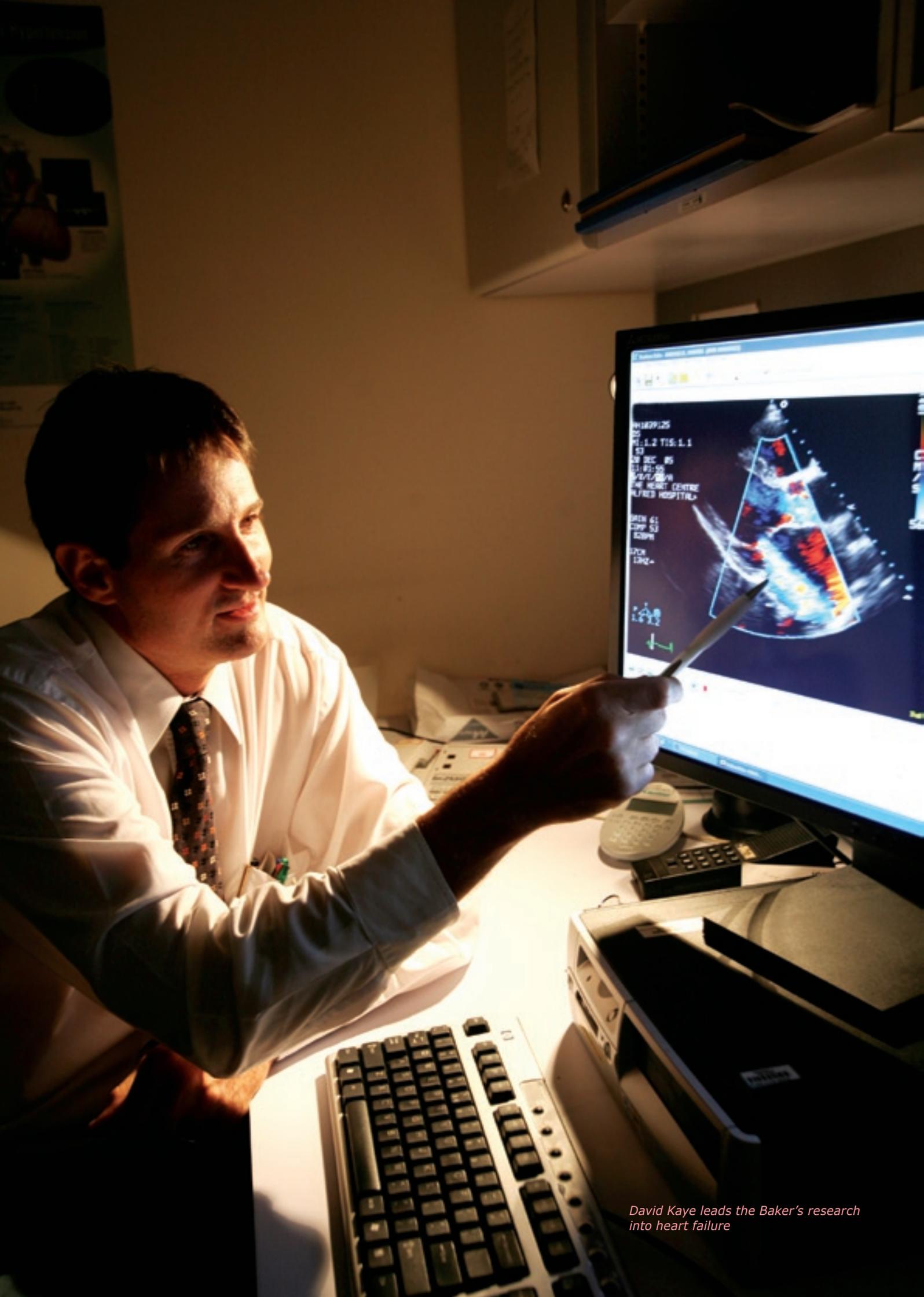
Murray Esler investigates the effects of stress on heart disease

Some research projects underway include:

- A specific cell type of the immune system, a regulatory T cell, has been shown by Baker scientists as important in controlling the development of atherosclerosis. This has important implications for the treatment of atherosclerosis and has the potential to be used in conjunction with other therapies to prevent the development of life-threatening lesions
- Marfan syndrome is a rare and devastating connective tissue disorder. Baker scientists are investigating the effects of ACE inhibitors in the treatment of this syndrome. Standard treatment to date has been beta blocker therapy, which has many side effects

- Baker research has revealed that the protein selectin is a significant contributor to heart disease in its own right, and not merely an active biomarker. As such, drug treatments for disease indicated by its presence can focus on switching off the effects of this protein
- The development of better-targeted treatments for blood pressure regulation through ongoing studies of the renin-angiotensin system
- The development of a drug therapy that will halt the formation of atherosclerotic plaques by preventing changes in proteoglycans, protein molecules that exist in the blood vessel wall
- New surgical treatments for the problem of atrial fibrillation, an increasingly common condition where the chambers of the heart beat out of "sync"
- Understanding the pathway within the body responsible for removing cholesterol from the blood vessel wall, known as reverse cholesterol transport. Research focuses on the balance between the delivery of cholesterol to the blood and its removal
- The neural control of the cardiovascular system during the onset of obesity and other metabolic disorders, and the mechanisms that cause cardiovascular diseases through environmental factors influencing the central nervous system
- Investigation of the link between different forms of stress and heart disease, including the link between panic disorder and cardiovascular disease, and the effects on heart risk of two different types of treatment: cognitive behavioural therapy and selective serotonin reuptake inhibitor (SSRI) medication





David Kaye leads the Baker's research into heart failure

Heart Failure



Research aims to improve the ability of a failing heart to pump blood

Despite the alarming increase in its prevalence, heart failure is commonly misunderstood as “heart attack”. In fact, heart failure is a debilitating, progressive condition that often begins 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. As more people survive heart attack, the incidence of heart failure is rising. The quality of life for a person with heart failure is dramatically reduced – normal daily activities like walking to the letterbox or making a bed can be an unpleasant, difficult and exhausting experience. In many cases heart failure leads to slow death. Understanding why the heart fails, and who is at risk of the progression of this disease is crucial given the rates of cardiovascular disease here and around the world.

- It is currently estimated that heart failure affects 300,000 Australians
- Up to 30,000 new cases develop each year
- It is the third largest cause of death among the various forms of cardiovascular disease in Australia

- Heart failure is a major cause of disability in the elderly
- The condition represents one of the biggest causes of hospital bed stays and as such is a significant drain on health budgets, costing millions of dollars in home and hospital care

The broad work of the Baker’s research into heart failure 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 transplant if they are to have any chance of survival. Investigations by Baker scientists range from efforts to improve the health of those who must undergo heart surgery to work on the cellular, molecular and genetic underpinnings of the progression from initial heart muscle damage to the condition of heart failure. Our scientists are hoping to not just treat heart failure better, but to cure it.

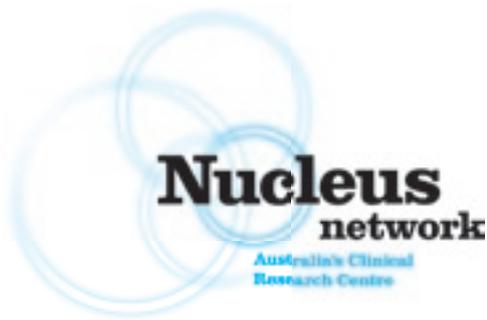
Our team has already made internationally renowned improvements to the understanding of heart failure and the treatment of those living with it. We are devoted to working on existing knowledge and building a better platform for scientists and clinicians to help those stricken with this condition, and the families who care for them. Under the Baker’s community arm, the Preventative Cardiology Unit, we are tracking and mapping areas in Australia where heart failure is most concentrated and conducting an analysis of the availability of health care services. This is highlighting the absence of adequate services in some parts of Australia with the greatest need, and will ensure patients have their health concerns understood.

Some research projects underway include:

- Studies of the enlarged heart (cardiac hypertrophy) – why it is beneficial to athletes but a harmful development in heart failure
- Investigations of the effects of diabetes on the muscle of the heart, and how diabetes contributes to heart disease
- Studies of the effects of the hormone relaxin on fibrotic heart tissue, and how it might improve the ability of a failing heart to pump blood
- Better cardiac surgical techniques, including a novel, non-surgical method for mitral valve repair
- The design of therapies that may regenerate hearts that have failed and how the muscle might be rebuilt to make it function better
- The study of mechanisms whereby the heart responds to stimulation and how these processes contribute to heart disease
- Ways to eliminate the risk of rupture of the ventricular wall, a serious complication of heart attack that almost always leads to sudden death. Research focuses on why it occurs and which drug treatments might prevent it



Scientists hope to cure heart failure, not just treat it



Nucleus Network applies rigorous standards to clinical research

Phase I drug trials, where a new drug therapy is tested in a healthy volunteer, are an integral part of the pharmaceutical industry, and the only way that new therapies and treatments can be introduced into the health system.

Nucleus Network, located in the Burnet Tower in the Alfred Medical Research and Education Precinct (AMREP) is a centre for excellence in clinical research and one of Australia's leading Phase I clinical research facilities. This not-for-profit business, a wholly-owned subsidiary of the Baker, operates a 24-bed early phase clinical research unit, with significant expansion planned in 2007. It is here that new drugs and compounds are administered to healthy volunteers in a strictly controlled environment, attended to 24 hours a day by Nucleus Network's specially trained medical support staff. Volunteers are watched closely for any reactions and have blood samples, blood pressure and other vital signs taken and carefully recorded at regular intervals. The information gathered monitors and protects the volunteer's health and also provides crucial information about the therapy being trialled. These volunteer profiles inform the pharmaceutical company's understanding of the drug and are a vital part of its development.

In a very successful year for the company, 2006 saw Nucleus Network achieve increased financial stability through strong growth. Importantly, Nucleus has also enhanced its operations in a number of key ways:

- A greater depth of staff (a 50 per cent increase on 2005) has enabled the core business to support specialised areas such as a technical laboratory; volunteer recruitment, screening and medical support;
- The development of a new Quality Management System has boosted quality standards through the introduction of internal audits and vendor assessment programs;
- The implementation of a risk management system and risk register has given Nucleus the edge over its competitors by identifying all areas of possible risk and applying best practice quality standard procedures at the earliest stage in the cycle of trials, and
- A greater spread of customers across all operations means that no one client represents more than 17 per cent of revenue.

These rigorous standards and unparalleled quality of service to clients has resulted in repeat work from six of the top 10 global pharmaceutical companies. To accommodate this expansion, the company's employee headcount doubled in 2006 to 41 permanent staff in 2006, up from 20 in 2005. Eighty per cent of this growth was funded from business and contracts from lucrative off-shore customers. This growth in the overseas client base is significant as the local biotechnology sector in Australia is not sufficiently large enough to exclusively support a Phase I unit such as Nucleus. Importantly, however, this local industry continues to benefit from the experience and infrastructure Nucleus Network is developing through work with big, international pharmaceutical companies.

This company growth makes Nucleus, one of only four specialist Phase I research units in Australia, and the only one in Melbourne, a productive and profitable AMREP partner. To date, core business has brought over \$1 million in contracts to the site and the company's growth and profit in 2006 was exponential. With the attention shown to the most important areas of the company – Nucleus Network's safety record and procedures are exceptional, as witnessed by strong repeat business –

this healthy growth is expected to continue.

NN divisional highlights

Centre for Clinical Studies:

- CCS conducted 28 studies in 2006
- 42 ethics submissions were sent to the Alfred Research Ethics Committee in 2006, with 31 approved, one not approved, four studies did not proceed and nine approvals are pending
- International clients generated export revenues of more than \$6 million. These clients include GSK, Roche, Merck, J&J, Sanofi-Aventis and Pfizer
- Successful conduct of six first-in-man studies

Clinical Trials Consulting:

- Consulted to over 14 Australian and NZ biotechnology companies
- Seven of these consulting projects have led to trials planned or conducted in the CCS unit
- Staff doubled

Nucleus Network Education:

- Delivered 257 training days
- ACRP membership has grown to 339
- 26 Nucleus staff trained in Good Clinical Practice (GCP)
- 79 trained in Queensland through franchisee

Nucleus Network is an industry leader, following strict adherence to the highest standards of clinical research, conducted in accordance with international regulatory requirements and expectations. The company is also committed to best practice clinical research and regularly provides training for researchers and medical staff around the country who are involved in trials. In 2006, Nucleus Network subsidised GCP training for 150 students.

Phase I drug trials are the only way new treatments can be developed



Commercialisation

An important adjunct to the work of our scientists at the Baker is our commercialisation team. The commercialisation of research activities is one of the most effective ways we have of ensuring the knowledge and ideas developed by our scientific team improve the lives of people living with, and at risk of, cardiovascular disease. To do this successfully we need to ensure that laboratory findings are translated into good results for patients.

MEDICAL RESEARCH COMMERCIALISATION FUND

Begun in 2006 and finalised in 2007, the Baker's commercialisation arm established Australia's first Medical Research Commercialisation Fund (MRCF). This unique venture, which represents many of the nation's leading medical research institutes, is supported by state-run superannuation firms and the Victorian and NSW governments and will provide critical funding to early stage medical research in Australia.

The \$30 million dollar venture capital fund aims to fill the shortfall in development dollars for early-stage medical innovations and comes as a boost to our medical research community.

MRCF founder, Baker commercialisation director Chris Nave, says the biggest obstacle to commercialisation of good ideas is the lack of a mature Australian venture capital industry. The new fund will go a long way to overcoming that obstacle.

The MRCF will allow good ideas with commercial potential time to come to fruition by providing crucial early support. The fund will put a \$2 million cap on individual investments, and seek to create separate companies from the more promising research ideas that would then have the funding to conduct their own phase-II clinical trials.

V-KARDIA

V-Kardia Pty Ltd, and its US operation, Osprey Medical, Inc, are medical device companies dedicated to the development of V-Focus™, a new, minimally invasive, percutaneous (delivered through the skin) system that offers a radically new and improved treatment for heart failure patients. This innovation 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. The first disease targeted for this new therapy is heart failure. This progressive disease, where the ailing heart cannot pump blood to meet the requirements of the body, can be a consequence of all forms of serious heart disease. This new therapy, developed by a team of Baker scientists led by David Kaye and John Power has been designed to overcome the problem of systemic leakage associated with traditional delivery of drugs intended for the heart. It has potential applications beyond heart failure, and clinical trials are expected to be underway this year.



David Kaye has developed a new treatment for heart failure

V-Kardia has recently attracted \$5 million of equity financing with Brisbane-based CM Capital Investments to further develop this exciting technology.

Other commercialisation highlights:

- The Baker commercialisation team now represents Bayside Health (The Alfred Hospital) in their commercial endeavours. Assistance ranges from advice on IP protection strategies to commercial negotiations
- More than 20 material transfer agreements have enabled Baker scientists to gain access to a range of compounds for in vitro and in vivo studies, and has fostered collaborations with other research organisations globally
- New collaborative commercial agreements have been entered into with companies Starpharma, Cytopia and MiniFab. Collaborations with George Washington University, the University of South Carolina, Roche Pharmaceutical, Johnson & Johnson, Pfizer and Speedel are continuing
- Nucleus Network has considerable expanded its operations under the strategic guidance of the Baker's commercialisation team
- Income was received from 15 newly executed research contracts in 2006
- Total consolidated revenue now \$17.8 million



V-Focus™ allows drugs to be delivered directly to the heart

Donor Listing

Major Institutional Support

Atherosclerosis Research Trust of the UK
Australian Rotary Health Research Fund
The Baker Foundation
Diabetes Australia Research Trust
Federal Government of Australia
Juvenile Diabetes Research Foundation
National Health & Medical Research Council
National Heart Foundation
National Institutes of Health (USA)
Victorian Government

Major Donors

BHP Billiton Limited
Casella Wines
CSYS Consulting Services Pty Ltd
H & K Johnston Family Foundation
Miller Foundation Ltd
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Leonie Cullen	Scientific Project Officer
Anita Wluka	Senior Research Fellow
Bronwyn Kingwell	Executive Director Science Policy
Jaye Chin-Dusting	Executive Director Science Strategy

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Paul Nestel
Kerin O'Dea

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Jenny Starr	Client Services Manager
Sally Kay	Nurse
James Shaw	Research Fellow
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Clinical Electrophysiology

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Preventative Cardiology

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Claudia Retegan	Data Manager
Diem Dinh	Research Officer
Ann Nadonza	Data Administrator
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Beverley Russell	Casual Research Nurse
Virginia Cable	Casual Research Nurse
Margaret Bruce	Casual Research Nurse
Kathryn Murphy	Casual Research Nurse

Risk Clinic/Gene Bank

Risk Reduction Clinic Nurses

Janis Jennings	Nurse
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Elizabeth Jenkins	Nurse
Marijke Tress	Nurse

Atherothrombosis & Vascular Division

Karlheinz Peter	Head
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Thrombosis & Myocardial Infarction Laboratory

Karlheinz Peter	Head
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Professional & Technical Staff

Dexing Huang	Senior Research Officer
Christoph Hagemeyer	Senior Research Officer
Steffen Eisenhardt	Research Officer
Juliana Jeyandra	Research Officer
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Yung Chih Chen	Technical Assistant

Clinical Physiology

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Tanya Medley	Research Fellow
Sonia Dougherty	Research Nurse
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Cell Biology Laboratory

Alex Bobik	Head
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Senior Scientific

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Georgia Kostolias	Research Assistant
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Human & Vascular Biology Laboratory

Stephen Duffy	Head
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Professional & Technical Staff

Beth Johnson	Research Assistant
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Cell Biology & Diabetes

Peter Little	Head
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Professional & Technical Staff

Narin Osman	Research Officer
Mandy Ballinger	Post Doctoral Fellow

Lipoproteins & Atherosclerosis

Dmitri Sviridov	Head
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Nigora Mukhamedova	Senior Research Officer
Anh Hoang	Research Assistant
Mohammad Hai	Research Assistant

Vascular Pharmacology

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David Spiteri	Operations Manager

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Neelima Yadlpalli	Casual Administration Assistant

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Samantha Hulme	Team Leader
Claire Doran	Team Leader
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John Crawford	Animal Technician
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Mia Ibrahim	Animal Technician
Clare Fritzlaff	Animal Technician
Megan Fettke	Animal Technician
Elissa Wells	Animal Technician
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Coralie McGuire	Casual Animal Technician

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Leia Demtschyna

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Gert Talbo	Head
Mustafa Ayhan	Proteomics Scientist
Vincent Strangis	Research Assistant

Biological Media Preparation

Katie Penfold	Media Services Officer
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Walter Thomas	Head
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Experimental Cardiology & Heart Failure Division

David Kaye	Head
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Wynn Department of Cardiology

David Kaye	Head
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Wei-Zheng Zhang	Senior Research Officer
Zhiyong Yang	Senior Research Officer
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Elizabeth Woodcock	Head
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James Bell	Research Officer

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Ziquo Ming	Research Assistant
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Kimberly Hewitt	Research Assistant

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JDRF Diabetes & Metabolism Division

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Kidney Disease in Diabetic Complications

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Assam El-Osta Head

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Oxidative Stress

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Atherosclerosis in Diabetic Complications

Terri Allen Head

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 Belinda Davis Research Officer
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 Audrey Koitka Research Officer
 Amy Gatt Research Assistant
 Kylie Gilbert Animal Technician
 Kim McMillan Animal Technician
 Steve Risis Animal Technician

Proliferation & Fibrosis in Diabetic Complications

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Mark Febbraio Head

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 Beata Skiba Senior Research Officer

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Nadine Watson	Technical Assistant
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Flora Soratous	Research Assistant
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Celia Brenchley	Research Assistant
Tye Dawood	Research Assistant
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James Armitage	Research Officer
Luisa La Grecia	Research Assistant
John-Luis Moretti	Research Assistant
Kristy Jackson	Research Assistant
John-Luis Moretti	Research Assistant
Scott Maxwell	Casual Research Assistant

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Gillian Barker	Research Assistant

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David Lloyd	Chief Operating Officer
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Carolyn Thomson	Executive Assistant
Barbara Spaccatore	Receptionist

Anna Nelson	Administration Assistant
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Gary Loetsch	Accountant
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Lydia Dong	Accounts Officer
Dale Hince	Accounts Clerk

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Noel Tresider	OH&S Chemical Project Officer
Tracey Oakes	OH&S Project Officer
Solveiga Hall	Bio Safety & Radiation Officer
Stephen Wyley	OH&S Specialist

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Eden Medway	Help Desk Officer

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Katrina Rajic	Advisor
Lisa Skigopoulos	Payroll Officer

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Elizabeth Veal	Fundraising Projects Manager

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Ebru Yaman	Media Relations Manager
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Steve Droste	Building Infrastructure Manager
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Blaze Gomes	Electronic Technician
Jeffry D'Souza	Handyman

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Beverley Thomas	Commercialisation Manager
Paul Howie	In-House Legal Counsel
Renee Dutton	Business Development Manager
Zoe Kristall	Business Development Associate
Elise Needham	Commercial Contracts Manager

Students

Name Supervisor

5th Year PhDs

Oliver Vasilevski	Liz Woodcock
David Barton	Murray Esler

4th Year PhDs

Anna Ahimastos	Bronwyn Kingwell
Jessica Chellappah	Chris Reid
Ming Hang (Stanley) Chan	Mark Febbraio
Jason Chung	Mark Febbraio
Nathan Connelly	Jaye Chin-Dusting
Tye Dawood	Murray Esler
Catherine Huggins	Sal Pepe
Ngan Huynh	Jaye Chin-Dusting
Nicola Smith	Wally Thomas
Tony White	Bronwyn Kingwell

3rd Year PhDs

Daniella Brasacchio	Assam El-Osta
Wendy Burns	Mark Cooper
Hsiu-Wen Chan	Wally Thomas
Maggie Chow	Assam el-osta
Michael Ditiatkowski	Alex Bobik
Brian Drew	Bronwyn Kingwell
Karen Fang Lu	Xiao-Jun Du
Darren Henstridge	Bronwyn Kingwell
Melanie Ivey	Peter Little
Swati Mukherjee	Anthony Dart
Cristina Oro	Wally Thomas
Honor Rose	Dmitri Sviridov
Freya Sheeran	Sal Pepe
Kristy Shield	Greg Rice
Georgia Soldatos	Mark Cooper
Ratana Lim	Gregory Rice

2nd Year PhDs

Jake Anderson	Gavin Lambert
John Huynh	Wally Thomas
Justin Mariani	David Kaye
Andrew Murphy	Jaye Chin-Dusting
Enzo Porello	Wally Thomas
Larissa Prior	Geoff Head
Vicky Thallas	Mark Cooper
Kelly Yen-Yon To	Alex Bobik
Yugang (William) Tu	Mark Cooper
Yie Chee Yuen	Mark Febbraio

Name Supervisor

1st Year PhDs

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Allison Bourne	Wally Thomas
Gabrielle Callander	Wally Thomas
Michelle Gordon	Mark Cooper
Brooke Harcourt	Josephine Forbes
Wendy Ip	Sal Pepe
Charlotte Keating	Murray Esler
Rajesh Nair	Jaye Chin-Dusting
Bronwyn Neill	Mark Febbraio
Hayley Nicholls	Mark Febbraio
Yen Pham	Zemin Cao
Adeline Tan	Mark Cooper
Gautam Vaddai	Murray Esler / David Kaye

Hons and Others

Lisa Chang	Assam El-Osta
Daian Chen	Geoff Head
Harsha Dadlani	Peter Little
Ann Du	Wally Thomas
Nicola Fotherington	Geoff Head
Sam Keating	Karin Jandeleit-Dahm
Miriam Koniuszko	Frank Rosenfeldt
Ruide (Ray) Koh	Karlheinz Peter
Charles Lang	David Kaye, Wei-Zheng Zhang
Jasmine Lyons	B De Courten
Genevieve Martin	Geoff Head
Scott Maxwell	Assam El-Osta
John-Luis Moretti	Geoff Head
Stefanie Nadendirarah	Diem Dihn
Thu-Phuc Nguyen-Huu	Geoff Head
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Yogeshwar Rajaram	Mark Cooper
Ahrathy Selathurai	Alex Boik
April Toh	Jaye Chin-Dusting
Vicki Wong	Karlheinz Peter
Charles Wong	Karlheinz Peter
Fanny Sampurno	Karin Jandeleit-Dahm
Abhirup Lobo	Helen Kiriazis
Sheng Chen	Karlheinz Peter
Arindam Chakravorty	Xiao Jun Du
Sacha Khong	Melissa Byrnes

Publication Listing 2006

Journal Articles

1. Adams DJ, Head GA, Markus MA, Lovicu FJ, van der Weyden L, Kontgen F, Arends MJ, Thiru S, Mayorov DN, Morris BJ. Renin enhancer is critical for control of renin gene expression and cardiovascular function. *J Biol Chem* 2006;281(42):31753-61.
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