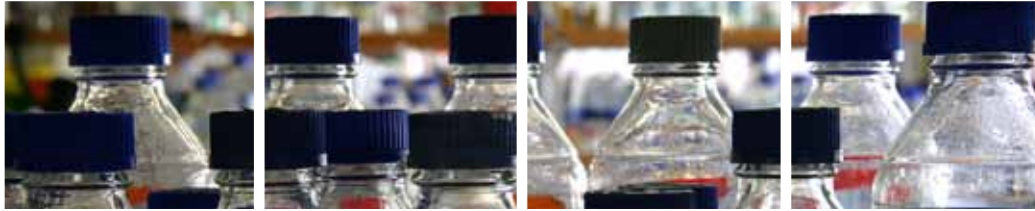


MAURICE WILKINS CENTRE

New Zealand's Centre of Research Excellence
for the discovery of new medicines

Annual Report 2008



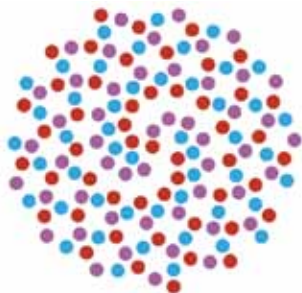
The Maurice Wilkins Centre

The Maurice Wilkins Centre (www.mauricewilkinscentre.org) brings together leading biologists, chemists, and computer scientists to target serious disease. The Wilkins Centre includes NZ researchers with world-class reputations for inventing new drugs targeting cancer, diabetes, and infectious disease, and several of these are in clinical trials by major international pharmaceutical companies.

As well as inventing new drugs, the Wilkins Centre develops new vaccines targeting infectious disease and cancer, and new tools to help basic research and clinical medicine, including sophisticated software for medical use. In bringing together scientists and doctors from a wide range of backgrounds, the Centre sponsors cutting-edge research that would not otherwise have happened. This intense research environment provides an outstanding training ground for the next generation of leaders in NZ biomedical science.

The Wilkins Centre now constitutes a national network of researchers at five Universities (Otago, Canterbury, Waikato, Victoria and Auckland), as well as the Malaghan Institute for Medical Research in Wellington, and Industrial Research Limited. This national network allows the Centre to draw the leading researchers across NZ into “dream teams” capable of targeting diseases of major importance to New Zealanders. The Wilkins Centre also provides world-class research infrastructure to its researchers, including both cutting-edge equipment and highly specialised technical training, often with international partners. These two fundamental activities – enabling nationwide multi-disciplinary collaboration, and maintaining internationally competitive research infrastructure – support our mission to ensure that New Zealand capitalises on its outstanding reputation for biomedical research.

For more information on New Zealand Centres of Research Excellence please go to www.tec.govt.nz/templates/standard.aspx?id=586



MAURICE WILKINS CENTRE
FOR MOLECULAR BIODISCOVERY

Director's Report	2
Contribution to National Goals	4
Highlights	7
Outreach.....	24
Organisational Development.....	28
Research Outputs	36
Financial Report	50
Directory	52
Contact Details	56

Director's Report

With this annual report, the Maurice Wilkins Centre proudly celebrates six years of achievement and development as one of New Zealand's founding Centres of Research Excellence (CoREs). The CoRE initiative was an innovative one that charged each Centre with building its own particular place in the New Zealand research scene. All the CoREs must meet the highest standards of national and international research excellence. Each has a unique focus, and each makes its own particular contribution to New Zealand's social and economic development. Collectively, the CoREs have the opportunity to innovate across a wide spectrum of activities.



The Maurice Wilkins Centre has two defining characteristics. First, it is highly multidisciplinary, crossing the disciplines of biology, chemistry and medicine, and incorporating strong elements of mathematics and engineering. This is important, because many of the most exciting developments in science come at the interface between disciplines. Second, our research focus is on human disease – discovering the molecular mechanisms of disease and developing new drugs, vaccines and other tools for therapy. It is thus a blend of fundamental discovery, development of innovative methods, and applications.

The past year was notable for a major new initiative, the roll-out of our flexible funding programme. This enables any member of the Centre to bid for PhD student support, for seed funding for a new project, or for financial support to access key infrastructure. We have also established new equipment at four of our partner institutions, the Malaghan Institute, and Waikato, Canterbury and Otago Universities. Our next goal is to expand the expertise within the Centre in order to consolidate it as the drug and vaccine development engine of New Zealand.

How should this year's report be read? On the one hand it is about people. Among our students, Hae Joo Kang, who in 2007 had her PhD research published in *Science*, was a prize-winner in the annual McDiarmid awards, and Danny Lee spent 3 stimulating months at the University of Chicago developing cutting-edge methods of glycoprotein synthesis. Among our leading investigators, Graham Le Gros, of the Malaghan Institute, won world recognition for a classic discovery in immunology, and Garth Cooper and Margaret Brimble were honoured as "Tall Poppies" in the 2008 World Class New Zealand awards – for Biotechnology and for Research, Science and Technology respectively. We are also delighted at Emily Parker's success in winning the Applied Biosystems Award, the premier prize of the NZ Society for Biochemistry and Molecular Biology. This continues a series of major awards to emerging new leaders in the Centre.

The report also celebrates our research. Many new projects have been initiated, providing a discovery pipeline that will feed future drug and vaccine development efforts. One example illustrates the path from new knowledge to development. The human enzyme phosphatidylinositol 3-kinase, otherwise known as PI3K, is a very “hot” target for the development of new anti-cancer drugs. A small seeding project in the Maurice Wilkins Centre, initiated by Peter Shepherd and Bill Denny in 2005, led to the discovery of an inhibitor that was better than any yet available. Health Research Council and Cancer Society funding followed, leading to the establishment of a start-up company, Pathway Therapeutics, which was able to attract \$12 million of venture capital funding from Australian investors.

I would like to finish on a personal note. This is my last report as Director of the Maurice Wilkins Centre. It has been a privilege to serve in this role, and I am immensely proud of the way in which the constituent groups that make up our Centre have come together to create an entity that is truly greater than the sum of its parts. The interdisciplinary mix is endlessly stimulating. We have a pipeline of new discoveries. And we are already seeing commercial applications arising from those discoveries, as a real contribution towards New Zealand's economic future.

Most of all, I do believe that our science is world class. I do not subscribe to the “Number 8 wire” philosophy. I believe we must do things properly, and aspire to and achieve the highest international standards – otherwise we sell New Zealand short. This can't be done “on the cheap”. This report is written at a time when we have a new government, yet to announce its full vision for science. Just as President Obama has re-dedicated the United States to placing science first, with a goal of devoting more than 3% of GDP to research and development, so we trust that the New Zealand government will also take this opportunity.

I returned to New Zealand after some years overseas because I wanted to do science here. So did many of my colleagues. We have a great education system in New Zealand and our graduates are in high demand overseas. But we need to provide the incentives to attract them back. I believe that this is a key role for our Centre, to reaffirm that world-class science can be done in New Zealand, and to help provide – with essential Government support – an environment that enables our best and brightest to fulfill their potential here, for national benefit.



Ted Baker
Director



Contribution to National Goals

The Centres of Research Excellence were collectively charged with making a contribution to national goals in terms of innovation, social and economic development, environmental sustainability, and fulfilment of the obligations of the Treaty of Waitangi. It was anticipated that the CoREs would each contribute to these goals in different ways and in different proportions, depending on their particular research focus. The Maurice Wilkins Centre has its own unique place in this spectrum. Our focus on the development of new therapies for human disease is based on a multidisciplinary platform that extends across chemistry, biology and medicine and combines key approaches and technologies from physics, engineering and mathematics.

Innovation

Innovation in research is often to be found at the interface between disciplines. Over the past five years we have integrated the research groups of internationally-eminent researchers in biology, chemistry, engineering and medicine, to develop a technology platform and knowledge base that is truly multidisciplinary. This acts as a springboard for new initiatives in biotechnology, and already a number of highly innovative new projects have emerged that were not envisaged at the outset. Such a multi-disciplinary platform, based on many collaborative projects, also gives an excellent training environment for the students and younger scientists in the Wilkins Centre, whose research takes place in an environment characterised by teamwork and exposure to the ethical, managerial and entrepreneurial aspects of translational science. Some of the methodological developments in the Wilkins Centre are also highly innovative, to the point of being world-leading.

Social Development

The Wilkins Centre's major contribution to social development in NZ is through the improvements it can make to human health. Our major focus is on the development of improved drugs and technologies to treat heart disease, cancer, and infectious bacterial diseases (particularly tuberculosis). At the same time, science is an important aspect of culture. Re-naming our Centre in honour of Maurice Wilkins expresses our pride in a famous NZ scientist, and advertises our national capabilities abroad. It is also important for our students to be able to see that research of the highest international quality can be done here, and that it can contribute in a real way to the social and economic well-being of their country. All of the research leaders in the Wilkins Centre could have followed careers overseas, at the top of their fields. All have chosen to return to NZ because they are committed to carrying out world-class research here. This belief, transmitted to students, is a powerful incentive for them to do likewise.

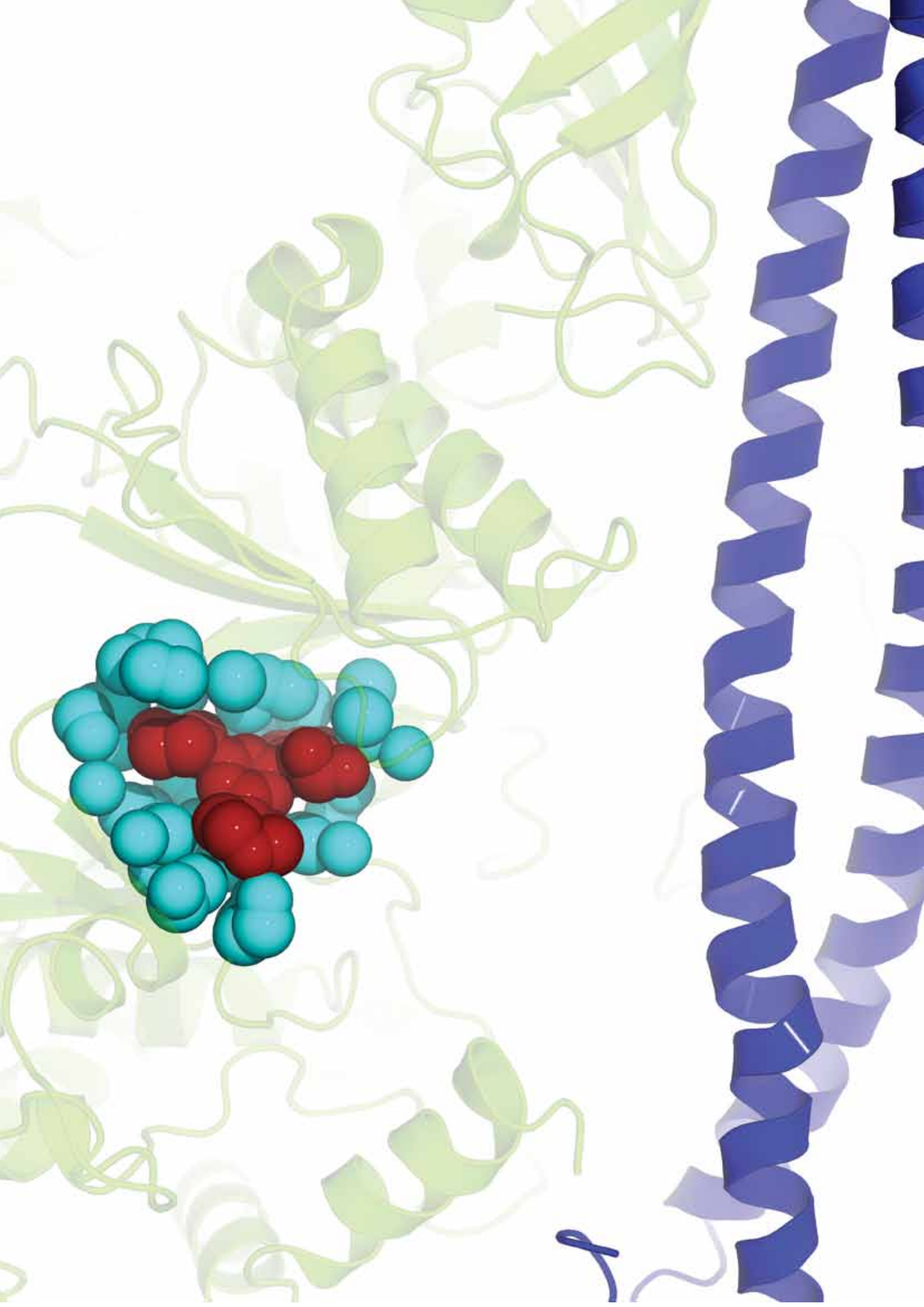
Economic Development

The primary focus of our Centre is on new therapies for disease. This has dual importance for New Zealand, in improving the health and bringing potentially huge economic gains; the biopharmaceutical sector already provides 90% of the global value of biotechnology. MWC investigators have to date been responsible for bringing 10 drugs to clinical trial, around two-thirds of the total for New Zealand. The intimate links between our research programme and start-up companies (Proacta, Symansis, Pathway) ensures that research findings can and will be developed for the national good. A pipeline of new drug and vaccine candidates, and diagnostic tools, is now being generated, to ensure the future of this paradigm.

Treaty of Waitangi

The main drug development projects in the Wilkins Centre are in areas (diabetes, heart disease and cancer) that have disproportionate effects on the Maori population. In addition the Wilkins Centre is committed to helping develop the Maori health research workforce by providing excellent opportunities for post-graduate research training.





Highlights

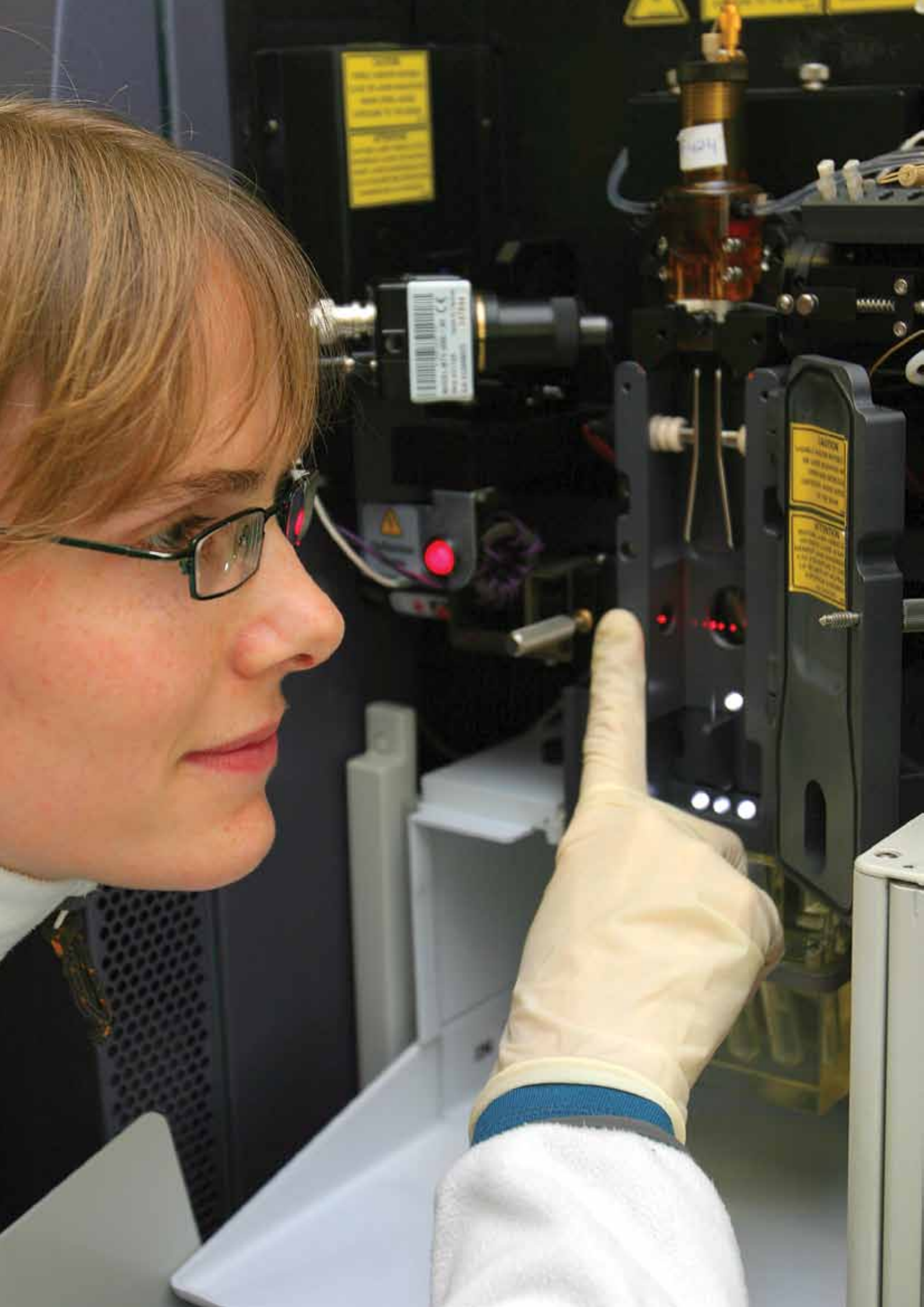
Wilkins Centre investigators led dozens of projects to success in 2008, as reflected in the list of Research Outputs below. Several highlights stand out as demonstrating the Centre's role in initiating new collaborative research to combat serious human disease.

Wilkins Centre seed funding spawns a major new drug discovery programme – and a spin-out company

In 2006 the Wilkins Centre initiated a new collaboration between the research groups of Peter Shepherd and Bill Denny, and medicinal chemist Gordon Rewcastle. The new team aimed to produce drugs that could inhibit a family of enzymes called “PI3 kinases”. It was already recognised that drugs targeting the PI 3-kinase family might make good anti-cancer drugs. However, the group wanted to investigate whether drugs that inhibit specific members of the family might be equally effective against cancer - and have fewer side effects. The project has now grown into a multi-disciplinary programme of research projects funded by grants from the Wilkins Centre, the Health Research Council, and the Cancer Society, as well as a commercially-funded drug development programme. These research projects employ five medicinal chemists and eight biologists. The drug development is funded by Pathway Therapeutics, a spin-out company founded in 2008 with \$12 million funding from two Australian venture capital firms.

In 2008 Wilkins Centre scientist Jack Flanagan introduced a technique that has allowed the drug designs to be refined using computer modeling. In the same year Ted Baker's lab group also joined the research programme, contributing specialised skills in producing recombinant proteins. These proteins are providing the basis for proteomic and structural studies to identify how the novel PI 3-kinase inhibitors work. The proteins are also being used to screen new drug candidates with the new high-throughput robot purchased by the Wilkins Centre. Industrial Research Limited chemist Gavin Painter has also contributed, by synthesising the most biologically important form of the lipid substrate for the PI3-kinase enzyme. This substrate is being used in enzyme assays to measure the drugs' effects. This unique research effort has rapidly grown to produce a wide range of basic and applied research outcomes. The scientists involved span several specialties in biology, chemistry and computation, and illustrate the importance of bringing together diverse research teams of New Zealand's leading scientists to discover new medicines.





Shining a light on human cells

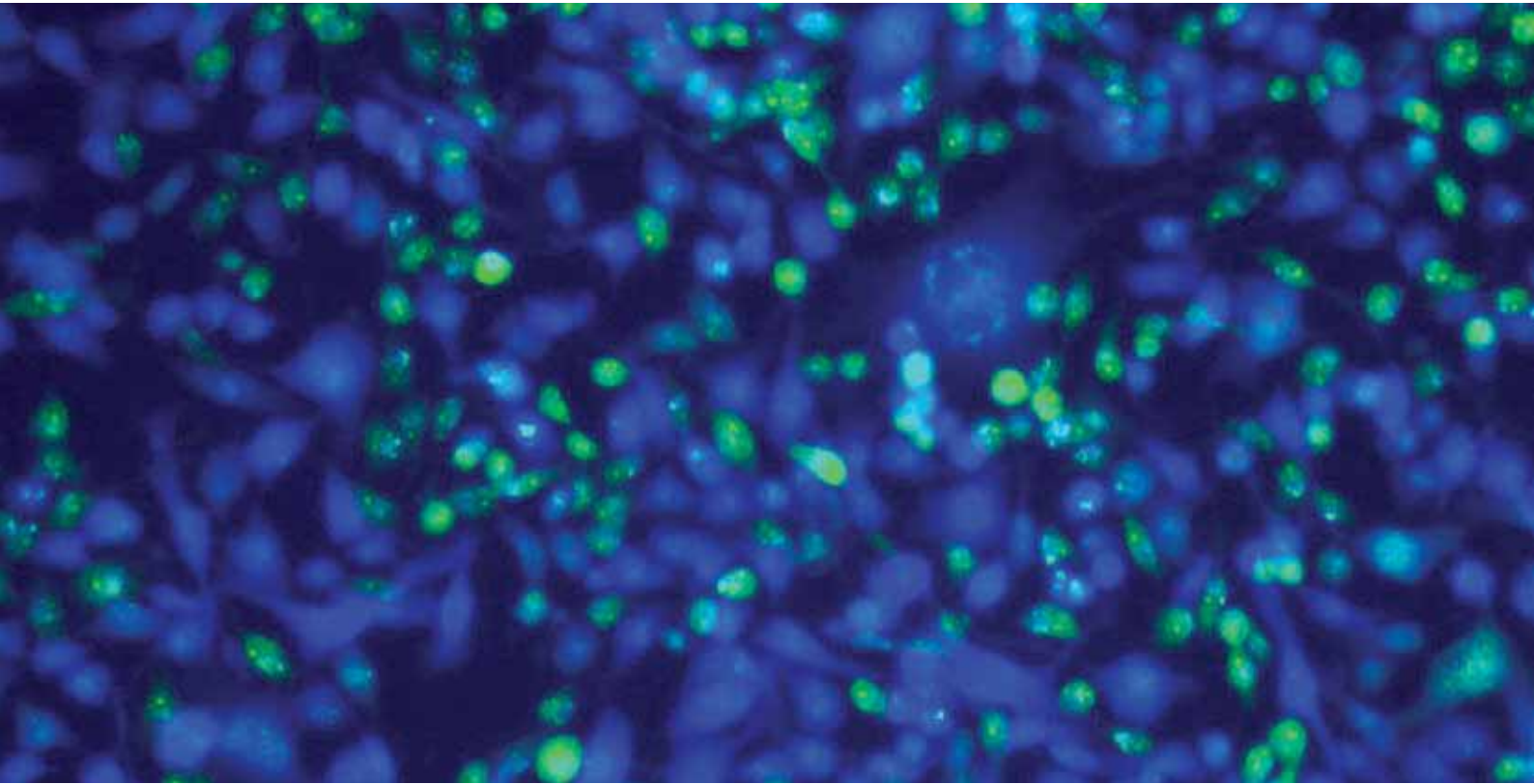
Two new pieces of equipment installed by the Wilkins Centre in 2008 demonstrate the Centre's national leadership in new technology platforms with wide applications in biological research.

The technique known as flow cytometry involves shining lasers on a stream of cells after they have been "painted" different colours. In the simplest flow cytometry experiments, a mixture of cells is labelled with an antibody that recognises a single marker on the outside of particular cells in the mixture. A coloured "tag" attached to the antibody glows when struck by the laser, so that the antibody-labelled cells can be identified and counted. For example, a coloured antibody to a cancer cell marker allows cancer cells to be identified and counted in blood samples from cancer patients.

The new machines installed by the Wilkins Centre illustrate how far the technology has come in recent years. The LSRII instrument sited at the Malaghan Institute of Medical Research in Wellington has five lasers, and the capability of simultaneously detecting up to 18 different colours. This allows many antibodies to be used to analyse the same sample, so that many different cell types can be identified and analysed in fine detail. The LSRII has enabled several new cutting-edge research platforms at the Malaghan Institute, to add to their existing programmes in cancer, asthma, multiple sclerosis, arthritis and tuberculosis. The new initiatives include a collaborative venture with Industrial Research Limited to unlock the commercial potential of the Malaghan Institute's cancer vaccine programme; and an invitation to join researchers from the Ludwig Institute in Melbourne and New York, and Harvard University, in a global Melanoma Research Alliance collaboration. The LSRII is also available to other Wilkins Centre investigators, and the Malaghan's Flow Cytometry Manager Kylie Price has already travelled to other centres to train potential users.

The second instrument, installed at the University of Auckland, has similar features to the LSRII, with 3 lasers and the capacity for up to 11-colour analysis, but it can also purify cells as well as analyse them. This is particularly important to the Wilkins Centre's immunology programme, where development of new vaccines and immune therapy for cancer depends on isolating the rare human immune cells with anti-cancer activity. However many other research programmes have been energised by the availability of this instrument – including the start-up biotech company, Androgenix, now a major client of the Wilkins Centre facility. The fact that Androgenix works mainly on applications to the livestock industry underscores the importance of the Wilkins Centre in establishing and maintaining new technology platforms that can benefit the wider economy as well as leading advances in human health. Facility manager Sintia Winkler visited two Swiss laboratories with similar instruments in 2008, to ensure the Wilkins Centre facility is benchmarked against the highest international standards in flow cytometry.





A new target for anti-cancer “pro-drugs”

Nitrogen mustards have a fearsome reputation from their original development as chemical warfare agents. Yet today they are being developed as powerful anti-cancer agents. The key to this is to maintain them in an inactive “pro-drug” form until they reach tumour cells, and then to selectively activate them. This is the rationale for the anti-cancer drug PR-104, which was discovered in the Auckland Cancer Society Research Centre, and is currently in stage II clinical trials for treatment of solid tumours, as one of the lead compounds being developed by NZ-based spin-out company Proacta.

PR-104 was designed to be activated only under the conditions of low oxygen supply (“hypoxia”) typical of the centre of many tumours. Surprisingly, Wilkins Centre investigators Adam Patterson, Bill Wilson and Jeff Smaill now find some cancers, including aggressive liver and lung cancers, have another way of activating PR-104, using an enzyme called AKR1C3. Understanding this novel activation mechanism has the potential to revolutionise anti-cancer chemotherapy, since it provides a new target molecule for pro-drugs. The structure of AKR1C3 has recently been solved by Wilkins Centre investigator Chris Squire, and a new inter-disciplinary collaboration between medicinal chemists and structural biologists has now been launched. Knowledge of exactly how PR-104 and related molecules bind will guide the design of new, improved anti-cancer compounds that exploit pro-drug activation inside tumours.



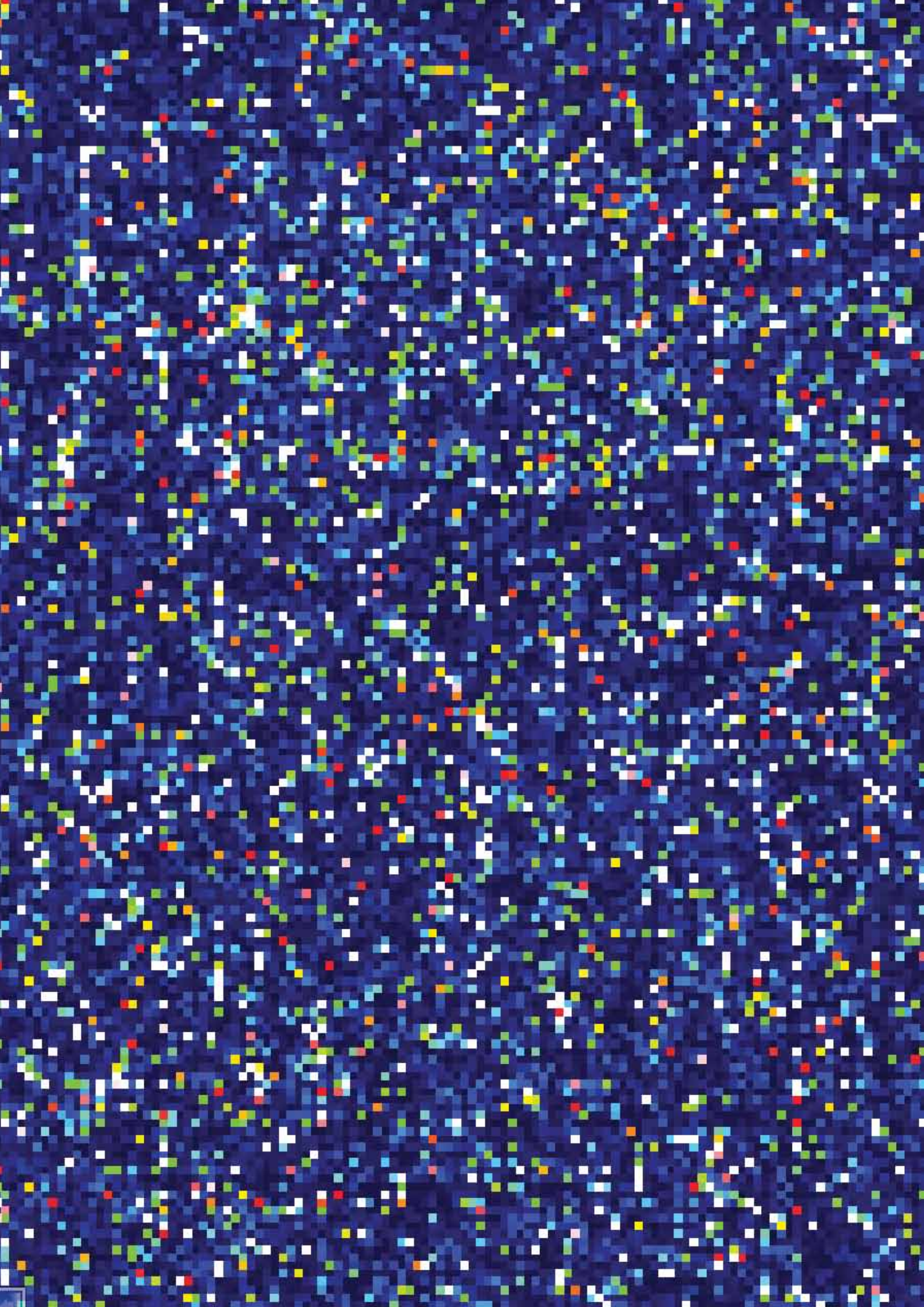


Wilkins Centre PhD student excels in the USA

Part of the Wilkins Centre's role is to train future leaders in biomedicine to the highest international standard. By exploiting our established global network of collaborators, we can place our best students in leading laboratories overseas for several weeks or months, to allow them to develop particular skills. The students then return to NZ, bringing back not only the latest techniques in their field, but also an appreciation of how their skills stack up against top international competition. In the case of PhD student Danny Lee, a 3-month placement in the USA funded by the Wilkins Centre went much further than building his skills.

Danny had been working with his supervisor, Margaret Brimble, to develop new chemical techniques for adding carbohydrate (sugar) molecules to biologically-active chemicals called peptides. Although the main driver of this work was a vaccine development project in collaboration with Wilkins Centre immunologists, the techniques turned out to have great value in other areas. Prof Steve Kent of the University of Chicago invited Danny to spend 3 months working in his lab, to learn how to build synthetic proteins from peptides, using a technique that Prof Kent invented ("native chemical ligation"). But while he was in Chicago, Danny was able to combine his new "glycopeptide" techniques with Prof Kent's technology, to produce new hybrid molecules. This combination of Danny's techniques, developed in the Brimble lab in Auckland, with the Kent lab's technology, was so groundbreaking that the team has already submitted a paper describing the advance to one of the world's leading chemistry journals. Danny returned to NZ not only bringing back new skills, but confident that the work he'd performed in NZ was internationally significant. As for Prof Kent, he was delighted both at the scientific outcome of the placement, and at the opportunity to work with Danny, who he describes as the equal of any of the young scientists he has ever helped train.





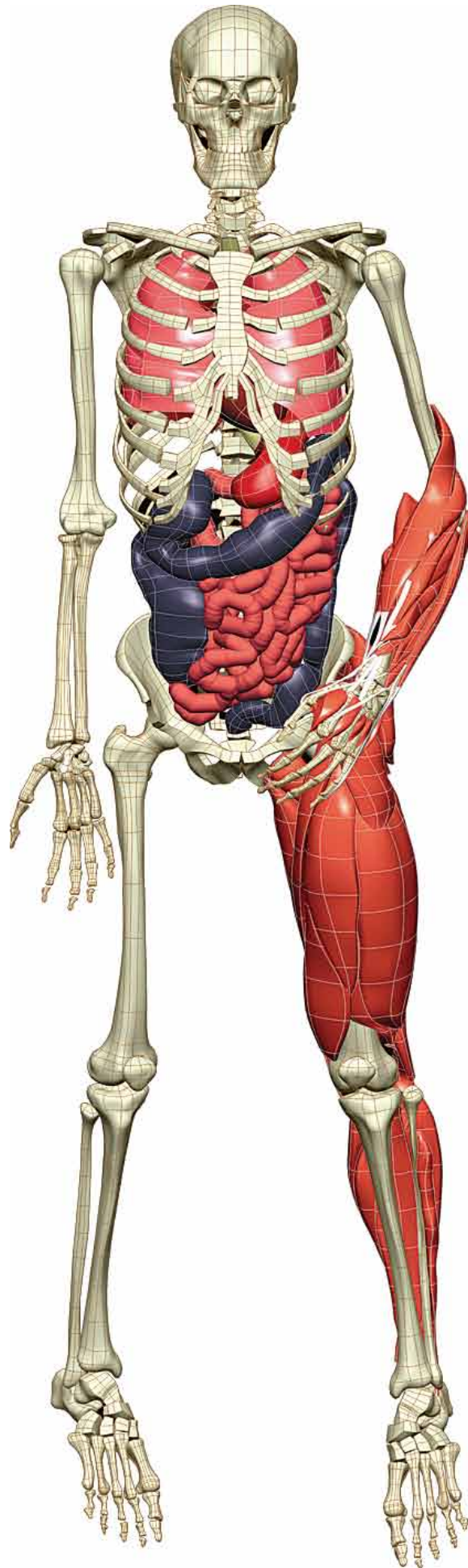
Supporting cancer diagnostics – and translation into clinical practice

Wilkins Centre funding is contributing to new molecular analysis of breast cancer and melanoma – and is also helping educate clinicians on the use of molecular diagnostics in cancer care.

In a multi-disciplinary collaboration incorporating oncology, molecular biology, and computer modeling, Wilkins Centre investigators Cristin Print, Peter Hunter and Edmund Crampin have been studying the networks of molecules that underlie both melanoma and breast cancer. These projects involve very high throughput techniques (especially micro-array analysis of gene expression) to look for patterns of molecules inside patient tumours. The same technology also allows the team to look at cancer cell lines grown in the laboratory, and to see how their molecular patterns change when they are exposed to different chemicals. The projects generate a massive amount of data, so the team uses mathematical modelling and computerised analysis to identify novel patterns of molecules that appear to be active in the tumours of patients, as well as individual molecules that appear to be key controllers in promoting the cancerous properties of the cells. The Wilkins Centre is funding PhD student Daniel Hurley to work on the projects. The Wilkins Centre also provided equipment infrastructure for the project, by purchasing an 'Experion' Bioanalyser. As is often the case for projects led by Wilkins Centre investigators, these projects also attracted funding from the Health Research Council's International Investment Opportunities Fund and from the Breast Cancer Research Trust.

It is sometimes difficult for doctors to reconcile existing approaches to therapy with the complex new age of molecular analysis of cancer they are reading about. In November, the Wilkins Centre sponsored a symposium held in the Faculty of Medical and Health Sciences at The University of Auckland, focussed on the future of molecular diagnostic and prognostic methods for breast cancer. The symposium attracted over 70 attendees and has resulted in closer links with clinicians in this area. For example, symposium organiser Cristin Print says one surgeon has applied for funding to start a PhD with his team to study how best to connect molecular analysis of tumours with patient care. Continuing Wilkins Centre support for improved contact between scientists and clinicians in these exciting but complex new areas is likely to improve uptake of new science into clinical practice within New Zealand.





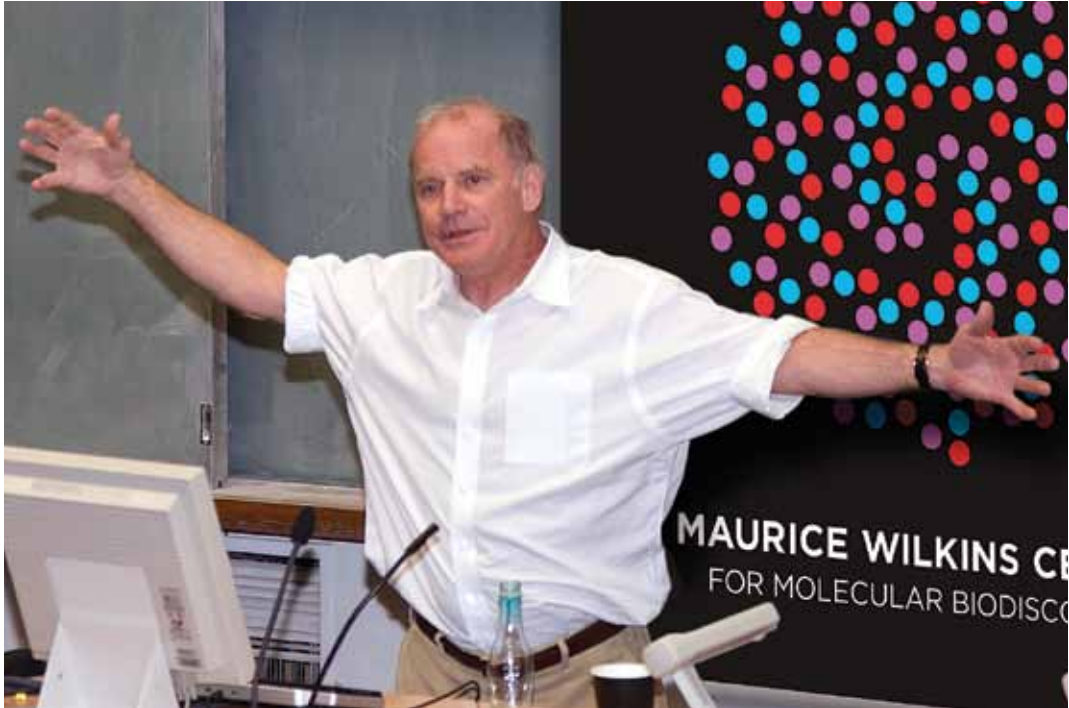
International recognition for Wilkins Centre computational biology

As the revolution in biology continues, huge amounts of information regarding all aspects of biological processes accumulate at an increasing rate. Making sense of all this new information requires high-level computation – and Wilkins Centre investigators lead the world in many aspects of computational biology, as recently recognised by several major international institutions.

In 2008, two of the world's leading research funders – the National Institutes of Health in the USA, and the European Commission – adopted three new standards for computational modelling of biological processes, and now require their scientists to use them. Two of these standard systems, called CellML and FieldML, were developed in NZ by Wilkins Centre investigators Peter Hunter and Poul Nielsen, and their colleagues based at the Auckland Bioengineering Institute. CellML is a method for allowing computer models of biological processes to work together using a standard language. Part of the CellML project involves Wilkins Centre investigators such as Catherine Lloyd collating and curating models in a “CellML library”, now replete with nearly 400 models from sources around the world. To enable use of CellML by scientists around the world, Catherine organises an annual meeting on Waiheke Island sponsored by the Wilkins Centre, that attracts many international participants. A focus in 2008 was the integration of the NZ-based systems with other international systems. The European Union has recognised the importance of this work by funding a “Virtual Physiological Human” project, founded on CellML and FieldML, along with a Network of Excellence to develop the project, with the Auckland group as the only non-European member.

This leadership in computational biology has enabled new inter-disciplinary collaborations. In 2008, Wilkins Centre computer modeler Gib Bogle and immunologist Rod Dunbar published the first stage of their computer model of immune cell behaviour in lymph nodes. The project aims to support the Wilkins Centre's vaccine development programme, since immune responses to vaccines begin with encounters between rare immune cells in lymph nodes. As a result of this work, Gib was invited to join a network of researchers in 11 countries, funded by the European Union under the International Research Staff Exchange Scheme. Access to this International Network in Theoretical Immunology (INTI) will enable visits by overseas scientists to the Wilkins Centre, as well as visits by Gib to research groups in Europe and the USA.





A science legend delivers the Maurice Wilkins Lecture

Mention the name Kary Mullis to anyone interested in molecular biology, and some animated conversation will inevitably follow. Certainly the students who mobbed Dr Mullis for his autograph after he delivered the 2008 Maurice Wilkins Lecture were in no doubt they were in the presence of a true star of world science. Dr Mullis invented the revolutionary DNA technology commonly known as “PCR” – the Polymerase Chain Reaction that is not only the workhorse of research laboratories around the world, but powers the forensic DNA analysis now familiar to many television viewers. Dr Mullis won the Nobel Prize for this work, and his landmark paper is now one of the most cited in all biology. But he is also noted for his disarmingly frank admissions about how he made his breakthroughs, and he has become a beacon for less conventional scientists the world over. His public lecture at The University of Auckland generated huge interest, with over 400 people attending, including more than 100 secondary school students. The lecture was highly entertaining and thought provoking, and will long remain in the memory of all those present. Dr Mullis was also very generous with his time, lingering for an hour after the lecture to answer questions – and sign more of those autographs.

From Iran to New Zealand – and a new insight into TB

Ghader Bashiri has come a long way, in every sense, since he left his home in northern Iran to pursue a PhD in New Zealand. Language was not a problem – he already spoke four languages – but there were the inevitable cultural and scientific adjustments. Now, however, Ghader has completed an outstanding PhD in structural biology, supervised by Ted Baker, joining a cohort of some 20 Wilkins Centre PhD students to complete in 2008. Ghader investigated a group of enzymes that were thought to be involved in the activation of a very promising new anti-TB drug called PA-824. In parallel, Brian Palmer and a team of medicinal chemists in the Wilkins Centre were developing improved versions of PA-824 under contract to the Global Alliance for TB Drug Development. Ghader’s work revealed the atomic structure of the enzyme FGD1 that carries out the first step of the activation of PA-824. This not only told him how this enzyme works, but it also provided information that can be used by the chemists in their drug development.

Ghader’s work has since been published in a high-profile American journal and he has now moved on to another project aimed at a new molecule in melanoma cells that has been discovered by Wilkins Centre investigators. Ghader has another souvenir of New Zealand – he and his wife Zahra (from Shiraz, Iran) have a new baby daughter called Sevin (meaning “happiness”).





Awards for both student and supervisor – and two Tall Poppies

In 2007, Wilkins Centre Director Ted Baker and his colleagues published a landmark paper in *Science* on the structure of the bacterial protein pilin, with PhD student HaeJoo Kang as first author. In 2008, both Ted and HaeJoo were honoured independently.

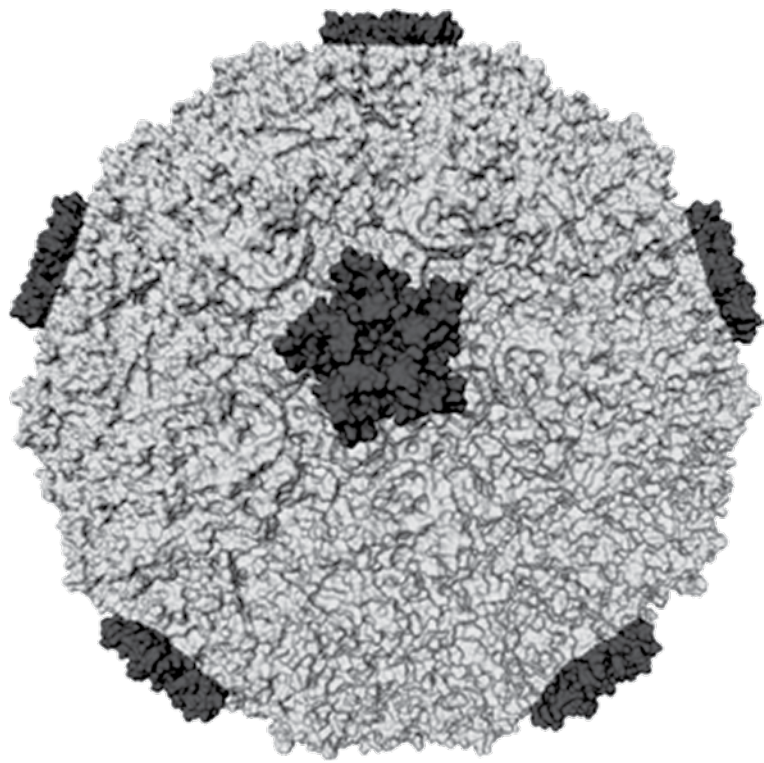
In August, HaeJoo was named as runner-up in the 2008 MacDiarmid Awards, in the category of Advancing Human Health and Wellbeing. The MacDiarmid Awards celebrate the achievements of New Zealand's future leaders in science and in 2008 there were a record 146 entries from young scientists. In November, Ted was awarded the Liley Medal for Excellence in Health Research by the Health Research Council of New Zealand. The Liley medal recognises research that has made an outstanding contribution to health and medical sciences, and is considered by many to be the premier award for life sciences in the country.

To top a stand-out year for the Maurice Wilkins Centre, two Principal investigators were named Tall Poppies in the 2008 World Class New Zealand Awards.

Garth Cooper was recognised with the Biotechnology award, and Margaret Brimble was acknowledged with the Research, Science, Technology and Academic award.

The awards, sponsored by Kea New Zealand and New Zealand Trade and Enterprise, recognise leaders who provide inspiration and leadership for the next generation of New Zealanders. Winners were selected across seven categories representing the diversity of the national economy, are acknowledged for the time, knowledge and skills they use to help New Zealand succeed internationally.





... and finally, the common cold

Wilkins Centre Investigators are dedicated to fighting serious disease of importance to New Zealanders, with a particular focus on cancer, diabetes, and infectious disease. But their skills can also be deployed against other disease targets – developing cutting edge research technology along the way.

Wilkins Centre scientists have begun an international collaboration to attack the virus family that causes most common colds, known as “rhinoviruses”. A new collaboration between the research groups of Margaret Brimble and John Fraser is focusing on novel compounds that inhibit an enzyme essential for the growth of rhinovirus. The “3C protease” enzyme is made by the virus and is essential for viral assembly, so drugs that can inhibit this enzyme have potential as treatment for the common cold. The science collaboration brings the medicinal chemistry of Margaret Brimble’s group together with the biochemistry and molecular biology expertise of John Fraser’s group. The team is also collaborating with the world-renowned Scripps Research Institute in San Diego, where structural biologist Ian Wilson has a particular interest in the rhinovirus enzyme. A natural compound called thysanone is known to inhibit the 3C protease, and the goal is to synthesise derivatives of this compound and test them in 3C assays to select for higher activity compounds. The group at Scripps will study the atomic structure of the 3C protease with thysanone bound to its active site, providing information that will help the chemists design the molecular structure of the new drugs – a process called “rational drug design”. As well as targeting the common cold, the project will allow Wilkins Centre investigators to build on New Zealand’s extensive drug design experience, and strengthen the pipeline of promising new medicines being developed here.





Outreach

Sponsorship

Maurice Wilkins Centre Prize for Excellence in Chemical Research

The Wilkins Centre has partnered with the New Zealand Institute of Chemistry to sponsor the annual Maurice Wilkins Centre Prize for Excellence in Chemical Research. This prize will be awarded to an NZIC member who has made a significant contribution to some branch of chemical science in the five years preceding the award.

In 2008, this prize was awarded to Professor Henrik Kjaergaard (Department of Chemistry, University of Otago) for his work in the area of theoretical chemistry. The award was presented at the NZIC conference, held in Dunedin in December.

Conferences and Meetings

Conferences and meetings are an important forum for knowledge transfer in the scientific community. The Wilkins Centre provides support for international scientific meetings to be held in New Zealand as well as for smaller local scientific meetings and networks.

In 2008 the Wilkins Centre sponsored:

- The 2008 Queenstown Molecular Biology meeting. This meeting attracted over four hundred delegates from New Zealand and overseas. In addition to the main meeting the programme included four satellite meetings. Two of these satellites, focused on signal transduction and structural biology, involved presentations by a number of Wilkins Centre investigators and students.
- Stratus, a network focused on emerging researchers at the University of Auckland. Stratus aims to identify and address issues of importance to emerging researchers, provide a support network for these researchers and raise the profile of emerging researchers and science within the academic and public communities.
- Breast Cancer Symposium, organised by Wilkins Centre Investigator Cris Print. As described earlier in this report, this meeting was very well attended and has resulted in closer links between researchers and clinicians in this area.
- The second CellML international workshop, organized by Wilkins Centre Research Fellow Catherine Lloyd, was held in March. Over 50 delegates attended the meeting, including visitors from England, Spain, the Netherlands, America, Japan, and Australia.

Public engagement

The Wilkins Centre actively engages the New Zealand public, to communicate exciting new research developments and successes, and provide commentary on current scientific issues. Wilkins Centre staff gave numerous media interviews and public lectures in 2008. Particular highlights for 2008 included:

- Margaret Brimble continued her role promoting science to the general public and women in particular. Her work was profiled in media articles in several magazines, including Mindfood Magazine, Jolie Magazine, Southern Cross Magazine, Unlimited Magazine, Management Magazine and Readers' Digest. She also delivered public lectures to the Aorangi Club and Federation of Graduate Women.
- The launch of biotech start up company Pathway Therapeutics (see Highlights) attracted considerable media coverage, including an interview of co-founder Peter Shepherd on TV3's ASB Business programme.
- The Maurice Wilkins Lecture given by Nobel Laureate Kary Mullis (see Highlights) attracted hundreds, and generated strong media interest.
- Wilkins Centre investigators played prominent roles at the NZ Melanoma Summit in Wellington, where hundreds of patients, clinicians, and researchers met, to mark the launch of the new guidelines for melanoma care in Australia and New Zealand, and to plot a path for improving outcomes for melanoma patients. Rod Dunbar and Graham LeGros provided an overview of New Zealand research into melanoma, and Rod Dunbar appeared on breakfast television along with radiation oncologist Graham Stevens to highlight current progress against melanoma.

Wilkins Centre staff helped launch the Royal Society launch the Science Media Centre at the Viaduct in Auckland. The Science Media Centre (www.sciencemediacentre.co.nz) aims to promote accurate, bias-free reporting on science and technology by helping the media work more closely with the scientific community, and the Wilkins Centre has offered its full support to this effort. This support included helping entertain the large throng of journalists and media types who gathered at the launch, with a colourful chemistry demonstration by members of the Brimble group at a stylised laboratory "bar" – and a keyboard performance with the hip-hop band *Misfits of Science* by an anonymous Wilkins Centre investigator.

Science education

Science education in New Zealand schools is important to encourage future generations of scientists. In 2008 the Wilkins Centre was involved in numerous science education initiatives, including:

- NZ Science Learning Hub – Wilkins Centre investigators provided research stories and videos for this national website which supports the school science curriculum.
- LENSscience (Liggins Education Network for Science) – Several Wilkins Centre investigators participated in this classroom-based programme that provides schools with access to research scientists, to maximise student potential with high quality learning opportunities for both students and teachers.
- Rotary National Science and Technology Forum – Wilkins Centre scientists Jodie Johnstone, Chris Squire and Paul Young designed and ran a practical laboratory session for 150 students at this national residential programme for outstanding all-round science, maths and technology students in Year 12.
- Incredible Science – At this open day for students interested in science and their parents, hosted by the University of Auckland, Margaret Brimble conducted a 'Women in Science' session with 25 children and teachers from 5 primary schools, while Wilkins Centre scientists led by Chris Squire and Jodie Johnstone ran a display called 'The Protein House of Fun' to show the importance of proteins in everyday life.

Service

Wilkins Centre investigators support both the New Zealand and international science communities in leadership roles and serving on many advisory boards and panels.

National roles

In 2008 senior members of the Wilkins Centre have served in advisory and governance roles in the following New Zealand organizations;

- Royal Society of NZ
- Marsden Fund Council
- NZ Health Research Council
- Foundation for Research Science and Technology, Leveraging New Zealand's Natural Resources (LNNR) Panel
- Rutherford Foundation
- NZ Cancer Control Council Research Advisory Group
- National Heart Foundation Science Panel
- Allan Wilson Centre for Molecular Ecology & Evolution (Massey University)
- NZBIO
- Queenstown Molecular Biology Meetings Organisation
- Nuffield Medical Research Fellowship for Oxford University
- Logan Campbell Medical Trust

David Ackerley, one of our younger investigators, was selected as a member of the Ministry of Research, Science and Technology delegation to the international biotechnology conference BIO2008, to represent and promote New Zealand biotechnology on the international stage.

International roles

In 2008 members of the Wilkins Centre have served in over 40 advisory, editorial and governance roles in international organizations based in the United States of America, Europe, Australia, the United Kingdom, Asia, Ireland, Iceland, Holland, France, Canada, and Norway.



Organisational Development

Flexible Research Fund

A major new research strategy in 2008 was the launch of a contestable funding mechanism to seed very early stage research collaborations. The Flexible Research Seeding Fund is open to all investigators within the Wilkins Centre, and is designed to support highly ambitious research initiatives, proposed by groups of investigators from different scientific disciplines. A Project Review Committee reviews the proposals rapidly, and funding is made available to top-ranked projects within 6-8 weeks of the call for new proposals. The Flexible Research Seeding Fund therefore allows the Wilkins Centre to respond very quickly to new ideas and new technology, and nurture the most exciting new collaborations between its investigators to the point where they can obtain sustained research funding from external sources.

In the December 2008 round, a total of \$137,580 was awarded to seed six new projects over 2009/2010. These projects focused on:

- *A diabetes drug target*: Kerry Loomes, The University of Auckland; Juliet Gerard, University of Canterbury; Ted Baker, The University of Auckland
- *A vaccine for TB*: Graham LeGros & Joanna Kirman, Malaghan Institute for Medical Research; Shaun Lott, The University of Auckland
- *A TB drug target*: Emily Parker, University of Canterbury; Heather Baker, The University of Auckland; Ted Baker, The University of Auckland
- *Melanoma gene analysis*: Edmund Crampin, Auckland Bioengineering Institute; Cris Print, The University of Auckland; Lai-Ming Ching, Auckland Cancer Society Research Centre; Rod Dunbar, The University of Auckland
- *Chemical probes for cell biology*: Margaret Brimble & Kathy Mountjoy, The University of Auckland
- *Drug leads for renal carcinoma*: Michael Hay & Jack Flanagan, Auckland Cancer Society Research Centre; Allen Rodrigo, Bioinformatics Institute; Nick Jones, BeSTGRID; Amato Giaccia, Stanford University

New Investigators

Three new Associate investigators were invited to join the Wilkins Centre in 2008.

Dr Jack Flanagan is a molecular modeller and Senior Research Fellow in the Auckland Cancer Society Research Centre (ACSRC) at the University of Auckland. Jack previously worked in the Institute for Molecular Bioscience in Brisbane, where he was Head of Computational Chemistry and Biology at the Australian Research Council Special Research Centre for Functional and Applied Genomics. He has providing modelling support and initiatives for many of the ACSRC's ongoing drug development projects, and is working with The University of Auckland's Bioinformatics Institute on high-speed computing for virtual screening.

Dr Debbie Hay received her PhD from Imperial College, London in 2002. She then moved to New Zealand on a postdoctoral fellowship and is now Senior Lecturer, leading the Molecular Pharmacology laboratory at the School of Biological Sciences, University of Auckland. Her main research interests are peptide G protein-coupled receptors.

Dr Kathy Mountjoy is a Senior Research Fellow in the Departments of Physiology and Molecular Medicine and Pathology at The University of Auckland. She graduated with a PhD in Medicine from the University of Auckland in 1987 before completing 6 years as a post-doctoral fellow in the USA. Three years were spent at Harvard University working with Professor Jeffrey Flier and another three years at Oregon Health Sciences University working with Dr Roger Cone. Together with Dr Cone she was the first to clone the melanocortin receptors and her research since returning to Auckland in 1993 has focused on understanding physiological roles for melanocortin peptides and how they signal through melanocortin receptors with a particular focus on roles in energy homeostasis.



Equipment & facilities

2008 was a busy year for the development of Wilkins Centre equipment facilities, as the 2007 allocation of CoRE capital equipment funding became available in June 2008. In total 9 of the 17 items on the Wilkins Centre capital equipment list were installed in 2008 with the remainder of the purchases scheduled for 2009.

In addition to the purchase of equipment to be located at the University of Auckland, the Wilkins Centre has also purchased equipment that has been located at four collaborating institutions – the University of Otago, Canterbury University, the Malaghan Institute for Medical Research in Wellington, and the University of Waikato.

While primarily used by Wilkins Centre investigators, the capital equipment purchased by the Centre has also provided valuable services for many New Zealand biotechnology companies and researchers based at CRIs and Health Boards. In 2008 the Centre client list included:

- ZyGEM Ltd
- DEC International Ltd
- Genesis R&D Ltd
- Vialactia Ltd
- Living Cell Technologies Ltd
- Androgenix Ltd
- Pathway Therapeutics Ltd
- Proacta Ltd
- Symansis Ltd
- ICPBio Ltd
- Cawthron Institute
- IRL
- HortResearch
- Canterbury District Health Board
- Green Lane Research & Educational Fund (Auckland City Hospital)

As noted in the Highlights the new flow cytometry and cell sorting facilities have already enjoyed heavy use, from both Wilkins Centre investigators and external users, including start-up biotech companies. The availability of high speed cell sorting and analysis based on large number of fluorophores have allowed new protocols to be established that were not previously possible within New Zealand. The proteomics facility has also been

heavily patronised. In particular the expertise of the Wilkins Centre staff in the cutting edge “iTRAQ” technique, for large-scale quantitative proteomic analysis, has proven very attractive to users. The availability of this technical platform has not only enabled many high-quality new publications, but has also spawned some major research into new algorithms for the interpretation of this kind of high-throughput proteomic experiment.

At the University of Canterbury, the installation of the new Wilkins Centre Differential Scanning Calorimeter (DSC) has enabled fascinating new studies of “thermophilic” organisms, capable of flourishing in extreme environments, such as hot springs and deep sea hydrothermal vents. Grant Pearce and Juliet Gerrard have been studying the stability of an enzyme from *Thermotoga maritima*, a bacterium that normally lives at 80 °C in thermal hot springs. They had not previously been able to measure the stability of these enzymes, as their high stability meant that most biochemical equipment was unable to provide the high temperatures, at least 90°C, required to melt the protein. However, with the new Wilkins Centre DSC, they have been able to study the enzyme at higher temperatures, and have been investigating the structural reasons for the high stability of the *Thermotoga* enzyme. This work has important implications both in biotechnology, where thermostable enzymes are crucial components of many industrial and research processes, and in medicine, where new knowledge of protein stability can enhance the production of new protein-based drugs.

Governance & management

Governing Board

During the period under review the Governing Board met on two occasions. Focus at its meetings has been on monitoring progress in the Centre’s endeavours to extend its reach to other scientific bodies, and to make its activities known to a wider public audience, the results of which are presented in this report. Routinely the Board reviews progress in the principal projects being conducted by the various arms of the Centre, and compliance with its budget. It is pleasing to report that nearly all of the Centre’s work is on target, and that no major variations have been required to the programmes which have been in place since the Centre’s inception. Work has been conducted within the budgetary parameters established when the programme was renewed last year.

W J Falconer CNZM
Chairman

Management Committee

The Wilkins Centre Management Committee, made up of the Wilkins Centre Principal Investigators and management staff, met three times during 2008.

Members of the Governing Board, Scientific Advisory Board and Principal Investigators are listed in the Directory at the end of this report.



Human capability

The multidisciplinary and collaborative nature of Wilkins Centre research provides an excellent training environment for younger scientists and students, the future science leaders.

PhD student support

The Wilkins Centre supports a large cohort of PhD and MSc students within its associated research groups by providing working expenses, travel funding and access to specialised research equipment and facilities. In 2008 the Wilkins Centre provided full or partial scholarship support for 14 PhD students.

There were 13 Wilkins Centre-associated PhD students who completed their studies in 2008. Almost all of these students are now working as Research Fellows either within Wilkins Centre research groups or in research groups overseas. Prominent examples of these graduates are the three 2008 PhD graduates from John Fraser's group, who all secured Research Fellowships in top UK research groups. Nicola Jackson was awarded the inaugural Freemansons Roskill Foundation Postdoctoral Fellowship by The Rutherford Foundation, to undertake post-doctoral research at the University of Cambridge, with Professor John Trowsdale and Dr Adrian Kelly. Natasha Willoughby obtained a position as a Research Fellow at the National University of Ireland, with Professor Sean Doyle. And Amanda Taylor became a Research Fellow at the Brighton and Sussex Medical School, with Dr Martin Llewelyn. The Wilkins Centre encourages its graduates to obtain experience in leading international research labs, and aims to provide a world-class environment for the return of these graduates, once they have gained wider experience of the global research effort against major human diseases.

Personnel Exchanges

In order to maintain a world class research programme it is important that Wilkins Centre investigators and students keep up to date with international developments in their research area. The Wilkins Centre provides support for staff and students to travel to conferences and visit other national and international research labs to learn new skills and techniques.

An example of a student placement was Danny Lee's time in the Kent lab in Chicago, as described in Highlights above. Staff exchanges are aimed at technical updates for key personnel. Wilkins Centre staff Martin Middleditch and Christina Buchanan attended Applied Biosystem's iTRAQ workshop hosted by the Institute for Molecular Biosciences at the University of Queensland in Brisbane, where they gained firsthand experience with the new 8-plex iTRAQ labeling system. This system has since been implemented in the Proteomics Facility at Auckland, representing another new technical platform accessible by researchers throughout the country.

International experts

The Wilkins Centre enables visits to New Zealand by international scientists, so that they can share their knowledge and research experiences with the New Zealand research community and establish research links.

Visitors hosted in 2008 were:

- Professor Eleanor Dodson FRS (University of York, UK)
- Professor Hong Xu (Shenshen University, China)
- Professor Mohammed Roayaei (Shahid Chamran University, Iran)
- Professor James Remington (University of Oregon, USA)
- Dr Clemens Vonrhein (Global Phasing, Cambridge, UK)
- Professor Richard Lewis (University of Newcastle, UK)
- Dr John Sanderson (Durham University, UK)
- Professor Charles Eason (Connovation Ltd./ Lincoln University)
- Dr David Foo (AMRI, Singapore)
- Dr Fraser Fleming (DuQuesne University, Pittsburgh, USA)
- Dr Andrew Philipps (University of Colorado, Boulder, USA)
- Dr Joel Tyndall (University of Otago)
- Professor Dieter Enders (University of Aachen, Germany)
- Associate Professor Andrew Hughes (La Trobe University, Melbourne)
- Professor Chris Moody (University of Nottingham, UK)
- Professor Chris Braddock (Imperial College London, UK)
- Professor David Knight (University of Cardiff, UK)



In particular the Wilkins Centre was pleased to support extended visits by highly distinguished expatriates Professors Steve Kent and Guy Dodson.



Professor Steve Kent

Director, Institute for Biophysical Dynamics, The University of Chicago, USA.

Prof Steve Kent, one of the world's leading peptide and protein synthetic chemists, visited the University of Auckland and the Wilkins Centre in March 2008, as an Adjunct Professor. During his visit Steve presented a Maurice Wilkins Centre seminar on his research entitled 'Through the looking glass, a new world of proteins enabled by chemistry'. He also advised on translation of the Wilkins Centre's vaccine development programmes towards clinical trials, and visited IRL in Wellington, and the AnQual laboratories in Auckland, to view the new drug development facilities at each site. While in Wellington, he delivered a seminar in the Ministry of Research, Science and Technology's "breakfast" seminar programme, to brief science policy leaders across the ministries on recent developments in the research environment in the USA, including his recent experience with commercialising scientific discoveries. Steve was particularly emphatic about the benefits of the multi-disciplinary research approach taken by the Wilkins Centre, which mirrors his own institute in Chicago, and he believes has strong potential for delivering important health and economic outcomes for New Zealand.



Professor Guy Dodson FRS

University of York, UK.

Prof Guy Dodson visited the Wilkins Centre and The University of Auckland during March 2008, also as an Adjunct Professor. Prof Dodson spent much of this time discussing research with postgraduate students and research staff in the Wilkins Centre and passing on some of his wealth of knowledge and experience. Prof Dodson gave two seminars while in Auckland; 'Careful crystallography and insights in to catalytic structure and mechanism', and 'The chemical and structural events in insulin biosynthesis and its relevance to neo-natal diabetes'.

External funding

Many of the research projects within the Wilkins Centre research programme are supported by additional grants from other funding sources. The Centre also targets a proportion of its research budget to seed and develop new projects to the point where they are successful in securing competitive funding.

NZ funding

In 2008 Wilkins Centre investigators were awarded new grants worth more than \$27 Million from New Zealand funding agencies for research projects to be carried out over the next two to five years. Success with major funding agencies is illustrated by the following:

- Health Research Council (6 grants, \$14.28 Million)
- Marsden Fund (3 grants, \$2.47 Million)
- Foundation for Science, Research and Technology (1 grant, \$10 Million)

International and commercial funding

In 2008 Wilkins Centre investigators secured new funding of more than \$17 Million from the following international and commercial sources to fund future research;

- Proacta Inc (NZ/USA)
- Agennix Inc (USA)
- Global Alliance for TB (USA)
- Ludwig Institute for Cancer Research (USA)
- European Commission FP7 (EU)

Of particular note is that this figure includes \$12 Million of venture capital funding for start-up company Pathway Therapeutics (GBS Ventures, CM Capital, UniServices Trans-Tasman Fund). As noted above under Highlights, this company was spun out as the direct result of research originally funded by the Wilkins Centre.





Research Outputs

Publications

In 2008 research outputs from Wilkins Centre investigators included over 200 peer reviewed scientific papers published in international journals and 14 patents. Research directly supported by the Wilkins Centre generated the following 80 scientific papers.

Papers and Reviews:

- 1 Anagnostou SH, Shepherd PR. Glucose induces an autocrine activation of the Wnt/beta-catenin pathway in macrophage cell lines. *The Biochemical Journal* (2008) **416**:211-18
- 2 Anderson RF, Shinde SS, Maroz A, Boyd M, Palmer BD, Denny WA. Intermediates in the reduction of the antituberculosis drug PA-824, (6S)-2-nitro-6-{{4-(trifluoromethoxy)benzyl}oxy}-6,7-dihydro-5H-imidazo[2,1-b] [1,3]oxazine, in aqueous solution. *Organic and Biomolecular Chemistry* (2008) **6**:1973-80
- 3 Andrey O, Sperry J, Larsen US, Brimble MA. An approach to an enantioselective synthesis of crisamicin A via a novel double Hauser-Kraus annulation strategy. *Tetrahedron* (2008) **64**:3912-27
- 4 Bachu P, Sperry J, Brimble MA. Synthesis of a C8 oxygenated pyranonaphthoquinone: a useful precursor to dimeric pyranonaphthoquinones. *Tetrahedron* (2008) **64**:3343-50
- 5 Bachu P, Sperry J, Brimble MA. Chemoenzymatic synthesis of deoxy analogues of the DNA topoisomerase II inhibitor eleutherin and the 3C-protease inhibitor thysanone. *Tetrahedron* (2008) **64**:4827-34
- 6 Baker E, Dauter Z, Guss M, Einspahr H. Deposition of diffraction images to be discussed at the Open Meeting of the Commission on Biological Macromolecules of the IUCr in Osaka. *Acta Crystallographica Section F: Structural Biology and Crystallization Communications* (2008) **64**:231-32
- 7 Barnett MPG, Phillips ARJ, Harris PM, Cooper GJS. Impaired insulin secretion in perfused pancreases isolated from offspring of female rats fed a low protein whey-based diet. *Journal of the Pancreas* (2008) **9**:477-88
- 8 Bashiri G, Squire CJ, Moreland NJ, Baker EN. Crystal structures of F420-dependent glucose-6-phosphate dehydrogenase FGD1 involved in the activation of the anti-tuberculosis drug candidate PA-824 reveal the basis of coenzyme and substrate binding. *Journal of Biological Chemistry* (2008) **283**:17531-41
- 9 Bogle G, Dunbar PR. Simulating T-cell motility in the lymph node paracortex with a packed lattice geometry. *Immunology and Cell Biology* (2008) **86**:676-87

- 10 Boughton BA, Dobson RCJ, Gerrard JA, Hutton CA. Conformationally constrained diketopimelic acid analogues as inhibitors of dihydrodipicolinate synthase. *Bioorganic and Medicinal Chemistry Letters* (2008) **18**:460-63
- 11 Boughton BA, Griffin MDW, O'Donnell PA, Dobson RCJ, Perugini MA, Gerrard JA, Hutton CA. Irreversible inhibition of dihydrodipicolinate synthase by 4-oxo-heptenedioic acid analogues. *Bioorganic and Medicinal Chemistry* (2008) **16**:9975-83
- 12 Brimble MA, Gibson JS, Sejberg JJP, Sperry J. A facile enantioselective synthesis of the dimeric pyranonaphthoquinone core of the cardinalins. *Synlett* (2008):867-70
- 13 Brimble MA, Kowalczyk R, Harris PWR, Dunbar PR, Muir VJ. Synthesis of fluorescein-labelled O-mannosylated peptides as components for synthetic vaccines: Comparison of two synthetic strategies. *Organic and Biomolecular Chemistry* (2008) **6**:112-21
- 14 Bunker RD, McKenzie JL, Baker EN, Arcus VL. Crystal structure of PAEO151 from *Pyrobaculum aerophilum*, a PIN-domain (VapC) protein from a toxin-antitoxin operon. *Proteins: Structure, Function and Genetics* (2008) **72**:510-18
- 15 Burgess BR, Dobson RCJ, Bailey MF, Atkinson SC, Griffin MDW, Jameson GB, Parker MW, Gerrard JA, Perugini MA. Structure and evolution of a novel dimeric enzyme from a clinically important bacterial pathogen. *Journal of Biological Chemistry* (2008) **283**:27598-603
- 16 Chan Y, Guthmann H, Brimble MA, Barker D. Diastereoselective synthesis of substituted 4-piperidones and 4-piperidols using a double mannich reaction. *Synlett* (2008):2601-04
- 17 Chia EW, Pearce AN, Berridge MV, Larsen L, Perry NB, Sansom CE, Godfrey CA, Hanton LR, Lu GL, Walton M, Denny WA, Webb VL, Copp BR, Harper JL. Synthesis and anti-inflammatory structure-activity relationships of thiazine-quinoline-quinones: Inhibitors of the neutrophil respiratory burst in a model of acute gouty arthritis. *Bioorganic and Medicinal Chemistry* (2008) **16**:9432-42
- 18 Choi KW, Brimble MA. Synthesis of spiroacetal-triazoles as privileged natural product-like scaffolds using "click chemistry". *Organic and Biomolecular Chemistry* (2008) **6**:3518-26
- 19 Choi KW, Brimble MA, Groutso T. ([plus-minus sign])-1-{8'-(tert-Butyldiphenylsilyloxymethyl)-1',7'-dioxaspiro[5.5]undecan-2'-yl}uridine. *Acta Crystallographica Section E* (2008) **64**:o715
- 20 Clow F, Fraser JD, Proft T. Immobilization of proteins to biacore sensor chips using *Staphylococcus aureus* sortase A. *Biotechnology Letters* (2008) **30**:1603-07
- 21 Cooling MT, Hunter P, Crampin EJ. Modelling biological modularity with CellML. *Systems Biology, IET* (2008) **2**:73-79
- 22 Crimmins D, Choi KW, Boyd PDW, Brimble MA. ([plus-minus sign])-2'-Phenylcyclohexanespiro-4'-(azepano[1,2-b]isoxazolidine). *Acta Crystallographica Section E* (2008) **64**:o1535
- 23 Crimmins D, Dimitrov I, O'Connor PD, Caprio V, Brimble MA. A facile synthesis of a spironitrone and a study of its cycloaddition and nucleophilic addition reactions. *Synthesis* (2008):3319-25
- 24 Danaher RN, Loomes KM, Leonard BL, Whiting L, Hay DL, Xu LY, Kraegen EW, Phillips ARJ, Cooper GJS. Evidence that β -calcitonin gene-related peptide is a neurohormone that controls systemic lipid availability and utilization. *Endocrinology* (2008) **149**:154-60
- 25 Devenish SRA, Gerrard JA, Jameson GB, Dobson RCJ. The high-resolution structure of dihydrodipicolinate synthase from *Escherichia coli* bound to its first substrate, pyruvate. *Acta Crystallographica Section F: Structural Biology and Crystallization Communications* (2008) **64**:1092-95



- 26 Dobson RCJ, Griffin MDW, Devenish SRA, Pearce FG, Hutton CA, Gerrard JA, Jameson GB, Perugini MA. Conserved main-chain peptide distortions: A proposed role for Ile203 in catalysis by dihydrodipicolinate synthase. *Protein Science* (2008) **17**:2080-90
- 27 Flint RS, Phillips ARJ, Power SE, Dunbar PR, Brown C, Delahunt B, Cooper GJS, Windsor JA. Acute pancreatitis severity is exacerbated by intestinal ischemia-reperfusion conditioned mesenteric lymph. *Surgery* (2008) **143**:404-13
- 28 Fraser JD, Proft T. The bacterial superantigen and superantigen-like proteins. *Immunological Reviews* (2008) **225**:226-43
- 29 Frederick R, Denny, W.A. . Molecular modeling approaches to the design and discovery of new drugs. The example of phosphoinositide-3-kinases (PI3Ks). *Chimie Nouvelle* (2008) **26**
- 30 Frederick R, Denny WA. Phosphoinositide-3-kinases (PI3Ks): Combined comparative modeling and 3D-QSAR to rationalize the inhibition of p110? *Journal of Chemical Information and Modeling* (2008) **48**:629-38
- 31 Garny A, Nickerson DP, Cooper J, Santos RWD, Miller AK, McKeever S, Nielsen PMF, Hunter PJ. CellML and associated tools and techniques. *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences* (2008) **366**:3017-43
- 32 Goldstone RM, Moreland NJ, Bashiri G, Baker EN, Shaun Lott J. A new Gateway® vector and expression protocol for fast and efficient recombinant protein expression in *Mycobacterium smegmatis*. *Protein Expression and Purification* (2008) **57**:81-87
- 33 Gong D, Lu J, Chen X, Reddy S, Crossman DJ, Glyn-Jones S, Choong YS, Kennedy J, Barry B, Zhang S, Chan YK, Ruggiero K, Phillips ARJ, Cooper GJS. A copper(II)-selective chelator ameliorates diabetes-evoked renal fibrosis and albuminuria, and suppresses pathogenic TGF- β activation in the kidneys of rats used as a model of diabetes. *Diabetologia* (2008) **51**:1741-51
- 34 Goodall K, Brimble M, Barker D. ¹H and ¹³C NMR spectra of C-6 and C-9 substituted 3-azabicyclo[3.3.1]nonanes. *Magnetic Resonance in Chemistry* (2008) **46**:75-79
- 35 Griffin MDW, Dobson RCJ, Pearce FG, Antonio L, Whitten AE, Liew CK, Mackay JP, Trehella J, Jameson GB, Perugini MA, Gerrard JA. Evolution of Quaternary Structure in a Homotetrameric Enzyme. *Journal of Molecular Biology* (2008) **380**:691-703
- 36 Gueret SM, Choi KW, O'Connor PD, Boyd PDW, Brimble MA. (1R,6R)-1-Methyl-8-azaspiro[5.6]dodecan-7-one. *Acta Crystallographica Section E* (2008) **64**:o1151
- 37 Harris PWR, Williams GM, Shepherd P, Brimble MA. The synthesis of phosphopeptides using microwave-assisted solid phase peptide synthesis. *International Journal of Peptide Research and Therapeutics* (2008) **14**:387-92
- 38 Hay MP, Hicks KO, Pchalek K, Lee HH, Blaser A, Pruijn FB, Anderson RF, Shinde SS, Wilson WR, Denny WA. Tricyclic [1,2,4]triazine 1,4-dioxides as hypoxia selective cytotoxins. *Journal of Medicinal Chemistry* (2008) **51**:6853-65
- 39 Hopkins PA, Pridmore AC, Ellmerich S, Fraser JD, Russell HH, Read RC, Sriskandan S. Increased surface toll-like receptor 2 expression in superantigen shock. *Critical care medicine* (2008) **36**:1267-76
- 40 Hunter P, Kurachi Y, Noble D, Viceconti M. Meeting Report on the 2nd MEI International Symposium - The Worldwide Challenge to Physiome and Systems Biology and Osaka Accord. *Journal of Physiological Sciences* (2008) **58**:425-31
- 41 Hunter PJ, Crampin EJ, Nielsen PMF. Bioinformatics, multiscale modeling and the IUPS Physiome Project. *Briefings in Bioinformatics* (2008) **9**:333-43

- 42 Jensen J, Grønning-Wang LM, Jebens E, Whitehead JP, Zorec R, Shepherd PR. Adrenaline potentiates insulin-stimulated PKB activation in the rat fast-twitch epitrochlearis muscle without affecting IRS-1-associated PI 3-kinase activity. *Pflugers Archiv European Journal of Physiology* (2008) **456**:969-78
- 43 Jüllig M, Hickey AJR, Chai CC, Skea GL, Middleditch MJ, Costa S, Choong SY, Phillips ARJ, Cooper GJS. Is the failing heart out of fuel or a worn engine running rich? A study of mitochondria in old spontaneously hypertensive rats. *Proteomics* (2008) **8**:2556-72
- 44 Kefala G, Evans GL, Griffin MDW, Devenish SRA, Pearce FG, Perugini MA, Gerrard JA, Weiss MS, Dobson RCJ. Crystal structure and kinetic study of dihydrodipicolinate synthase from *Mycobacterium tuberculosis*. *Biochemical Journal* (2008) **411**:351-60
- 45 Klenerman P, Dunbar PR. CMV and the Art of Memory Maintenance. *Immunity* (2008) **29**:520-22
- 46 Lena G, Trapani JA, Sutton VR, Ciccone A, Browne KA, Smyth MJ, Denny WA, Spicer JA. Dihydrofuro[3,4-c]pyridinones as inhibitors of the cytolytic effects of the pore-forming glycoprotein perforin. *Journal of Medicinal Chemistry* (2008) **51**:7614-24
- 47 Linke C, Caradoc-Davies TT, Proft T, Baker EN. Purification, crystallization and preliminary crystallographic analysis of *Streptococcus pyogenes* laminin-binding protein Lbp. *Acta Crystallographica Section F: Structural Biology and Crystallization Communications* (2008) **64**:141-43
- 48 Lithander FE, Keogh GF, Wang Y, Cooper GJS, Mulvey TB, Chan YK, McArdle BH, Poppitt SD. No evidence of an effect of alterations in dietary fatty acids on fasting adiponectin over 3 weeks. *Obesity* (2008) **16**:592-99
- 49 Lloyd CM, Phillips ARJ, Cooper GJS, Dunbar PR. Three-colour fluorescence immunohistochemistry reveals the diversity of cells staining for macrophage markers in murine spleen and liver. *Journal of Immunological Methods* (2008) **334**:70-81
- 50 Lorimer AV, O'Connor PD, Brimble MA. Buchwald-Hartwig Mono-N-arylation with 2,6-dihaloisonicotinic acid derivatives: A convenient desymmetrization method. *Synthesis* (2008):2764-70
- 51 Mitsakos V, Dobson RCJ, Pearce FG, Devenish SR, Evans GL, Burgess BR, Perugini MA, Gerrard JA, Hutton CA. Inhibiting dihydrodipicolinate synthase across species: Towards specificity for pathogens? *Bioorganic and Medicinal Chemistry Letters* (2008) **18**:842-44
- 52 Mittal A, Flint RJ, Fanous M, Delahunt B, Kilmartin PA, Cooper GJ, Windsor JA, Phillips AR. Redox status of acute pancreatitis as measured by cyclic voltammetry: initial rodent studies to assess disease severity. *Critical care medicine* (2008) **36**:866-72
- 53 Mittal A, Middleditch M, Ruggiero K, Buchanan CM, Jullig M, Loveday B, Cooper GJS, Windsor JA, Phillips ARJ. The proteome of rodent mesenteric lymph. *American Journal of Physiology - Gastrointestinal and Liver Physiology* (2008) **295**:G895-G903
- 54 O'Connor PD, Körber K, Brimble MA. Novel use of N-carboalkoxy α,β -unsaturated iminium ions as dienophiles in Diels-Alder reactions. *Synlett* (2008):1036-38
- 55 Payne LS, Brown PM, Middleditch M, Baker E, Cooper GJ, Loomes KM. Mapping of the ATP-binding domain of human fructosamine 3-kinase-related protein by affinity labelling with 5'-[p-(fluorosulfonyl)benzoyl]adenosine. *The Biochemical Journal* (2008) **416**:281-88
- 56 Pearce FG, Dobson RCJ, Weber A, Lane LA, McCammon MG, Squire MA, Perugini MA, Jameson GB, Robinson CV, Gerrard JA. Mutating the tight-dimer interface of dihydrodipicolinate synthase disrupts the enzyme quaternary structure: Toward a monomeric enzyme. *Biochemistry* (2008) **47**:12108-17



- 57 Pearce FG, Sprissler C, Gerrard JA. Characterization of dihydrodipicolinate reductase from *Thermotoga maritima* reveals evolution of substrate binding kinetics. *Journal of Biochemistry* (2008) **143**:617-23
- 58 Poppitt SD, Keogh GF, Lithander FE, Wang Y, Mulvey TB, Chan YK, McArdle BH, Cooper GJS. Postprandial response of adiponectin, interleukin-6, tumor necrosis factor- α , and C-reactive protein to a high-fat dietary load. *Nutrition* (2008) **24**:322-29
- 59 Radcliff FJ, Fraser JD, Wilson ZE, Heapy AM, Robinson JE, Bryant CJ, Flowers CL, Brimble MA. Anti-*Helicobacter pylori* activity of derivatives of the phthalide-containing antibacterial agents spiroloxine methyl ether, CJ-12,954, CJ-13,013, CJ-13,102, CJ-13,104, CJ-13,108 and CJ-13,015. *Bioorganic and Medicinal Chemistry* (2008) **16**:6179-85
- 60 Rathwell DCK, Tsang KY, Choi KW, Boyd PDW, Brimble MA. 3-Allyl-2-hydroxy-5,6,8-trimethoxynaphthalene-1,4-dione. *Acta Crystallographica Section E* (2008) **64**:o1929
- 61 Schmid DS. Superantigens: Molecular Basis for Their Role in Human Diseases. *Emerging Infectious Diseases* (2008) **14**:866-67
- 62 Sejberg JJP, Sperry J, Choi KW, Boyd PDW, Brimble MA. (1R,1'R,3S,3'S)-5,5',10,10'-Tetramethoxy-1,1',3,3'-tetramethyl-3,3',4,4'-tetrahydro-1H,1'H-8,8'-bi[benzo[g]isochromene]. *Acta Crystallographica Section E* (2008) **64**:o758
- 63 Sharpe ML, Gao C, Kendall SL, Baker EN, Lott JS. The Structure and Unusual Protein Chemistry of Hypoxic Response Protein 1, a Latency Antigen and Highly Expressed Member of the DosR Regulon in *Mycobacterium tuberculosis*. *Journal of Molecular Biology* (2008) **383**:822-36
- 64 Showalter HDH, Denny WA. A roadmap for drug discovery and its translation to small molecule agents in clinical development for tuberculosis treatment. *Tuberculosis* (2008) **88**:S3-S17
- 65 Smail JB, Baker EN, Booth RJ, Bridges AJ, Dickson JM, Dobrusin EM, Ivanovic I, Kraker AJ, Lee HH, Lunney EA, Ortwine DF, Palmer BD, Quinn J, Squire CJ, Thompson AM, Denny WA. Synthesis and structure-activity relationships of N-6 substituted analogues of 9-hydroxy-4-phenylpyrrolo[3,4-c]carbazole-1,3(2H,6H)-diones as inhibitors of Wee1 and Chk1 checkpoint kinases. *European Journal of Medicinal Chemistry* (2008) **43**:1276-96
- 66 Smail JB, Lee HH, Palmer BD, Thompson AM, Squire CJ, Baker EN, Booth RJ, Kraker A, Hook K, Denny WA. Synthesis and structure-activity relationships of soluble 8-substituted 4-(2-chlorophenyl)-9-hydroxypyrrrolo[3,4-c]carbazole-1,3(2H,6H)-diones as inhibitors of the Wee1 and Chk1 checkpoint kinases. *Bioorganic and Medicinal Chemistry Letters* (2008) **18**:929-33
- 67 Smith GC, Chaussade C, Vickers M, Jensen J, Shepherd PR. Atypical antipsychotic drugs induce derangements in glucose homeostasis by acutely increasing glucagon secretion and hepatic glucose output in the rat. *Diabetologia* (2008) **51**:2309-17
- 68 Sperry J, Brimble MA. An efficient enantioselective synthesis of the 3C protease inhibitor (-)-thysanone. *Synlett* (2008):1910-12
- 69 Sperry J, Gibson JS, Sejberg JJP, Brimble MA. Enantioselective synthesis of the dimeric pyranonaphthoquinone core of the cardinalins using a late-stage homocoupling strategy. *Organic and Biomolecular Chemistry* (2008) **6**:4261-70
- 70 Swan A, Hunter P, Tawhai M. Pulmonary gas exchange in anatomically-based models of the lung. *Advances in experimental medicine and biology* (2008) **605**:184-89

- 71 Terkildsen JR, Niederer S, Crampin EJ, Hunter P, Smith NP. Using Physiome standards to couple cellular functions for rat cardiac excitation-contraction. *Experimental Physiology* (2008) **93**:919-29
- 72 Tong ST, Barker D, Choi KW, Boyd PDW, Brimble MA. ([plus-minus sign])-Cyclohexane-1,2-diyl bis(4-nitrobenzoate). *Acta Crystallographica Section E* (2008) **64**:o2174
- 73 Tong ST, Barker D, Choi KW, Boyd PDW, Brimble MA. ([plus-minus sign])-N-(3-Hydroxy-1,2-diphenylpropyl)-4-methylbenzenesulfonamide. *Acta Crystallographica Section E* (2008) **64**:o1990
- 74 Tong ST, Harris PWR, Barker D, Brimble MA. Use of (S)-5-(2-methylpyrrolidin-2-yl)-1H-tetrazole as a novel and enantioselective organocatalyst for the aldol reaction. *European Journal of Organic Chemistry* (2008):164-70
- 75 Turcotte S, Chan DA, Sutphin PD, Hay MP, Denny WA, Giaccia AJ. A Molecule Targeting VHL-Deficient Renal Cell Carcinoma that Induces Autophagy. *Cancer Cell* (2008) **14**:90-102
- 76 Watkins HA, Baker EN. Cloning, expression, purification and preliminary crystallographic analysis of the RNase HI domain of the Mycobacterium tuberculosis protein Rv2228c as a maltose-binding protein fusion. *Acta Crystallographica Section F: Structural Biology and Crystallization Communications* (2008) **64**:746-49
- 77 Wong WP, Scott DW, Chuang CL, Zhang S, Liu H, Ferreira A, Saafi EL, Choong YS, Cooper GJ. Spontaneous diabetes in hemizygous human amylin transgenic mice that developed neither islet amyloid nor peripheral insulin resistance. *Diabetes* (2008) **57**:2737-44
- 78 Young PG, Smith CA, Metcalf P, Baker EN. Structures of Mycobacterium tuberculosis folylpolyglutamate synthase complexed with ADP and AMPPCP. *Acta Crystallographica Section D: Biological Crystallography* (2008) **64**:745-53
- 79 Zhang L, Cannell MB, Phillips AR, Cooper GJ, Ward ML. Altered calcium homeostasis does not explain the contractile deficit of diabetic cardiomyopathy. *Diabetes* (2008) **57**:2158-66
- 80 Zhang S, Liu H, Yu H, Cooper GJS. Fas-associated death receptor signaling evoked by human amylin in islet β -cells. *Diabetes* (2008) **57**:348-56



Patents

Patents awarded

1. Atwell, G.J., Denny, W.A., Yang, S. , *Processes for preparing asymmetric dinitrobenzamide mustard compound, intermediate compounds, useful therein and products obtained therefrom*. 2008: PCT. pp. 67.
2. Brimble, M., P.M. Harris, and F. Sieg, *Analogs of Glycyl-Prolyl-Glutamate*. 2008: USA. pp. 48.
3. Cooper, G.J., Xu, A., Wang, Y., *Adiponectin and uses thereof*. 2008: USA.
4. Cooper, G.J., J. Cornish, and I. Reid, *Adrenomedullin agonists*. 2008: USA.
5. Denny, W.A., Yang, S. , *Synthesis of 5,6-dimethyl-9-oxo-9h-xanthen-4-yl- acetic acid (DMXAA)*. 2008: PCT. pp. 20.
6. Denny, W.A., Baguley, B.C., Marshall, E.S., Sutherland, H.S., *Substituted ring fused azines and their use in cancer therapy*. 2008: PCT. pp. 67.
7. Denny, W.A., Wilson, W.R., Stevenson, R.J., Tercel, M., Atwell, G.J., Yang, S., Patterson, A.V.,Pruijn, F.B., *Nitrobenzindoles and their use in cancer therapy*. 2008: PCT. pp. 67.
8. Phiasivongsa P, R., S., Gamage, S.A., Brooke, D., Denny, W.A., Bearss, D.J., *Quinoline derivatives for modulating DNA methylation*. 2008: PCT. pp. 79.
9. Stribbling, S.M., Mountjoy, K.G., Tercel, M., Wilson, W.R., Denny, W.A., Stevenson, R.J., Lu, G-L. *Indoline derivatives and uses thereof*. 2008: PCT. pp. 77.

Patents pending

1. Rewcastle, G.W., Shepherd, P.R., Chaussade, C., Denny, W.A., *Substituted pyrimidine and triazine derivatives and their use in cancer therapy*. 2008: USA.
2. Trapani, J.A., Smyth, M.J., Spicer, J.A., Denny, W.A., Lena, G., *Dihydrofuro[3,4-c]pyridine-3(1H)-ones, preparation and uses thereof*. 2008: USA. pp. 112.
3. Trapani, J.A., Smyth, M.J., Spicer, J.A., Denny, W.A., Lena, G., *Dihydrofuro[3,4-c]pyridine-3(1H)-ones, preparation and uses thereof*. 2008: USA. pp. 86.
4. Trapani, J.A., Smyth, M.J., Spicer, J.A., Denny, W.A., Lena, G., *Therapeutic compounds, their preparation and uses thereof*. 2008: USA. pp. 110.
5. Turcotte, S., Sutphin, P.D., Chan, D.A., Hay, M.P., Denny, W.A., Giaccia, A.J., *Heteroaryl compounds and compositions therefrom for therapeutic use in cancer treatments*. 2008: USA.

Presentations

The international significance of Wilkins Centre research is demonstrated by Wilkins Centre investigators being invited to give 69 international and national presentations in 2008. Presentations include invited lectures at conferences and seminars to academic institutions in Italy, the USA, Japan, the UK, Germany, Australia, India, Denmark, China, Sweden, Iceland, France and New Zealand, as shown in the diagram below.



List of presentations

David Ackerley

- Special Symposium on Directed Evolution at the Australian COMBIO 2008 meeting (Canberra, Australia)

Ted Baker

- International School of Crystallography (Erice, Italy)
- Northwest Crystallography Workshop (Eugene, USA)
- 21st Congress of the International Union of Crystallography (Osaka, Japan)
- EMBO World Lecture Series (Pune, India)
- QMB Proteins Meeting (Queenstown)
- Rutherford Symposium at NZIC-NZSBMB conference (Dunedin)
- Invited seminars at Department of Chemistry, University of Naples (Italy), Novartis Vaccines, Siena (Italy), University of York (UK), Ascitis Institute, Griffith University (Australia), Institute of Molecular Biosciences and School of Molecular and Microbial Sciences, University of Queensland (Australia).



Margaret Brimble

- Symposium to honour the centenary of the Indian Institute of Science (Bangalore, India)
- Melbourne University Chemical Society Lecture; Victorian Institute of Chemical Sciences Distinguished Visiting Research Fellow (Australia)
- Australasian Society for Clinical and Experimental Pharmacology and Toxicology (ASCEPT) Conference (Queenstown)
- Association of Women in Science Conference (Christchurch)
- Rotary National Science and Technology Forum (Auckland)
- L'Oreal-UNESCO Women in Science 10 year reunion, French Academy of Science, (Paris, France)
- University of Chicago, Department of Chemistry (USA)
- Invited seminars to the Bio21 Institute, the Howard Florey Institute, the Royal Melbourne Institute of Technology, Monash University, the Victorian School of Pharmacy and the Royal Australian Institute of Chemistry, Victoria Branch (Melbourne, Australia).

Christina Buchanan

- Pacific Rim International Conference on Protein Science/ Australia Oceania Human Proteome Organisation conferences (Cairns, Australia).

Garth Cooper

- University of Manchester, Plenary Lecture in the Faculty of Life Sciences AstraZeneca 2008 Seminar Series (UK)
- MRC Immunochemistry Unit Symposium, Department of Biochemistry, University of Oxford (UK)
- University of Iceland
- deCODE Genetics (Reykjavik, Iceland)
- Institut de Biologie Structurale (Grenoble, France)
- Departments of Pharmacology and Biochemistry, University of Oxford (UK)

Bill Denny

- NZBio Conference (Auckland)
- Halpern Symposium, University of Wollongong (Australia)
- Cancer Research Technology Memorial Symposium for Dr Lloyd Kelland. University College (London, UK)
- NZBio Conference (Auckland)
- American Association for Cancer Research 2008 Annual Meeting (San Diego, USA)
- Malaghan Institute (Wellington)
- Molecular Biology (QUEST) Meeting (Queenstown)
- Global Alliance for TB Drug Development (New York, USA)
- Australian Medical & Health Research Congress (Brisbane, Australia)
- Australasian TB Conference (Auckland)
- Rutherford Medallist Forum, NIZC Conference (Dunedin)

Rod Dunbar

- Cancer Trials NZ meeting (Auckland)
- NZ Melanoma Summit (Wellington)
- Mater Medical Research Institute (Brisbane, Australia)
- Peter Medawar Institute for Pathogen Research, University of Oxford (UK)
- Kroto Research Institute, University of Sheffield (UK)

John Fraser

- 2008 International Congress on Staphylococci (Cairns, Australia)
- Annual Biology Symposium, (Greifswald, Germany)
- Australasian Society for Immunology (Canberra, Australia)
- Bernard Notcht Institute (Hamburg, Germany)
- Imperial College London, Hammersmith Hospital (UK)

Juliet Gerrard

- Gordon Conference on Biomolecular Interactions (Ventura, USA)

Peter Hunter

- UK Institute of Mechanical Engineers Prestige Smith & Nephew Lecture for 2008 (London, UK)
- Inaugural MERIT Research lecture at the University of Melbourne (Australia)
- Japanese Society for Medical and Biological Engineering, 47th Annual Meeting (Kobe, Japan)
- International Physiome Symposium (Seoul, Korea)
- Healthgrid Conference (Chicago, USA)
- 2nd International Workshop on Systems Biology (Kildare, Ireland)

Peter Shepherd

- University of Bath (UK)
- Queen Mary and Westfield College (UK)
- Western Pacific International Diabetes Federation Meeting (Wellington)
- Hegdorn Institute (Copenhagen, Denmark)
- EU Meeting on Insulin Action (Oslo, Sweden)
- Guanzhou Institute of Biomedicine and Health (China),



Collaborations

The Wilkins Centre benefits from a vast network of national and international collaborations which have been built up over a number of years by Wilkins Centre investigators. The research funded through the Centre has strengthened these and helped to establish new collaborations.

The international and national reach of these collaborations is shown in the diagram below.



New academic collaborations

In 2008 new collaborations have been established between the Wilkins Centre and

- The University of Greifswald (Germany)
- Leukaemia Research Foundation Laboratories at The University of Oxford (UK)
- The University of Manchester School of Medicine and Manchester Interdisciplinary Biocentre (UK)
- The University of Oxford Department of Chemistry (UK)
- The University of London Kings College (UK)
- The University of Iceland
- The European Synchrotron Radiation Facility (France)
- The University of Texas Medical Center (USA)

Uptake of Wilkins Centre research and expertise

The primary focus of the Wilkins Centre is to carry out research into new therapies for disease. The successful translation of this research into the development phase requires uptake by the commercial biotechnology sector. This is enabled by the close links that the Wilkins Centre has with the biotechnology companies ProActa Inc, Pathway Therapeutics Ltd and Symansis Ltd. As noted under the Highlights above, projects initiated by the Wilkins Centre, and subsequently developed with support from other research funding agencies, are now on the path to commercialisation. This Wilkins Centre-initiated activity extends the Wilkins Centre's established role in supporting progression to commercial uptake of discoveries made under funding from other sources.

As part of the research process, Wilkins Centre investigators have developed knowledge and expertise in areas of science that are vital to the biotechnology sector. In addition to participating in academic collaborations, Wilkins Centre investigators also act as consultants and contractors for biotechnology companies. The Wilkins Centre also makes its equipment and service facilities and expertise available for use by these companies.

In 2008 the expertise of Wilkins Centre investigators was sought by the following companies:

- Paraco Ltd.
- Mattersmiths Holdings
- Proacta Inc
- Pathway Therapeutics Ltd
- Symansis Ltd
- Neuren Pharmaceuticals Ltd
- Aquapharm Biodiscovery Ltd (Scotland)
- InvivoGen (France)
- Androgenix Ltd
- Orico Ltd

As noted above under Organisational Development, Wilkins Centre equipment services were also used by a large number of companies and institutions.

Awards and Honours

Pillar of Immunology



Graham Le Gros has received a major international honour by being selected as a “Pillar of Immunology”. Graham is the Director of the Malaghan Institute of Medical Research, a leading immunology research centre based in Wellington, and a Wilkins Centre Associate Investigator.

A Pillar of Immunology is a cornerstone scientific discovery that has revolutionised the way we think about and understand how our immune systems function. They are selected by a panel of world-renowned immunologists on behalf of the Journal of Immunology, a premier publication for the field of immunology. To date

there have only been 30 such published scientific pieces of work (out of the many hundreds of thousands going back to the 1960s) that have been awarded this prestigious title.

“The research paper demonstrated how simple cell based assays could be used to understand what happens during immune responses,” said Graham. “It revealed unexpected properties for the T cell produced cytokine IL-4 and how it coordinated the allergic immune response.”

The extraordinary scientific insight provided by Graham and his colleagues’ ingenious approach to understanding the basic biology of interleukin-4 (IL-4) is as relevant today as it was when it was first published back in 1990.

Early Career Researcher Award

David Ackerley was recognized in 2008 with a Victoria University of Wellington Early Career Researcher Award. David is a Senior Lecturer in the School of Biological Sciences at Victoria University.

2008 Applied Biosystems Award

The 2008 Applied Biosystems Award, the premier prize of the New Zealand Society of Biochemistry and Molecular Biology was awarded to Emily Parker at the New Zealand Institute of Chemistry conference in December 2008.

Top Student Poster

Gareth Prosser, a PhD student working with David Ackerley at Victoria University, won the top student poster prize at the NZ Microbiology Society conference in Christchurch in November, with his poster entitled “The SOS-chromotest and anticancer prodrug activation: New applications for an old technique”.

World Class New Zealand Awards

As noted above in Highlights, both Garth Cooper and Margaret Brimble were honoured with awards at the 2008 World class New Zealand Awards.

Liley Medal

As noted above in Highlights, Ted Baker was awarded with the Liley Medal for Excellence in Health Research.

MacDiarmid Awards

As noted above in Highlights, PhD student HaeJoo Kang was the runner up in the 'Advancing Human Health and Wellbeing' section of the 2008 MacDiarmid Awards.

Financial Report 2008

<u>Operating Fund^a</u>	<u>\$ 2008</u>	<u>\$ 2007</u>
<u>Income</u>		
CoRE grant	3,373,067	2,773,333
Equipment User charges ^b	226,958	244,832
Balance from previous year ^c	1,559,186	1,615,962
Total Income	5,159,211	4,634,127
<u>Expenditure</u>		
Salaries	1,195,280	928,809
Overheads	909,174	889,609
Project costs ^d	478,742	472,128
Student support (PhD and other) ^d	206,588	278,457
Travel	93,592	67,287
Depreciation ^e	494,543	438,649
Total Expenses	3,377,919	3,074,941
Commitments^f	587,511	564,638
Income less expenditure and commitments^g	1,193,781	994,548
 <u>Capital Expenditure Fund</u>		
<u>Income</u>		
Balance of TEC grant 2002	42,866	
TEC grant 2008	2,732,726	
Total Income	2,775,592	
<u>Expenditure</u>		
Capital expenditure 2008	2,052,718	
Funds carried forward to 2009^h	722,874	

Notes

- a) This financial report is for the period 1st January to 31st December 2008 and covers the second six months of the Wilkins Centre Year 6 (CoRE grant 2002 to 2008) and the first six months of Wilkins Centre Year 7 (CoRE grant 2008 to 2014). This report only details income and expenditure relating to the CoRE grant funding that the Wilkins Centre receives from the Tertiary Education Commission. It does not contain details of external operating funding to Centre investigators from other funding agencies, which in 2008 was estimated to be \$21M.
- b) These equipment user charges are collected by the Wilkins Centre from users of the large items of capital equipment purchased with funding from the Centre capital equipment fund. The charges are used to offset the operational costs of the equipment.
- c) This brought forward balance is unspent funding from previous years of the Wilkins Centre that will be used to fund research initiatives in 2009/2010.
- d) These costs include the costs of subcontracts for Associate Investigator's research projects during 2008. Expenditure in direct costs was significantly less than budget in 2008 due to deferment of the first flexible funding round to December 2008. Corresponding increases in expenditure is forecast for 2009/2010 now that the flexible funding process is operational.
- e) Depreciation costs were less than budget due to delays in installation of capital equipment.
- f) These commitments refer to contracts or agreements to fund staff, students and associated costs that were in place as of the 31st December 2008 and will be deducted from the unspent funding brought forward from previous years of the Wilkins Centre.
- g) This balance of funding will be used to fund research initiatives to support the MWC research programme in 2009 and 2010.
- h) As of 31st December 2008 there was a total of \$109,826 of purchase order commitments against this balance.



Directory

Governing Board Members

Mr. Bill Falconer (Chair)

Prof Dick Bellamy

Prof Gary Hook

Mr John Loof

Prof Iain Martin

Prof George Peterson

Ms Maxine Simmons.

Scientific Advisory Board Members

Dr Jim Watson (Chair)

Prof Peter Andrews

Prof Sir Tom Blundell

Prof Suzzane Cory

Dr Jilly Evans

Prof Shankar Subramaniam

Prof Dick Wettenhall

Principal Investigators

Prof Ted Baker (Director)
School of Biological Sciences,
The University of Auckland

Prof John Fraser (Deputy Director)
Department of Molecular Medicine
and Pathology,
The University of Auckland

Assoc Prof Rod Dunbar (Director Elect)
School of Biological Sciences,
The University of Auckland

Prof Margaret Brimble
Department of Chemistry,
The University of Auckland

Prof Garth Cooper
School of Biological Sciences,
The University of Auckland

Prof Bill Denny
Auckland Cancer Society Research Centre,
The University of Auckland

Prof Peter Hunter
Auckland Bioengineering Institute,
The University of Auckland

Prof Peter Shepherd
Department of Molecular Medicine
and Pathology,
The University of Auckland

Associate Investigators

Dr David Ackerley
School of Biological Sciences,
Victoria University of Wellington

Assoc Prof Vickery Arcus
Department of Biological Sciences,
University of Waikato

Prof Paul Atkinson
School of Biological Sciences,
Victoria University of Wellington

Prof Bruce Baguley
Auckland Cancer Society Research Centre,
The University of Auckland

Dr Gib Bogle
Auckland Bioengineering Institute,
The University of Auckland

Prof Peter Browett
Department of Molecular Medicine
and Pathology,
The University of Auckland

Dr Christina Buchanan
Department of Molecular Medicine
and Pathology,
The University of Auckland

Assoc Prof Gregory Cook
Department of Microbiology
and Immunology,
University of Otago

Dr Edmund Crampin
Auckland Bioengineering Institute,
The University of Auckland

Dr Andrew Dingley
Department of Chemistry,
The University of Auckland

Dr Gary Evans
Industrial Research Ltd

Prof Mike Findlay
Department of Oncology,
The University of Auckland

Dr Jack Flanagan
Auckland Cancer Society Research Centre,
The University of Auckland

Dr Richard Furneaux
Industrial Research Ltd

Assoc Prof David Greenwood
Plant and Food Research

Prof Juliet Gerrard
School of Biological Sciences,
University of Canterbury

Dr Mark Hampton
Free Radical Research Group,
University of Otago, Christchurch

Dr Paul Harris
Department of Chemistry,
The University of Auckland

Dr Debbie Hay
School of Biological Sciences,
The University of Auckland

Assoc Prof Michael Hay
Auckland Cancer Society Research Centre,
The University of Auckland

Dr Ian Hermans
Malaghan Institute of Medical Research

Dr Tony Hickey
School of Biological Sciences,
The University of Auckland

Prof Geoffrey B. Jameson
Institute of Fundamental Sciences,
Massey University

Dr Richard Kingston
School of Biological Sciences,
The University of Auckland

Prof Graham Le Gros
Malaghan Institute of Medical Research

Dr Kerry Loomes
School of Biological Sciences,
The University of Auckland

Dr Shaun Lott
School of Biological Sciences,
The University of Auckland

Assoc Prof Peter Metcalf
School of Biological Sciences,
The University of Auckland

Dr Kathy Mountjoy
Department of Physiology,
The University of Auckland

Dr Richard Newcomb
Plant and Food Research

Assoc Prof Poul Nielsen
Auckland Bioengineering Institute,
The University of Auckland

Assoc Prof Brian Palmer
Auckland Cancer Society Research Centre,
The University of Auckland

Assoc Prof Emily Parker
Department of Chemistry,
University of Canterbury

Dr Adam Patterson
Auckland Cancer Society Research Centre,
The University of Auckland

Dr Anthony Phillips
School of Biological Sciences,
The University of Auckland

Assoc Prof Cristin Print
Department of Molecular Medicine
and Pathology,
The University of Auckland

Dr Thomas Proft
Department of Molecular Medicine
and Pathology,
The University of Auckland

Dr Matt Templeton
Plant and Food Research

Dr Peter Tyler
Industrial Research Ltd

Prof Thomas Rades
National School of Pharmacy,
University of Otago

Assoc Prof Gordon Rewcastle
Auckland Cancer Society Research Centre,
The University of Auckland

Dr Franca Ronchese
Malaghan Institute of Medical Research

Dr Jeff Smaill
Auckland Cancer Society Research Centre,
The University of Auckland

Prof Nic Smith
University Computing Laboratory,
The University of Oxford

Prof James Sneyd
Department of Mathematics,
The University of Auckland



Dr Christopher Squire
School of Biological Sciences,
The University of Auckland

Dr John Taylor
School of Biological Sciences,
The University of Auckland

Dr Moana Tercel
Auckland Cancer Society Research Centre,
The University of Auckland

Dr Yu Wang
Department of Pharmacology and
Pharmacy,
University of Hong Kong

Prof William Wilson
Auckland Cancer Society Research Centre,
The University of Auckland

Assistant Prof Aimin Xu
Department of Pharmacology and
Pharmacy,
University of Hong Kong

Dr Shaoping Zhang
School of Biological Sciences,
The University of Auckland

CoRE funded research fellows

Dr Indira Basu
Department of Molecular Medicine
and Pathology,
The University of Auckland

Dr Christina Buchanan
Department of Molecular Medicine
and Pathology,
The University of Auckland

Dr Claire Chaussade
Department of Molecular Medicine
and Pathology,
The University of Auckland

Dr Jack Flanagan
Auckland Cancer Society Research Centre,
The University of Auckland

Dr Paul Harris
Department of Chemistry,
The University of Auckland

Dr Nicola Jackson
Department of Molecular Medicine
and Pathology,
The University of Auckland

Dr Mia Jullig
School of Biological Sciences,
The University of Auckland

Dr Jerome Le Nours
School of Biological Sciences,
The University of Auckland

Dr Catherine Lloyd
Auckland Bioengineering Institute,
The University of Auckland

Dr Grant Munro
Department of Molecular Medicine
and Pathology,
The University of Auckland

Dr Gordon Rewcastle
Auckland Cancer Society Research Centre,
The University of Auckland

Dr Jeff Small
Auckland Cancer Society Research Centre,
The University of Auckland

Dr Christopher Squire
School of Biological Sciences,
The University of Auckland

Dr Hiliary Sheppard
School of Biological Sciences,
The University of Auckland

CoRE funded research technicians

Mr Richard Bunker
School of Biological Sciences,
The University of Auckland

Ms Fiona Clow
Department of Molecular Medicine
and Pathology,
The University of Auckland

Mr Ivan Ivanovic
School of Biological Sciences,
The University of Auckland

Ms HaeJoo Kang
School of Biological Sciences,
The University of Auckland

Ms Renata Kowalczyk
Department of Chemistry,
The University of Auckland

Mr James Lawson
Auckland Bioengineering Institute,
The University of Auckland

Mr Tiong Lim
Auckland Bioengineering Institute,
The University of Auckland

Mr Justin Marsh
Auckland Bioengineering Institute,
The University of Auckland
Mr Martin Middleditch
School of Biological Sciences,
The University of Auckland

Ms Sintia Winkler
School of Biological Sciences,
The University of Auckland

Ms Zhening Zhang
School of Biological Sciences,
The University of Auckland

CoRE funded PhD students

Ms Sasha Anagnostou
Department of Molecular Medicine
and Pathology,
The University of Auckland

Ms Jessica Chaston
School of Biological Sciences,
The University of Auckland

Ms Melanie Collings
School of Biological Sciences,
The University of Auckland

Ms Mridula Dogra
Department of Molecular Medicine
and Pathology,
The University of Auckland

Ms Orla Finch
Department of Chemistry,
The University of Auckland

Mr Daniel Hurley
Auckland Bioengineering Institute,
The University of Auckland

Ms Nicola Jackson
Department of Molecular Medicine
and Pathology,
The University of Auckland

Mr Andrew Marshall
Auckland Cancer Society Research Centre,
The University of Auckland

Ms Hayley Reynolds
Auckland Bioengineering Institute,
The University of Auckland

Ms Jennifer Sweny
School of Biological Sciences,
The University of Auckland

Ms Sophie Syddall
Auckland Cancer Society Research Centre,
The University of Auckland
Ms Amanda Taylor
Department of Molecular Medicine and
Pathology,
The University of Auckland

Ms Natasha Willoughby
Department of Molecular Medicine and
Pathology,
The University of Auckland

Ms Zhening Zhang
School of Biological Sciences,
The University of Auckland

CoRE funded management

Mr Peter Lai
Maurice Wilkins Centre,
The University of Auckland

Ms Rochelle Ramsay
Maurice Wilkins Centre,
The University of Auckland



Contact Details



Director/Principal Investigator

Professor Ted Baker

School of Biological Sciences
Faculty of Science
The University of Auckland
Private Bag 92019
Auckland 1142, New Zealand
Ph +64 9 373 7599 ext 84415
email: ted.baker@auckland.ac.nz



Deputy Director/Principal Investigator

Professor John Fraser

School of Medical Sciences
Faculty of Medical and Health Sciences
The University of Auckland
Private Bag 92019
Auckland 1142, New Zealand
Ph +64 9 373 7599 ext 86036
email: jd.fraser@auckland.ac.nz



Director-Elect/Principal Investigator

Associate Professor Rod Dunbar

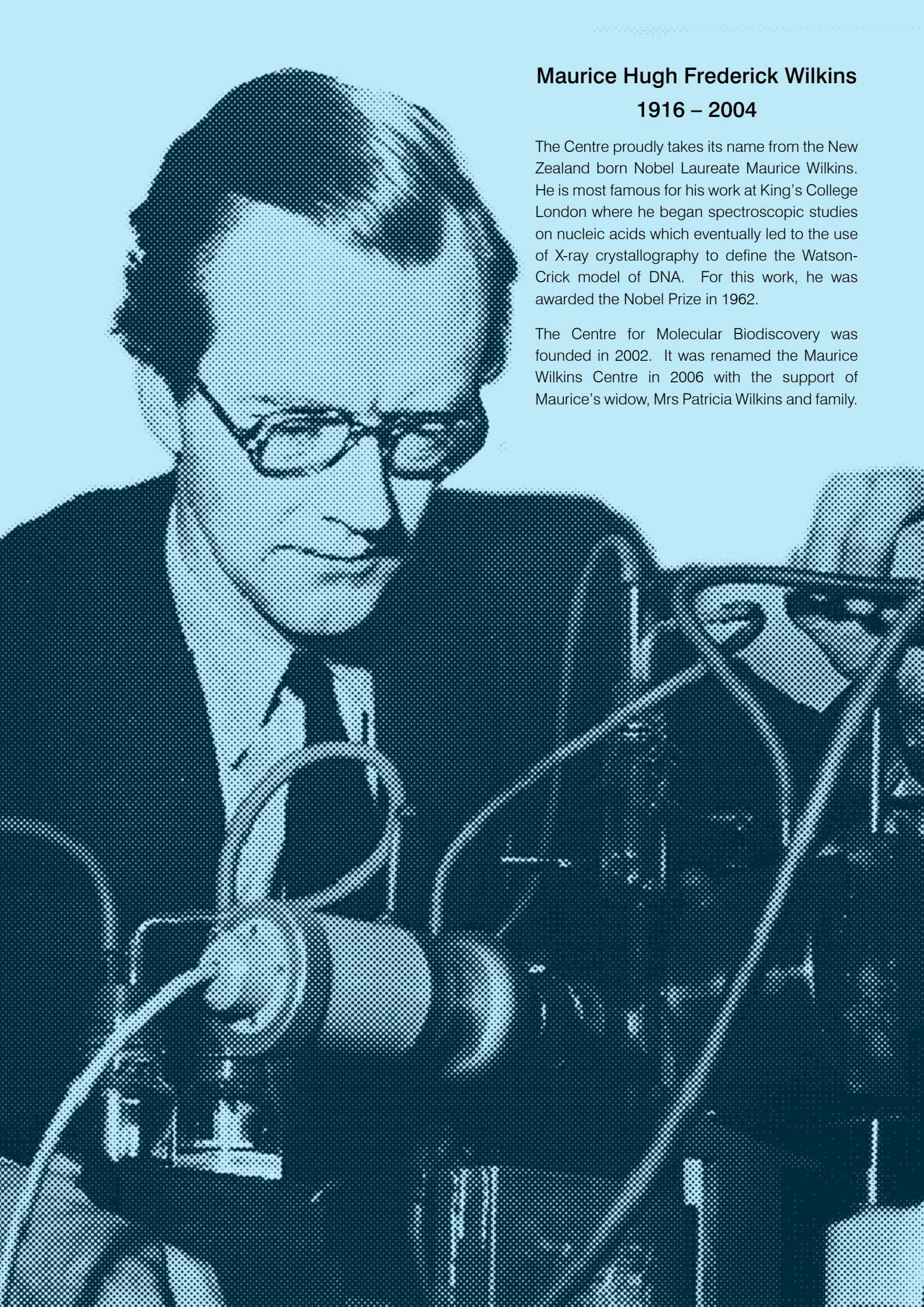
School of Biological Sciences
Faculty of Science
The University of Auckland
Private Bag 92019
Auckland 1142, New Zealand
Ph +64 9 373 7599 ext 85765
email: r.dunbar@auckland.ac.nz



Research Manager

Ms Rochelle Ramsay

Maurice Wilkins Centre
c/o School of Biological Sciences
Faculty of Science
The University of Auckland
Private Bag 92019
Auckland 1142, New Zealand
Ph +64 9 373 7599 ext 85533
email: rj.ramsay@auckland.ac.nz



Maurice Hugh Frederick Wilkins

1916 – 2004

The Centre proudly takes its name from the New Zealand born Nobel Laureate Maurice Wilkins. He is most famous for his work at King's College London where he began spectroscopic studies on nucleic acids which eventually led to the use of X-ray crystallography to define the Watson-Crick model of DNA. For this work, he was awarded the Nobel Prize in 1962.

The Centre for Molecular Biodiscovery was founded in 2002. It was renamed the Maurice Wilkins Centre in 2006 with the support of Maurice's widow, Mrs Patricia Wilkins and family.

