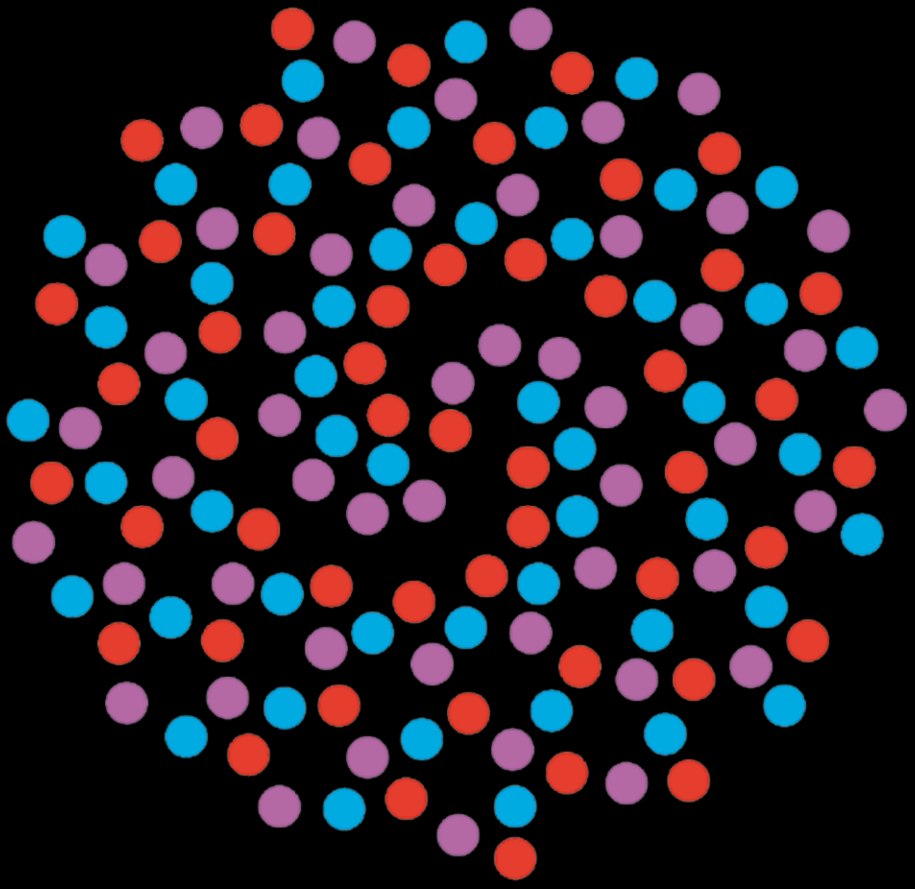


MAURICE WILKINS CENTRE

New Zealand's Centre of Research Excellence
targeting human disease

Annual Report 2010

Maurice Wilkins Centre

The Maurice Wilkins Centre is New Zealand's Centre of Research Excellence targeting major human diseases. It focuses on cancer, diabetes and infectious disease.

New Zealand has an outstanding reputation for biomedical research. The Centre aims to harness this expertise to develop cutting-edge drugs and vaccines, tools for early diagnosis and prevention, and new models of disease. In addition to translational research that directly targets human disease the Maurice Wilkins Centre encourages innovative fundamental science that has the potential for high impact on human health.

The Maurice Wilkins Centre is a multidisciplinary network that brings together leading biologists, chemists and computer scientists. It comprises 97 investigators throughout the country, and over 100 early-career affiliates, linking researchers from six Universities, three Crown Research Institutes and a private research institute.

The Centre incorporates the majority of New Zealand researchers who have discovered new drugs that have progressed to clinical trials, most of the investigators developing new vaccines targeting human infectious disease and cancer, and many of those developing new diagnostic tools.

As the national hub for molecular biodiscovery the Centre provides a point of contact for a broad range of local scientific expertise. It cultivates collaborations with international researchers and engages with industry and the medical profession. It is committed to building scale in the New Zealand biomedical research sector and thereby delivering optimal health and economic outcomes for the country.

For more information see www.mauricewilkinscentre.org

For more information on New Zealand Centres of Research Excellence see www.acore.ac.nz

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND
Te Whare Wānanga o Tāmaki Makaurau

UNIVERSITY of OTAGO
Te Whare Wānanga o Otāgo
NEW ZEALAND

TE WHARE WĀNANGA O TE ŪPOKO O TE IKA A MĀUI
VICTORIA
UNIVERSITY OF WELLINGTON

THE UNIVERSITY OF WAIKATO
Te Whare Wānanga o Waikato

UC
UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

INDUSTRIAL RESEARCH LIMITED
Te Tauihu Pūtaiao
IRL

MALAGHAN INSTITUTE
OF MEDICAL RESEARCH

agresearch

MASSEY UNIVERSITY

Plant & Food RESEARCH
RANGAHAU AHUMĀRA KAI

MAURICE WILKINS CENTRE
FOR MOLECULAR BIODISCOVERY

Director's Report

As you will find in this report, the Maurice Wilkins Centre continues to grow, and to contribute strongly to New Zealand science and culture, through its intertwined scientific and educational programmes. The report of the international Scientific Advisory Board, which reviewed the Centre's progress over two days in April, included a resounding endorsement of the quality of the Centre's science. Amongst many highlights, we once again celebrate new drugs invented in New Zealand progressing to international clinical trials – further evidence that our scientific community has the capacity to mount new attacks on serious human disease.

But beyond these wonderful scientific achievements this report also shows how the Maurice Wilkins Centre is fulfilling the other roles originally envisioned for Centres of Research Excellence (CoREs) – building scientific capability, developing human capital, and fostering linkages between the scientific community and other communities within New Zealand.

This year, the Tertiary Education Commission asked all the CoREs to review their activities, and their strategies for future growth. In common with the seven other CoREs, the Maurice Wilkins Centre has evolved since its founding in 2002. Systemic changes introduced in late 2008 have increased the impact of the Maurice Wilkins Centre on New Zealand biomedical research. In particular the flexible research seeding programme has now sparked almost 50 exciting new projects involving collaborations across seven institutions

As the Maurice Wilkins Centre evolves, so does its vision of how it can best contribute to the New Zealand science and innovation system. Much of this vision stems from asking a simple question: what are the unique roles that the Maurice Wilkins Centre can play? To a degree, all the CoREs need to consider this question – not least to justify continuing support from the taxpayer – but the answers for the Maurice Wilkins Centre are coloured by the unique opportunities offered by the scientific space it occupies.

One of the unique roles of the Maurice Wilkins Centre is to build scale in New Zealand's biomedical research. Why should building scale be necessary? Our individual investigators consistently win international recognition, and our research institutions provide infrastructure and people to enable their research, supported by both public and charitable funding. Yet for a variety of reasons – some cultural, some institutional – New Zealand has often forgone opportunities to forge scientific partnerships capable of scaling up its science. The Maurice Wilkins Centre now has a crucial role to play in bringing together scientists from across our research institutions to build biomedical research

programmes on a scale that is more ambitious – and more internationally competitive. This role may be particularly important in a country that has tended to lionise the pioneering individual – and still expects such individuals to succeed alone in the wilderness armed with nothing more than some fencing wire and a cheerful disposition.

The Maurice Wilkins Centre is also uniquely placed to foster inter-disciplinary research. Developing new ways to prevent, detect, and treat human disease necessitates co-operation across scientific boundaries – for example most new drugs come from intense collaboration between chemists and biologists. Yet learning each others' scientific dialects can be daunting, and inter-disciplinary collaboration needs to be carefully nurtured over time-scales beyond 3 year research grant cycles. In fact some New Zealand institutions already have a proud and sustained record in inter-disciplinary biomedical research, with the success of the Auckland Cancer Society Research Centre over several decades perhaps being the most impressive example. A second crucial role for the Maurice Wilkins Centre is now to build on these successful local models, and enable inter-disciplinary collaboration across a much larger national network. Here New Zealand might make an advantage of its relatively small size and geographic isolation: having less opportunity to collaborate with local colleagues in your own discipline perhaps makes inter-disciplinary work more attractive. But over time, the Maurice Wilkins Centre aims to completely remove such traditional scientific boundaries from the vision of our future biomedical research leaders, by steeping them in the language and practice of each others' science. As described in this report, many of our younger investigators are already developing just such breadth of vision in their research.

A third unique role for the Maurice Wilkins Centre is in linking top biomedical scientists to other networks. In 2010 two initiatives were emblematic of this function – one involving outreach to medical specialists, the other to business.

In the first initiative, the Maurice Wilkins Centre convened a national symposium focused on "superbugs", bringing its scientists together with clinicians from the front line in the defence against infectious agents. This event engendered a two-way exchange that is all too rare, at once updating Maurice Wilkins Centre scientists about the actual microbial threats facing the nation, and providing the clinical community with a vision of national research capability. This interaction has already stimulated plans for new research projects responding to urgent clinical needs. The event also garnered a major feature in one of the Sunday newspapers that eschewed media hyperbole about "superbugs" in favour of communicating the symposium's conclusions to the public. Given the heavy demands on clinicians' time, the Maurice Wilkins Centre sees an important role in initiating and enabling clinically-focused research projects, on issues of national importance that are prioritised by the clinicans themselves.

The second initiative was active consultation with New Zealand businesses involved in the manufacture of therapeutic agents. While it might be assumed that business knows how to access academic expertise, in practice many businesses report patchy knowledge of national research capability, and some degree of bafflement about how to access services that can advance their business. Direct contact with Maurice Wilkins Centre leaders has stimulated several major New Zealand businesses to invest in new research projects, and ongoing consultation has led to new strategic initiatives to deepen the links between New Zealand businesses and Maurice Wilkins Centre researchers. New Zealand already has long experience of commercialising its research into human therapeutic agents, through contract research, licensing, and spin-out companies. But the Maurice Wilkins Centre sees new opportunities to capture both the health and economic benefits of New Zealand biomedical research by working more closely with major employers domiciled within New Zealand. Importantly this does not mean that the Centre focuses on close-to-market applied research – New Zealand businesses recognise that the greatest value is likely to lie in highly innovative, world-first discoveries, such as those reported in the following pages.

These unique roles provide the Maurice Wilkins Centre with some guidance about where to invest its resources. Building scale in New Zealand's biomedical research, sparking innovative inter-disciplinary research collaborations, and linking national research capacity to medical imperatives and business opportunities, are activities that dovetail well with other parts of the science and innovation system.

Finally it must be said that the Maurice Wilkins Centre can only prosper and grow with the support of a wide community. I would like to express particular thanks to the members of the Management Committee and the Governing Board, who guide Maurice Wilkins Centre strategy. Pauline Curtis from the University of Auckland's Communications office has developed our new communications strategy, and has played a central role in preparing this report. I also extend my congratulations to Rochelle Ramsay, the Maurice Wilkins Centre Research Manager, who co-ordinates an extraordinary amount of activity with minimal administrative resources, ably supported by Peter Lai. But at the heart of the Maurice Wilkins Centre is the network of talented scientists and students whose work is documented in this report. Their continued enthusiastic contribution to Centre activities is what powers the Maurice Wilkins Centre's success.

Rod Dunbar
Director

Associate Professor Michael Baker and Dr Christian Linke at the ‘Superbugs’ symposium.
Image courtesy of Godfrey Boehnke.

Contribution to National Goals

The Centres of Research Excellence are 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 is anticipated that the CoREs will 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 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

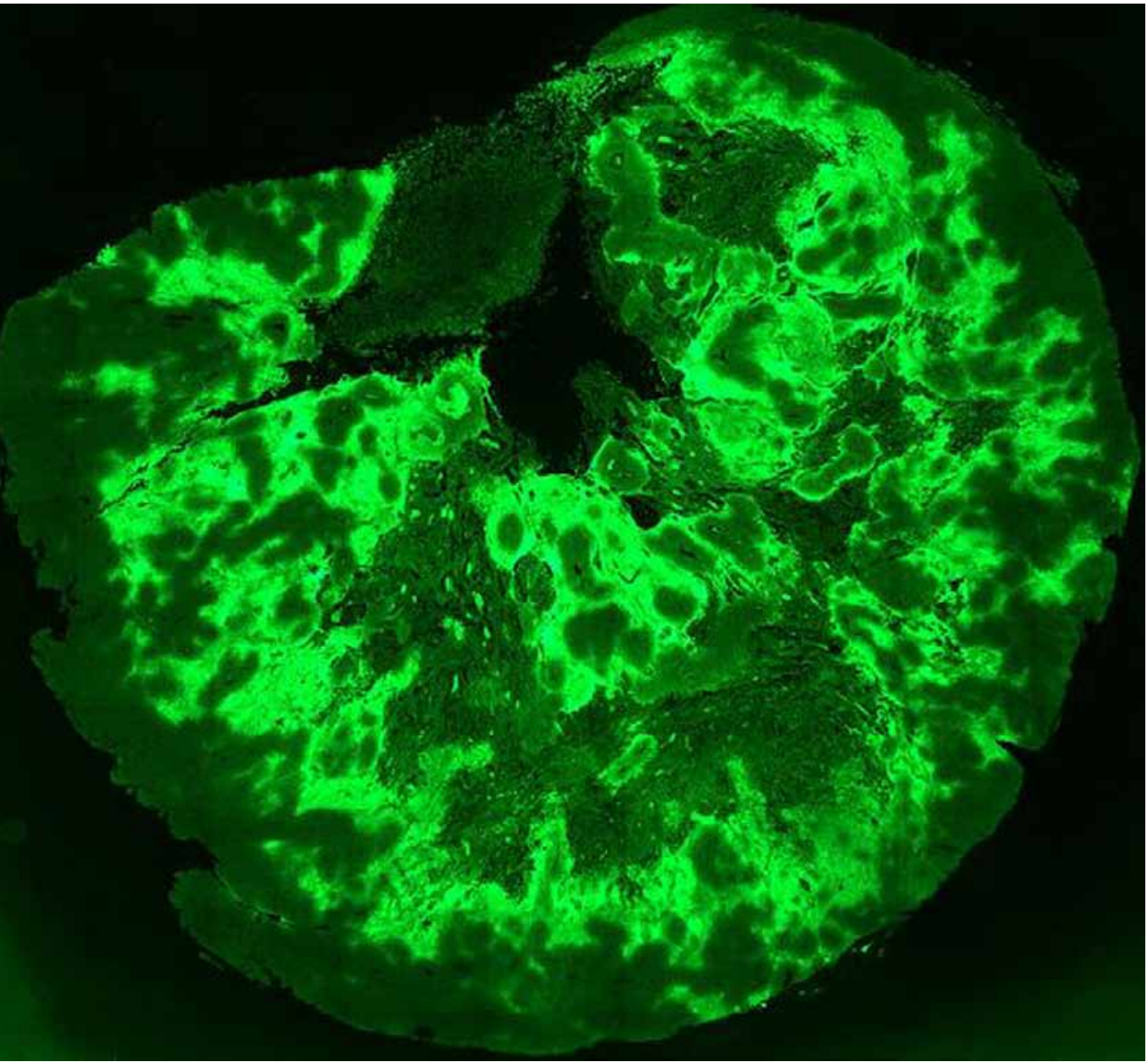
The Maurice Wilkins Centre conducts highly innovative research and enables innovation in the wider research and business sector. Its goal is to become New Zealand's engine for the discovery of new therapies and diagnostic tests. Innovation in research is often to be found at the interface between disciplines, through cross fertilisation of ideas and technology. The Maurice Wilkins Centre brings together researchers from a range of disciplines to tackle complex questions that no one field could address alone. It also encourages a more collegial approach within the biomedical research sector in New Zealand. The Centre's work leads to the establishment of new spin-out companies and contributes directly to innovation within established companies through contract research, consultation, and sharing of facilities and expertise. Fundamental scientific discoveries and novel technologies developed within the Centre enable new lines of research, advance our understanding of human health and disease, accelerate the development of new approaches for human disease, and advance other research fields (including demonstrable impact on New Zealand's primary industries).

Social Development

One of the Maurice Wilkins Centre's contributions to social development in New Zealand is through improvements to human health. Our major focus is to improve the diagnosis and treatment of diseases such as cancer, diabetes, and infectious disease – all increasing challenges for New Zealand society. At the same time, science is an important aspect of our culture, and the Maurice Wilkins Centre plays a role in increasing the impact of science within New Zealand, as well as connecting us strongly to the international scientific community. The multi-disciplinary and collaborative ethos of the Maurice Wilkins Centre ensures an excellent training environment for graduate students and younger scientists, including exposure to the ethical, managerial and entrepreneurial aspects of translational science. It is particularly important for students at all levels of education to see that scientific research of the highest international quality can be done in New Zealand, and that it can make major contributions to the social and economic well-being of their country. The example set by Maurice Wilkins Centre leaders in choosing to return from research posts overseas, committed to carrying out world-class research in New Zealand, provides a powerful incentive for our top students to do likewise in future.

Economic Development

The Maurice Wilkins Centre's focus on new approaches to human disease has dual importance for the New Zealand economy, in both improving health and providing direct economic gains. Maurice Wilkins Centre investigators have to date been responsible for bringing a large portfolio of drugs to clinical trial, with a deep pipeline of new projects in pre-clinical development. This strong portfolio means that New Zealand maintains its exciting potential in the biopharmaceutical sector, one of the few economic sectors capable of driving explosive economic growth. The intimate links between the Maurice Wilkins Centre research programme and recent start-up companies demonstrates that research findings can and will be developed for the national good. Direct economic gains also come from international research contracts, and milestone and licensing revenue from overseas partnerships – effectively a "weightless" export industry. Less direct economic gains come from Maurice Wilkins Centre investigators' significant impact on the international rankings of our educational institutions, which affect their ability to attract international students. The Maurice Wilkins Centre also plays an important role in promoting and validating our national scientific capabilities abroad, increasing the reputation of New Zealand as a source of high-value research.



Fluorescence imaging showing areas of hypoxia in a tumour.
Image courtesy of Dr Maria Abbattista and Dr Adam Patterson (Translational Therapeutics Team, Auckland Cancer Society Research Centre).

Highlights

The following stories describe 2010 highlights in research, training and science education .

Cancer stealth drug enters clinical development

The first of an exciting new class of anticancer drugs will proceed to clinical development under an international deal announced in early 2011.

Eliminating cancer cells without harming healthy tissue is one of the greatest challenges facing cancer scientists. “Standard cancer therapies are indiscriminate in their attack against cancer cells and normal cells, and their toxicity in healthy tissues limits the dose that can safely be given to patients,” says cancer biologist Dr Adam Patterson.

To overcome this, Adam and medicinal chemist Dr Jeff Smaill have designed an exciting new class of anticancer “stealth” drugs that only become active once they reach a tumour. The compounds use the low oxygen levels (hypoxia) found in many tumours to convert from inactive “prodrugs” into highly active anticancer agents.

“About two thirds of tumours contain zones that cannot be reached by oxygen,” says Jeff. “Cancer cells in these zones are more resistant to treatment, making them an important cause of treatment failure and cancer relapse, and scientists have been searching for a way to eliminate these cells for many years. There is also growing evidence that other parts of a tumour cycle through periods of hypoxia lasting from minutes to days.”

“Our prodrugs not only selectively target tumours but reside there for an unusually long time, releasing their active form slowly. So we can effectively deliver much more of our drug into a tumour than is possible with standard chemotherapy. Our research to date suggests that this is associated with far greater efficacy against tumours.”

The prodrugs target Human Epidermal growth factor Receptors (HERs) that are important for normal cell growth but become overactive or mutated in many cancers. Since the prodrugs cannot convert into toxic form in the presence of oxygen, normal HER activity in healthy tissue is protected. Unlike drugs approved to date, the prodrugs inhibit all members of the HER family and may therefore be effective against a wider range of tumours, and provide permanent rather than temporary inhibition of HER activity.

PR509 is part of a pipeline of hypoxia-activated prodrugs from The University of Auckland licensed to pharmaceutical company Proacta Incorporated, a spin-out from the university founded by Professors Bill Wilson and Bill Denny. A deal between Proacta and Yakult Honsha Co Ltd (Tokyo) will see PR509 developed for non-small cell lung cancer and likely evaluated in other cancers such as gastric, breast, and pancreatic cancer.

Adam and Jeff are Auckland Cancer Society Research Centre members and Maurice Wilkins Centre investigators. The Maurice Wilkins Centre provided partial salary support for the research, which has also been supported by grants from the Foundation for Research, Science and Technology, Health Research Council of New Zealand and Proacta.

Dr Sally Roberts speaking at the Superbugs Symposium
Photo courtesy of Godfrey Boehnke.

Joining forces against infectious disease

The 2010 Superbugs Symposium convened by the Maurice Wilkins Centre brought together more than 350 medical professionals and scientists fighting infectious disease.

"As the national Centre of Research Excellence focusing on human disease, we have an important role to play connecting medical professionals who face challenging clinical problems with scientists who can study those problems in depth," says Director Professor Rod Dunbar. "The rising burden of infectious disease in New Zealand and the breadth and depth of our infectious disease research made 'superbugs' a natural focus for the symposium."

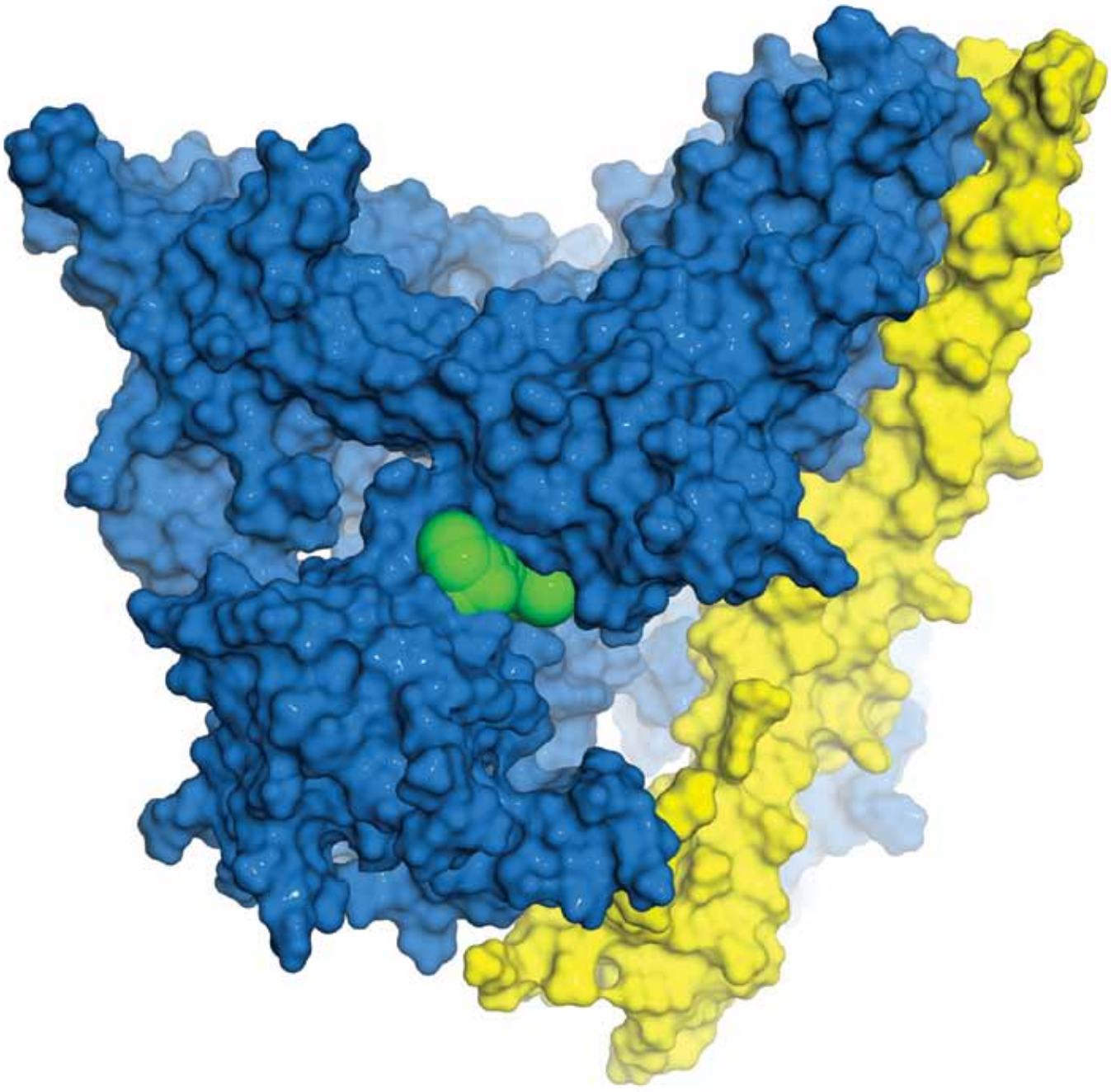
"Until fairly recently, the conventional wisdom was that infectious diseases were disappearing," said University of Otago epidemiologist Associate Professor Michael Baker, who presented new findings at the event. "In fact our research shows that over the last 20 years the burden of infectious disease in New Zealand has increased significantly. Infectious disease as a cause of hospitalisations rose from 18 to 26 percent in the period 1989 to 2008, which translates to 20,000 extra hospital admissions each year."

Dr Sally Roberts, Clinical Head of Microbiology, Labplus at Auckland District Health Board, said that one of the greatest challenges facing clinicians is the rise of anti-microbial resistant organisms like ESBLs* which are becoming a problem in hospitals and the community. Diseases caused by *Streptococcus pyogenes*, such as rheumatic fever, were also major clinical concerns."It's valuable for clinicians to meet with scientists doing the basic research that can help us to answer some of these questions and to allow future collaboration between the medical and scientific community. We don't often meet to discuss problems in this manner and this day has been fantastic for that," she said.

A panel discussion at the conclusion of the symposium highlighted the importance of basic preventive measures such as fastidious hospital hygiene and rapid and aggressive responses when outbreaks occur. But the panel advised that high-technology approaches are also needed, to develop new diagnostic techniques, vaccines, and antibiotics capable of dealing with organisms that escape infection control. "The science presented on the day, including new antimicrobial drugs entering clinical trials, clearly demonstrated that New Zealand has the scientific capability to attack many of the problems and threats highlighted by the clinical community, a process the Maurice Wilkins Centre will continue to foster" says Rod

The symposium followed a similar Maurice Wilkins Centre event in 2009 focusing on the links between science and business. "We aim to build a comprehensive national network extending from the medical profession through to commercial partners who can apply and add value to our scientific discoveries," says Rod.

** ESBL: Bacteria carrying a gene encoding Extended Spectrum Beta-Lactamase, an enzyme that confers resistance to many common antibiotics.*



Representation of the 3D structure of the PI3K alpha protein (blue) bound to the regulatory subunit p85 (yellow) with the compound A66 (green) modelled in the nucleotide binding site of the PI3K alpha kinase domain.
Image courtesy of Dr Jack Flanagan (Auckland Cancer Society Research Centre).

Drug selection a milestone for spin-out

In 2010 Maurice Wilkins Centre investigators Professors Bill Denny and Peter Shepherd selected a new anticancer drug candidate for clinical development, triggering US $4.5 million investment in the pharmaceutical company they founded two years earlier.

Professors Bill Denny and Peter Shepherd established Pathway Therapeutics in New Zealand to discover and develop inhibitors of phosphatidylinositol-3-kinase (PI3K) to treat cancer and inflammatory disease. The scientists credit the Maurice Wilkins Centre with bringing their research groups together. Bill is a medicinal chemist who co-directs the Auckland Cancer Society Research Centre while Peter is an expert in cell signalling. They collaborate on creating new drugs to inhibit PI3K, a family of four signalling proteins (alpha, beta, gamma and delta) that controls critical cell processes, from growth and proliferation to metabolism and survival.

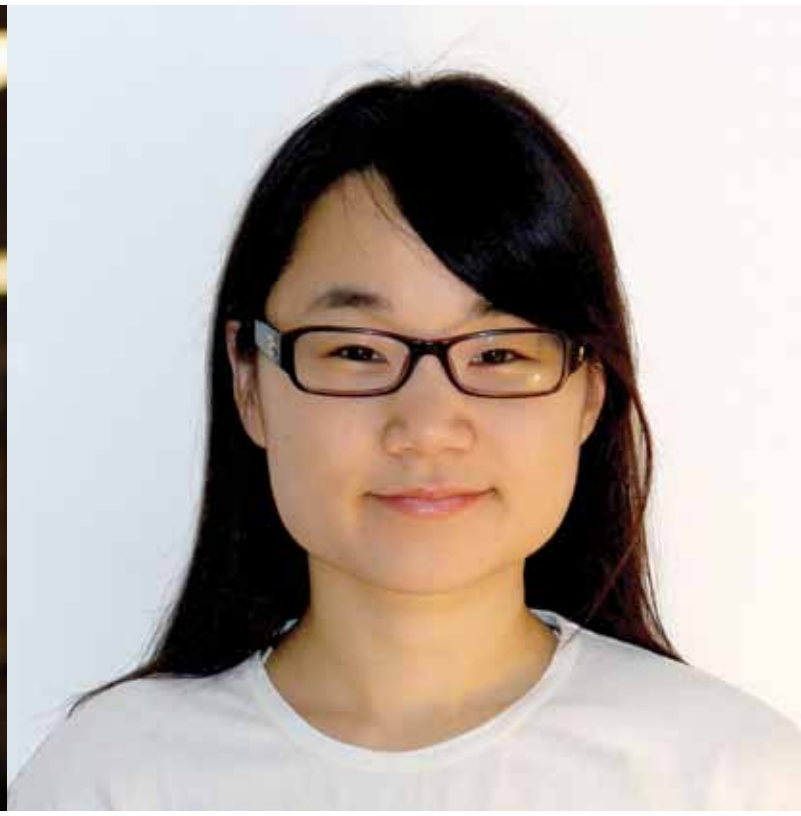
Abnormal PI3K activity is implicated in several diseases, including cancer, and PI3K inhibition is a “hot topic” in international cancer research. Mutations in PI3K alpha are some of the most common genetic abnormalities in cancer, with errors or multiple copies of the gene found in a wide range of tumour types such as breast, colon, and lung cancers.

The new drug candidate, PWT33597, is a dual inhibitor of PI3K alpha and mTOR, one of the most important molecules activated by PI3K. Inhibiting both proteins provides a back-up should cancer cells find a way to overcome either one of the blockades. Laboratory research completed by the New Zealand scientists in 2010 confirmed that PWT33597 is selective for its targets, and very effectively inhibits the signalling pathway they regulate. It also showed that the compound is suitable for oral administration, achieving excellent activity at doses that seem suitable for use in patients.

Pathway Therapeutics announced that the investment triggered by the selection of PWT33597 will be used to advance the compound to clinical trials. PWT33597 is currently in preclinical development and an Investigational New Drug application is anticipated in 2011. While PWT33597 is their most advanced compound, Pathway Therapeutics has several other PI3K inhibitors in the pipeline and the funds will support further research on these candidates overseas.

“Our work also demonstrates how commercially-focused research can synergise with traditional scientific outcomes,” says Peter. “It has already led to two successful grant applications to the Health Research Council of New Zealand as well as eleven scientific papers and many more to come.”

The Maurice Wilkins Centre has provided long-term salary support for two key scientists in the PI3K inhibitor programme and purchased a computer-controlled robot critical for screening the drug candidates.



Dr Zoe Wilson and Dr Dominea Rathwell.

Doctoral students win international recognition

Two medicinal chemistry PhD students supervised by Maurice Wilkins Centre investigator Professor Margaret Brimble have won prestigious international postdoctoral fellowships.

The natural world provides many of the drugs used to treat human disease. Medicinal chemists like Professor Margaret Brimble and her team create synthetic copies of promising natural compounds, to produce sufficient quantities for research and commercialisation and so that modifications can be made to further improve their activity.

For her PhD in Margaret's laboratory, Dominea Rathwell synthesised γ-rubromycin, a potent inhibitor of the enzyme telomerase, that has potential anticancer activity. Telomeres are the protective "caps" at the end of chromosomes that are worn down with each cell division. Telomerase counters this by extending the chromosomes to protect the genetic information within. Most cells die after a certain number of divisions because the telomeres become too short, but some cancer cells have increased telomerase activity that effectively makes them immortal. The synthesis of γ-rubromycin opens up exciting avenues for fighting cancer and, with international colleagues, Margaret is investigating the inhibitor's potential as a new drug.

Dominea's work was a cover story in the prestigious journal *Angewandte Chemie* and was selected as one of its top five percent of papers. She was awarded a 2010 Humbolt Research Fellowship to the Max Planck Institute in Berlin, and the 2010 Hatherton Award from the Royal Society of New Zealand for the best scientific paper by a doctoral student.

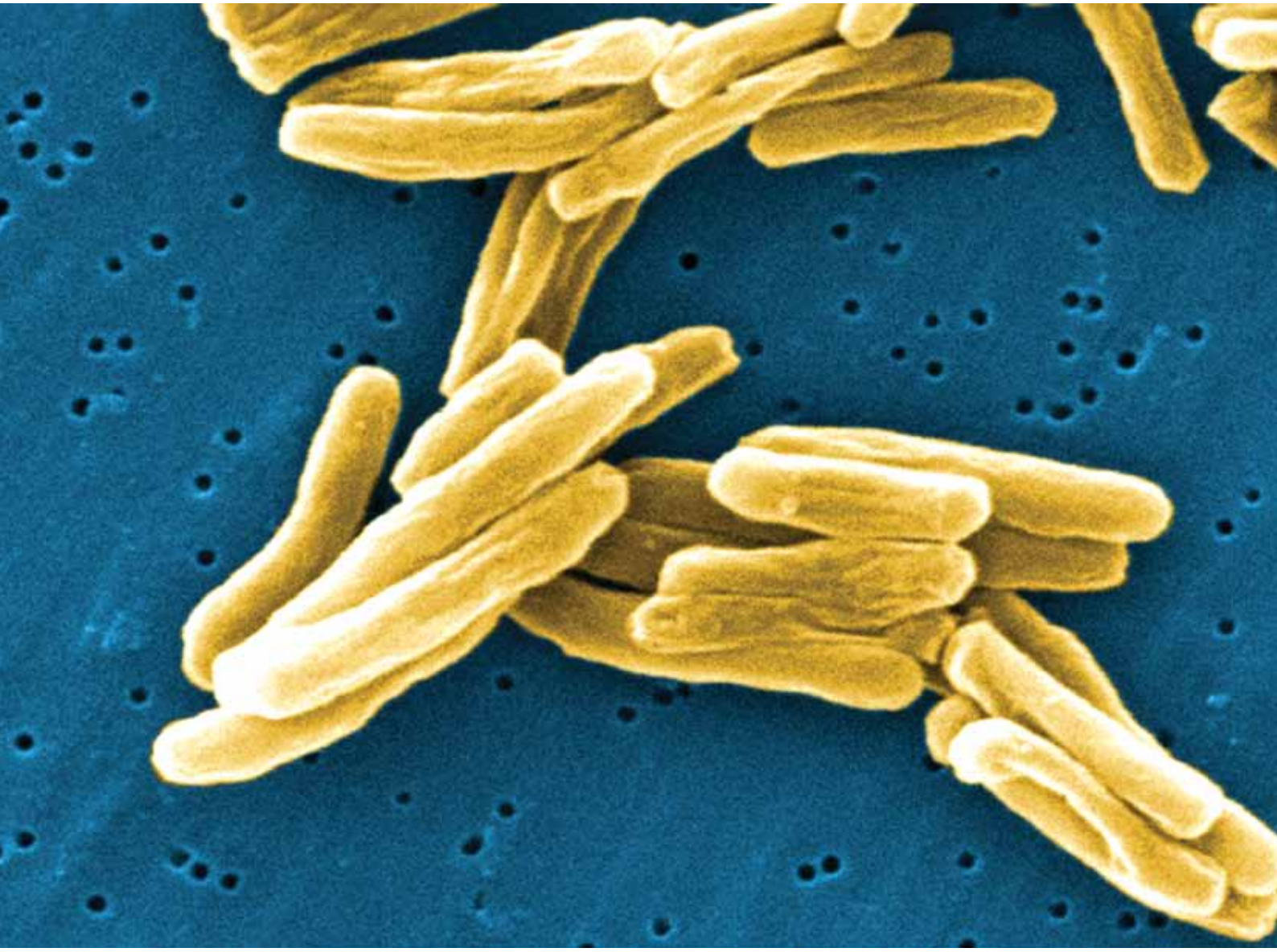
Fellow student Zoe Wilson's work focused on another natural product with anticancer activity, produced by a micro-organism from an extreme environment. The compound, berkelic acid, was isolated from a fungus growing in Berkeley Pit Lake, Montana. The lake, which formed when an abandoned copper mine filled with water, is acidic and laden with metals, and the organisms that live there produce natural products with unique structures.

Routine screening indicated that berkelic acid may be effective against cancer, but the natural source provides only small amounts and will disappear if the lake is drained. Zoe successfully synthesized the core of the complex compound, allowing further analysis and modifications. Her work was published in *Organic & Biomolecular Chemistry* and she was awarded a 2010 Newton International Fellowship to the University of Cambridge.

"It's quite incredible for two students from the same research group to win such prestigious international fellowships," says Margaret. "Since the fellowships provide ongoing support to maintain international research, the scientists and their New Zealand colleagues will continue to benefit even after they return home."

The Maurice Wilkins Centre supported both students by funding their PhD research expenses and project extensions.

See story on page 62 about Professor Margaret Brimble's Royal Society of Chemistry (UK) award.



Micrograph of *Mycobacterium tuberculosis*.
Image courtesy of Dr Ray Butler and Janice Carr (*Centres for Disease Control)*

Modern approaches to an ancient disease

Scientists associated with the Maurice Wilkins Centre have created new drugs for tuberculosis.

Tuberculosis (TB) is one of the oldest known human diseases and is again becoming a major concern. The bacterium responsible, *Mycobacterium tuberculosis*, is developing resistance to current antibiotics, especially in the "persistent" form of the disease, and treatment regimens are lengthy and difficult to follow. As a result of the HIV epidemic millions of people are also becoming more susceptible to infection.

Despite a major international research effort, only a few new drugs for persistent TB have entered clinical development in the last 40 years. The first of these, PA-824, is currently in phase II clinical trials under the stewardship of the non-profit Global Alliance for TB Drug Development (TB Alliance) in New York.

Scientists from the Auckland Cancer Society Research Centre, who are members of the Maurice Wilkins Centre, have worked with the TB Alliance to learn more about the biological activity of PA-824 and design improved "second generation" analogues of the drug. In the course of their research, they have also come up with a new method for synthesising the drugs, which will simplify and reduce the cost of production.

In 2010 Associate Professor Brian Palmer and Professor Bill Denny, who led the collaboration with the TB Alliance and University of Chicago, completed a contract to deliver a second-generation drug candidate to the Alliance. Their work involved designing and synthesising nearly a thousand second-generation compounds, refining them based on laboratory tests, and selecting the most promising candidates for further development. The final three candidates are now being evaluated by their international collaborators,

Also in 2010, Maurice Wilkins Centre PhD student Mridula Dogra and colleagues published research that improves understanding of how PA-824 behaves in the body. Given to patients as an inactive "prodrug", PA-824 converts to an active antibiotic when it encounters a particular *M. tuberculosis* enzyme. Mridula's research confirmed that PA-824 was selectively activated by *M. tuberculosis*, and not by a closely related bacterium or normal human enzymes. This provides reassurance that it is unlikely to be activated in tissues unaffected by TB.

"New Zealand can be very proud that its scientists feature so prominently in the work of the TB Alliance alongside colleagues from some of the world's top medical research institutes," says Maurice Wilkins Centre Director, Professor Rod Dunbar. "Their achievements are an indication of the strength of drug discovery in this country and its global reach."

The research group is now working with the Alliance on an improved "second-generation" analogue of another new TB drug, TMC207, which is currently in clinical trials.
See www.tballiance.org/new/portfolio.php

An artistic impression of the human lymph system.

Clues to life-threatening organ failure

Relatively little is known about lymph but there is growing evidence that it can carry disease-causing toxins from the intestines throughout the body. Researchers associated with the Maurice Wilkins Centre have conducted the first comprehensive analyses of the proteins that may be involved.

Our tissues and organs are bathed in fluid that provides nutrients and removes waste. Excess fluid from around the body is collected in the lymphatic system and eventually returned to the blood. This fluid, called lymph, contains proteins and other biologically-active factors secreted by the tissues. Lymph from the intestine and its mesentery (supporting tissues) takes a unique anatomical route that, in contrast to blood, bypasses detoxification in the liver. Biologically-active factors released by the intestines into the lymph therefore pass directly to the bloodstream, encountering the heart and lungs before being circulated to the rest of the body.

In the last decade, research has shown that mesenteric lymph can contain toxic factors that contribute to the development of multiple organ dysfunction syndrome (MODS) and other inflammatory diseases. MODS is a potentially life-threatening syndrome in which two or more organ systems cannot maintain normal activity without medical intervention. The precise series of events leading to MODS is unknown, but it typically develops during severe illness such as acute pancreatitis, sepsis or haemorrhagic shock (caused by the rapid loss of large amounts of blood).

Surgeons and Maurice Wilkins Centre investigators Professor John Windsor and Dr Anthony Phillips from The University of Auckland are leading research examining mesenteric lymph and its role in disease. Their work focuses on identifying proteins and other components in lymph that may provide clues about how critical illnesses develop, and how the conditions might be managed to avoid MODS.

In 2008 the research team, working with PhD student Anubhav Mittal, published the first description of the full protein complement (proteome) of normal mesenteric lymph, based on animal studies. The researchers then studied changes in two severe illness states.

Eight of a total of 245 identified proteins in mesenteric lymph were found to be elevated in acute pancreatitis, all but one of which was a pancreatic enzyme. This supports further research into the use of enzyme-blocking protease inhibitors to treat the condition. The latest study, in 2010, found that sixty proteins increased during hemorrhagic shock. Several of the proteins are worthy of further study, either as contributors to the disease or markers of its severity, suggesting new avenues for its management.

The studies significantly advance the understanding of lymph composition. The work was made possible by a unique collaboration between surgeons and biologists expert in proteomics, including Martin Middleditch and Professor Garth Cooper of the Maurice Wilkins Centre and by the use of a liquid chromatography-tandem mass spectrometry machine purchased by the Centre.

GMP manufacturing facilities at Glycosyn, Industrial Research Limited.
Photo courtesy of Industrial Research Limited.

Major new cancer vaccine programme

Maurice Wilkins Centre investigators are involved in a major new research programme that aims to develop and trial anti-cancer vaccines in New Zealand.

The body's immune system is capable of killing tumour cells, and researchers around the world are searching for ways to ramp up this response in cancer patients using vaccines. Unlike traditional vaccines, cancer vaccines are designed to be given after the disease has developed, and can be added to standard cancer treatments due to their relative lack of side effects.

A major new cancer vaccine research programme began in 2010 with a $4.5 million grant from the Health Research Council of New Zealand. The five-year programme aims to create one new vaccine and test it in patients, and also lay the groundwork for others. It builds on new ideas for producing vaccine components capable of strongly stimulating cancer patients' immune cells, and will use state-of-the art manufacturing facilities at Industrial Research Limited (IRL), the Malaghan Institute of Medical Research, and The University of Auckland.

Programme head, Dr Ian Hermans from the Malaghan Institute, says that although the focus is on melanoma, the techniques being developed can be applied to other cancers in the future. "Many cancers may respond to immune activation, so an effective vaccine-based strategy with a good safety profile could alleviate suffering on a large scale."

"Our vision is to bring together the best expertise in New Zealand to deliver more effective cancer vaccines. New Zealand's leading immunologists and chemists will design and manufacture the vaccines and the country's leading clinical researchers will test them in patients. We aim to capitalise on the world-class knowledge and expertise that has developed here through publicly funded research across a range of disciplines, and to move forward with that knowledge in a collaborative way. As scientists we want to see more of our work making it into the clinic and this programme takes a truly "bench-to-bedside" translational approach. It also establishes structures that will allow us to do more work with patients in the future."

The programme links investigators at the Malaghan Institute with a team at IRL led by Dr Gavin Painter and groups at The University of Auckland led by Professors Rod Dunbar and Margaret Brimble. Professor Michael Findlay of Cancer Trials New Zealand will coordinate clinical aspects of the programme and the trial will be led at Wellington Hospital by Dr Catherine Barrow. Dr Katrina Sharples from the University of Otago will provide statistical analysis.

The Maurice Wilkins Centre provides a forum to bring together many of the lead researchers, and has contributed funding for the synthetic chemistry required to manufacture one of the vaccine components.

High-performance computer equipment at the BeSTGRID facility at The University of Auckland.
Photo courtesy of Godfrey Boehnke

Virtual screening boosts drug discovery

A high-powered new virtual environment that allows researchers to screen thousands of molecules as potential new drug leads was launched in 2010, providing a major boost to Maurice Wilkins Centre researchers and their collaborators.

"Virtual screening helps us find molecules that have the potential to become new drugs," explains Dr Jack Flanagan, a molecular modeller from the Auckland Cancer Society Research Centre and Maurice Wilkins Centre investigator. "Commercial compound libraries have put millions of chemicals at our disposal, and by screening with computer models that can predict molecular behaviour, we can identify compounds that might be a good starting point for new drugs."

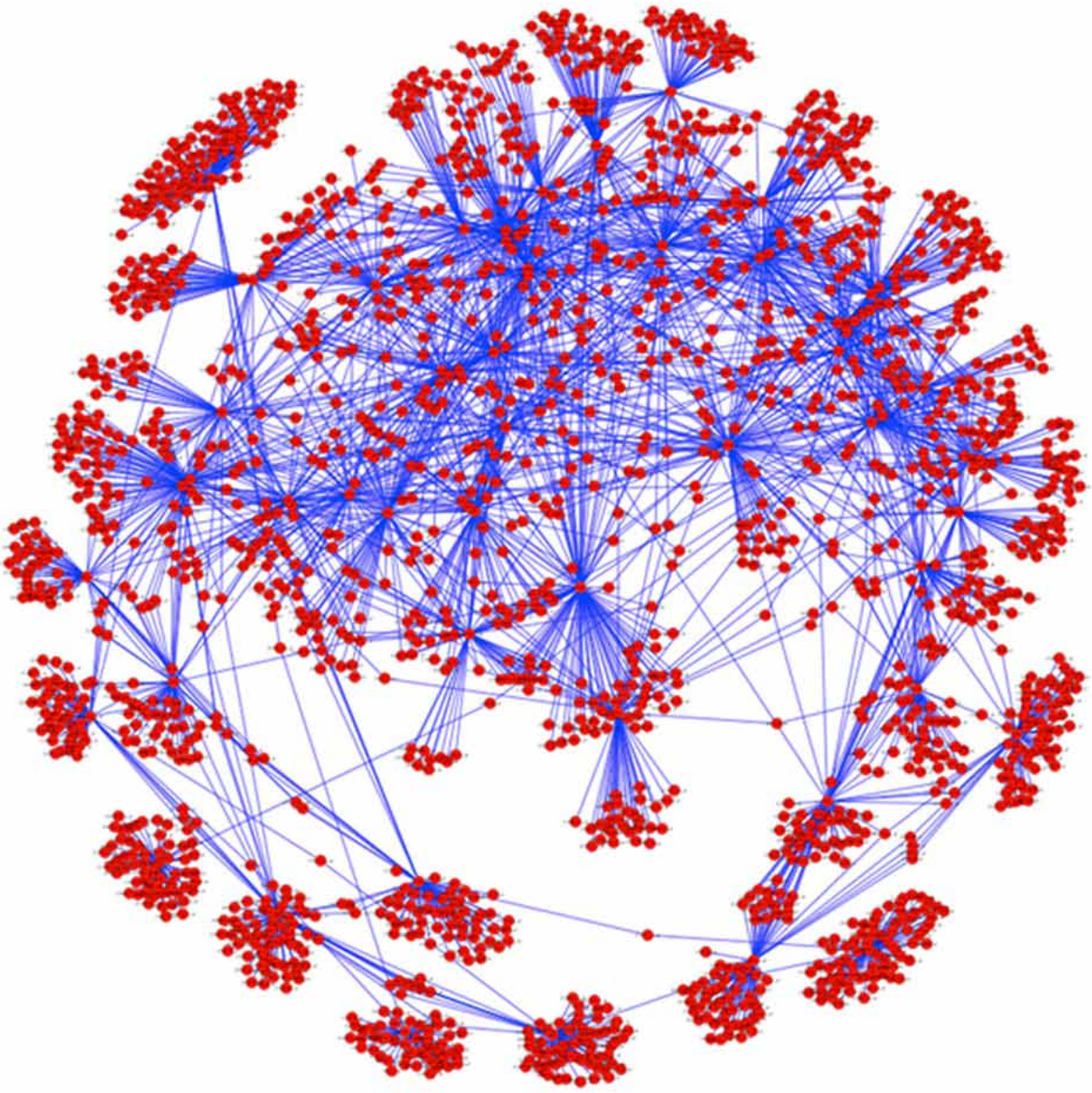
Jack and his team use two main approaches. The first is to begin with the 3D structure of a protein implicated in disease and search for compounds capable of binding to it, thereby altering its function. The second is to start with a compound that has useful biological activity and search for others that may behave in a similar way but are more suitable as new drug leads.

"We might start by selecting a hundred thousand compounds from libraries we're interested in and filter them through the virtual screening process. From the prioritised results we can select a much smaller number – tens to hundreds of compounds – for testing in the laboratory," says Jack. "Once a promising compound has been shown to have biological activity, our medicinal chemists can begin to synthesise variations on that lead."

With the computer resources in Jack's laboratory, it used to take several weeks to screen around 100,000 compounds. With funding from the Auckland Medical Research Foundation, he worked with Nick Jones from The University of Auckland's Centre for eResearch to custom-build a new virtual discovery environment that has already cut the process down to days, and may eventually reduce it to hours.

Launched in 2010, it uses the high-performance computer infrastructure and custom solutions provided by the Centre for eResearch's broadband-enabled science and technology grid (BeSTGRID). With support from the university's BioPharma Research Initiative, a user-friendly interface was developed to aid collaboration with researchers outside Jack's laboratory.

The virtual screening environment is already being used by other Maurice Wilkins Centre investigators. For instance, Dr Chris Squire, from The University of Auckland's School of Biological Sciences, is using the system to search for new inhibitors of an enzyme that alters the activity of an anticancer drug. The system also opens up new opportunities for postgraduate students, who are now doing work that would not previously have been possible within the timeframe of their research projects.



Cluster of co-expressed genes in melanoma cells identified by Daniel Hurley and colleagues.
Image courtesy of Daniel Hurley (Auckland Bioengineering Institute).

Mapping cellular networks

Maurice Wilkins Centre PhD student Daniel Hurley and colleagues are mapping signalling networks in cancer and have identified "master regulators" associated with patient survival.

"Tumour growth is driven by a complex network of cell signals and systems biology is a very powerful approach for understanding these pathways" says Maurice Wilkins Centre investigator Associate Professor Cristin Print."The recent explosion in our knowledge of the human genome, and the complexity of the signalling pathways that control gene activity, means that biologists routinely work with massive amounts of data. Collaboration with computational scientists has become extremely important to manage and find patterns in the information."

Student Daniel Hurley, his supervisors Associate Professors Edmund Crampin and Cristin Print, and colleagues Li Wang and Anita Muthukaruppan, are mapping the molecular networks responsible for tumour growth using a combination of laboratory experiments and advanced computer modelling. To date they have measured changes in the activity of more than 30,000 genes in human melanoma and breast cancer cells subjected to more than 70 genetic modifications in the laboratory. By identifying genes switched on or off under different conditions, they could build computer models of the signalling pathways within the cells.

Multiple computer modelling techniques were used to extract as much information from the data as possible. "Combining several different techniques to generate our model was a real challenge. It represents a significant advance in computer modelling of biological systems, and we have been invited to present the work at international meetings," says Daniel.

An important outcome was the identification of a set of potential "master regulators" of melanoma cell signalling, several of which control whole clusters of genes. The master regulators controlled tumour cell growth and DNA repair in the laboratory and were strongly associated with the survival of melanoma and breast cancer patients. The research team hopes to investigate their role in cancer further.

As well as laying the groundwork for new computer models of cancer cells, Cristin says that Daniel's work provides an important link with whole tissue research. "Our colleagues Edmund Crampin and Professor Peter Hunter at the Auckland Bioengineering Institute are building virtual models of major tissues and organs, and to do that effectively it will be important to understand what is happening down to the level of cells and molecules."

The researchers are now making their techniques available to others. Daniel has created a suite of web-based tools for scientists to build and compare their own virtual gene networks and identify key features for further evaluation in the laboratory.

Daniel's research, completed in 2010, was funded by a University of Auckland Scholarship with additional support from the Maurice Wilkins Centre and the Auckland Bioengineering Institute.

Professor Sir Peter Gluckman speaking at the Future Science Day
Photo courtesy of Godfrey Boehnke.

Supporting New Zealand's future scientists

The inaugural Future Science Day convened by the Maurice Wilkins Centre in 2010 provided advice, mentorship, networking, and science communication opportunities to 150 New Zealand postgraduate students and young scientists.

"The Maurice Wilkins Centre is committed to training New Zealand's future leaders in biomedicine," says Director Professor Rod Dunbar. "Future Science Day is an opportunity for some of our most experienced and successful investigators to share tips and pass the torch to the next generation."

Professor Bill Wilson of the Auckland Cancer Society Research Centre spoke about creating and sustaining successful research relationships, Professor Peter Hunter discussed productive interdisciplinary collaborations involving the Auckland Bioengineering Institute, and Dr Anthony Phillips described how to build connections between scientists and clinicians, based on his experience in The University of Auckland's School of Biological Sciences and Department of Surgery.

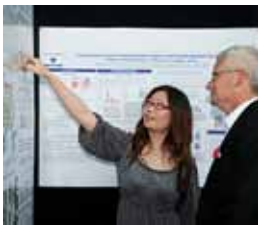
The Prime Minister's Chief Science Advisor, Professor Sir Peter Gluckman, spoke more broadly about changes in New Zealand science and its future. He highlighted the importance of science to the economy, and the value of bridging the boundaries between traditional scientific disciplines and between public and private sector science.

Young scientists learned about career prospects in New Zealand, with representatives from the public (Industrial Research Limited) and private sector (Douglas Pharmaceuticals and Androgenix Ltd), outlining their recruitment criteria. Professor Gillian Lewis from The University of Auckland offered insight into academic careers and Professor Margaret Brimble, chair of the Rutherford Foundation selection panel, spoke about fellowship opportunities.

"Through events like these we want to promote networking and interdisciplinary collaboration between young investigators, but we also need to encourage them to learn each others' languages," says Rod. Students were therefore challenged to explain their research, in three minutes or less, with the mixed-discipline audience scoring their ability to communicate with non-specialists. Thirty-one students took part, speaking on topics from immunology to medical imaging and drug design. First, second and third prizes went, respectively, to University of Auckland students Stefan Hermans and Kimiora Henare (Molecular Medicine and Pathology) and Lucia Tang (Biological Sciences).

The delegates also learnt about Maurice Wilkins Centre funding opportunities, including a new research seeding programme that allows emerging scientists to pilot ideas outside their main projects, fostering key skills such as scientific creativity and independent grant-writing.






Outreach

2010 Maurice Wilkins Centre Lecture

The 2010 Maurice Wilkins Centre Lecture was delivered at The University of Auckland in November, by Professor R. John Collier, Presley Professor of Microbiology and Molecular Genetics from Harvard Medical School, USA.

In his lecture entitled "An ode to the study of diphtheria toxin", Professor Collier outlined the history of studies on diphtheria toxin and how these have yielded broad insights into bacterial pathogenesis and led to novel therapeutics and vaccines for diseases unrelated to diphtheria.

Professor Collier has devoted his career to elucidating the structures and modes of action of bacterial protein toxins. He was elected to the National Academy of Sciences in 1991 and has received many other honours for his scientific achievements.

Sponsorship

Maurice Wilkins Centre Prize for Excellence in Chemical Research

The annual Maurice Wilkins Centre Prize for Excellence in Chemical Research is sponsored by the Centre in partnership with the New Zealand Institute of Chemistry (NZIC). It is awarded to an NZIC member who has made a significant contribution to chemical science in the past five years.

In 2010 the prize was awarded to Professor Keith Gordon from the University of Otago. Professor Gordon has made particularly significant contributions to the field of molecular electronic materials. Specifically, he has developed methods and strategies to understand and predict the electronic properties of large molecular materials such as metal complexes, porphyrins and thiophene polymers.

Conferences, meetings and organisations

Scientific conferences, meetings and networks are important fora to share knowledge and form collaborative relationships. The Maurice Wilkins Centre supports international scientific meetings held in New Zealand as well as smaller local scientific meetings and networks.

In 2010 the Maurice Wilkins Centre sponsored:

- The Queenstown Research Week. This meeting attracts delegates and speakers from around New Zealand, including many from the Maurice Wilkins Centre, as well as over 100 invited international speakers.
- The joint New Zealand Microbiological Society and New Zealand Society of Biochemistry and Molecular Biology conference. This meeting attracted over 300 delegates and featured international and national speakers, including many Maurice Wilkins Centre investigators.
- The 7th International Symposia on the CGRP Family. This specialised meeting is held every three years and in 2010 focused on the physiological roles of the CGRP family of peptides and their receptors in areas including satiety, pain, hypertension, cancer, migraine, and lymphatic development. The program included presentations from Maurice Wilkins Centre investigators working in this area.
- The 2010 CellML workshop. This workshop on the computational biology language invented at the Auckland Bioengineering Institute attracted delegates from Japan, Canada, the United Kingdom, India and Germany. People unable to attend the meeting in person were able to participate through the internet.
- The New Zealand Bioinformatics Conference. The goal of this conference was to map out the future of bioinformatics and identify capability gaps in New Zealand. The conference involved over 100 delegates from New Zealand and overseas.
- The Medical Sciences Congress. The 2010 meeting highlighted how basic understanding of biomedical science has contributed to advances in clinical medicine.
- NZ Structural Biology meeting. This is an annual event which enables interaction between all New Zealand researchers and students working in structural biology.
- Stratus. This network at The University of Auckland supports emerging researchers and works to raise their profile in both academic and public communities.
- NZBIO. The Maurice Wilkins Centre also supports NZBIO, a national organisation representing bioscience based industries in New Zealand. NZBIO's functions include interacting with government agencies and providing national and international networking opportunities.

Industry engagement

The Maurice Wilkins Centre supports innovation in the biotechnology and drug development sectors by providing companies with the expertise and facilities that their research and development programmes require. In 2010 the Maurice Wilkins Centre provided expertise and / or facilities to:

- AFT Pharmaceuticals Ltd. This full service pharmaceutical company, which also undertakes drug development, has operations in Australia and New Zealand. It has an ongoing contract with Maurice Wilkins Centre investigator Professor Margaret Brimble to synthesise an established anti-rheumatic drug in sufficient quantities for testing.
- Androgenix Ltd. This Auckland biotechnology company applies genomic technology to the development of products for the world-wide livestock industry. The company needs access to state-of-the-art cell sorting technology and continues to be the major external user of the Maurice Wilkins Centre's cell sorting facility established in 2007.
- Bomac Laboratories Ltd. This Auckland-based company develops and manufactures animal health products for sale in New Zealand and around the world. Maurice Wilkins Centre investigator Professor Margaret Brimble is conducting research designing and synthesising new molecules based on a lead compound identified by the company. In addition, in 2010, Maurice Wilkins Centre investigator Vinod Suresh led a pilot project for Bomac modelling rumen metabolism.
- Cancer Research Technology Ltd (UK). This is the cancer-focused technology development and commercialisation arm of Cancer Research UK, the world's largest cancer charity. Maurice Wilkins Centre investigator Professor Bill Denny collaborates with the company on research into inhibitors of AKR1C3, a molecular target in cancer.
- GlycoSyn. This is the discovery, development and manufacturing arm of Industrial Research Limited, working with biotechnology clients to develop high-value small molecules. In 2010 Maurice Wilkins Centre investigator Professor Margaret Brimble showed the company how to make neoglycosylated amino acid building blocks that it now sells commercially.
- Landcare Research New Zealand Ltd. This Crown Research Institute provides solutions and advice for sustainable development and the management of land-based natural resources. Their interest in developing humane rat-selective toxins led to them funding a project in the laboratory of Maurice Wilkins Centre investigator Professor Margaret Brimble. Based on this work Professor Brimble, Dr David Rennison and Olivia Laita, a PhD student involved in the research, have patented a new generation of rat-selective toxins.

- ParaCo Technologies Ltd. This subsidiary of AgResearch Limited screens libraries of novel molecules for potential animal health activity. Access to established compound libraries is required for this work, and the company has an ongoing agreement that gives it exclusive animal health screening (and subsequent commercialisation) rights to the libraries of Maurice Wilkins Centre investigators Professor Margaret Brimble and Professor Bill Denny. Professors Brimble and Denny also have contracts to synthesise promising molecules in sufficient quantities for further evaluation.

- Pathway Therapeutics Inc (USA). This San Francisco-based company was established to discover and develop the next generation of PI3-kinase inhibitors being developed at The University of Auckland for the treatment of cancer. Maurice Wilkins Centre investigators Professors Bill Denny and Peter Shepherd are the company's scientific founders and continue to provide consultancy and contract research services. Pathway Therapeutics requires screening facilities to search for potential PI3-kinase inhibitors, and the purchase of a computer-controlled robot by the Maurice Wilkins Centre has enabled this work to proceed (see page 13).

- Proacta Inc (USA). This clinical-phase biopharmaceutical company, headquartered in San Diego, is developing hypoxia-activated prodrugs for the treatment of cancer. Maurice Wilkins Centre investigators Professors Bill Denny and Bill Wilson are two of the company's scientific founders and, along with investigators Dr Jeff Smaill and Dr Adam Patterson, provide consultancy and contract research services. The investigators use mass spectrometry capabilities purchased by the Maurice Wilkins Centre as part of their ongoing research into new compounds (see page 9).

- Ruga Corporation (USA).This is a private biopharmaceutical company that discovers and develops novel targeted therapeutics in oncology. In 2010 Maurice Wilkins Centre investigator Associate Professor Michael Hay led research into novel agents that selectively target renal cell carcinomas. Synthesis and structure-activity relationship studies for two classes of molecules were carried out by Dr Muriel Bonnet and Associate Professor Hay, partly funded by the Maurice Wilkins Centre. The project has been jointly licensed by Uniservices and Stanford University to Ruga Corp for commercial development, resulting in a new research contract with the company.

- Symansis Ltd. This company, with facilities in the South Island and at the Institute for Innovation in Biotechnology at The University of Auckland, produces high-quality reagents for use by cell biologists. Maurice Wilkins Centre investigator Professor Peter Shepherd founded the company in the United Kingdom and brought it to New Zealand in 2004. He continues to act as its Chief Scientific Officer.

In addition to these examples the Maurice Wilkins Centre investigators have established a variety of other relationships with companies and non-profit organisations that drive the translation of their research and expertise into new approaches to fighting human disease (see page 60).

Public engagement

The Maurice Wilkins Centre actively engages with the public by sharing news of its research and successes and providing commentary on topical scientific issues. It communicates with New Zealanders through the news media and science blogs, through public lectures and presentations, and through interactions with school students.

In 2010 Centre members generated significant national and regional media coverage on a variety of scientific topics:

- The New Zealand Superbugs Symposium (see page 11), organised by the Centre in September captured the interest of national media. Rod Dunbar, Maurice Wilkins Centre Director, appeared on television to discuss the potential threats to New Zealand and a feature story on 'Superbugs' was published in the Herald on Sunday. The topic was also reported in regional and internet media.

- Significant research showing how the superbug *Staphylococcus aureus* evades key human immune defences, carried out by Maurice Wilkins Centre scientists led by Professor John Fraser and collaborators at The University of Aarhus in Denmark, was reported in national media and on several internet media sites following the publication of this work in the prestigious journal *Proceedings of the National Academy of Sciences USA* (PNAS) in February.

- Maurice Wilkins Centre investigator Professor Peter Hunter, the recipient of the 2009 Rutherford Medal, gave four public Rutherford Lectures in Napier, Palmerston North, Wellington and Nelson during August and September 2010 entitled "Maths, Maps and the Human Heart". In these lectures Professor Hunter explained the concept of 'virtual medicine' and how New Zealand is at the forefront of mapping the incredible functions of the human body.

- Local print media featured stories on the high school students awarded Maurice Wilkins Centre travel scholarships to attend the 2010 Asian Science Camp (see page 33).

- The research of Maurice Wilkins Centre investigators has also been featured on the Radio New Zealand programme "Our Changing World" throughout 2010. Professor Margaret Brimble was interviewed about making new medicines based on chemicals found in nature. Earlier in the year, the flow cytometry facilities at the Malaghan Institute of Medical Research in Wellington were featured. Other Maurice Wilkins Centre investigators who featured in 2010 were Dr Richard Furneaux and Dr Peter Tyler from IRL Ltd, Professor Graham Le Gros from the Malaghan Institute of Medical Research, Associate Professor Vic Arcus from The University of Waikato and Associate Professor Peter Metcalf from The University of Auckland.

- Professor Margaret Brimble's involvement with commercial research by ParaCo Technology Ltd to discover new molecules that may combat livestock parasites was reported in national agricultural media.

- An announcement about the first-ever royalty-free license agreement between two not-for-profit drug developers, the Drugs for Neglected Disease Initiative and a medicinal chemistry group led by Professor Bill Denny at The University of Auckland, received international media coverage.
- Several Maurice Wilkins Centre investigators provided expert commentary to media on a number of topics including the H1N1 influenza virus, the NIWA supercomputer, the Australian Synchrotron — and the chemicals in hair dye.

Science education

Supporting high-quality science education in New Zealand schools not only encourages the next generation of scientists but also helps others to understand and value science. In 2010 Maurice Wilkins Centre investigators were involved in numerous science education initiatives, including:

- 2010 Asian Science Camp, Mumbai, India. The Maurice Wilkins Centre co-ordinated a New Zealand delegation to this camp, which brings together more than 200 students from the Asian region to attend a week of lectures by world class scientists in chemistry, physics and biology. The Centre ran a national competition to select two Year 13 students and one secondary school teacher to attend the camp. The successful students were Olivia Tidswell from Tauranga Girls' College and Yuenho Wong from Auckland Grammar School and the teacher selected was Sharra Martin from Alfriston College in Manukau. Olivia and Yuenho both were awarded travel scholarships from the Indian Government and the Maurice Wilkins Centre sponsored the balance of their travel costs. The MacDiarmid Institute sponsored a further two students, Max Wilkinson from Papanui High School in Christchurch and Tianheng Zhai from Macleans College in Auckland. The delegation found it to be a valuable experience. "The camp has certainly affected how I think of my future, both reigniting my passion for biology and stimulating my curiosity for other disciplines," said Olivia. "It was amazing to see people of different ethnicities all coming together. Science itself is a common language," observed Yuenho.
- Maurice Wilkins Centre biology teacher development scholarships. In a new initiative in 2010 the Maurice Wilkins Centre sponsored scholarships for high-school biology teachers to attend the 20th annual Queenstown Molecular Biology meeting. The aim of the new scholarships is to give New Zealand teachers the opportunity to attend an international conference on contemporary biological research and to network with colleagues and practicing biologists from around the world. The scholarships covered conference registration, accommodation, and travel to the meeting. Recipients of the inaugural awards were Su Mukund from Papatoetoe High School, Rachel Heeney from Epsom Girls Grammar, Robbie Richards from Shirley Boys' High School, and Paul Scott from Mercury Bay Area School. The teachers said that the meeting was a very worthwhile professional development experience and gave them an up-to-date perspective on cutting-edge molecular biology.

- The Science Learning Hub. This national project provides resources for teachers for school years 5-10. In 2010 the research of Maurice Wilkins Centre investigators Professor Graham Le Gros and Dr Joanna Kirman, and colleagues at the Malaghan Institute of Medical Research, was profiled as part of a learning context on “Fighting Infection”.
- LENScience (Liggins Education Network for Science). This classroom-based programme provides secondary school students and teachers with access to practicing scientists and high-quality learning opportunities. Again in 2010 several Maurice Wilkins Centre investigators participated in the programme’s popular “Meet the Scientist” sessions.
- Rotary National Science and Technology Forum. This national residential programme is for outstanding all-round science, maths and technology students about to start Year 13. By popular request and for the third consecutive year, Maurice Wilkins Centre scientists Jodie Johnstone, Chris Squire and Paul Young ran a practical laboratory session for around 150 students, providing hands-on experience in the purification of green fluorescent protein.

Service

Maurice Wilkins Centre investigators support both the national and international science communities through service in leadership roles and on many advisory boards and panels.

National roles

In 2010 Maurice Wilkins Centre investigators served in advisory and governance roles in many New Zealand organisations including:

- Royal Society of New Zealand
- Marsden Fund Council and Panels
- Health Research Council of New Zealand
- Rutherford Foundation
- National Heart Foundation Science Committee
- NZBIO
- Queenstown Molecular Biology Meetings Society
- New Zealand Bioinformatics Institute
- MoRST Oxygen Group
- Nutrigenomics New Zealand
- Institute of Environmental Science and Research

- New Zealand Society for Biochemistry and Molecular Biology
- New Zealand Institute of Chemistry
- Arthritis New Zealand
- Diabetes NZ Auckland
- National Institutional Biosafety Committee Board, ERMA
- The New Zealand Association of Scientists
- New Zealand Society for Oncology
- Cancer Society of New Zealand
- Auckland Medical Research Foundation
- Wellington Medical Research Foundation
- New Zealand Genomics Ltd
- The Melanoma Network of New Zealand
- New Zealand Institute for Rare Disease Research Ltd

International roles

In 2010 members of the Maurice Wilkins Centre served in more than 60 advisory, editorial and governance roles in international organisations based in the United States of America, Australia, the United Kingdom, the Netherlands, Canada, France, Sweden, Malaysia, Egypt, Korea, Belgium and Norway.




Organisational Development

Research Seeding Programme

One the Maurice Wilkins Centre's main objectives is to encourage early-stage research collaborations between investigators from different scientific disciplines, and its contestable research seeding programme has helped achieve this objective. Three rounds of the programme were held in 2010 and a total of $975,935 was awarded to seed 18 new projects, including support for 7 new PhD students under the multidisciplinary training category of the programme.

New initiatives

The Maurice Wilkins Centre fosters new multidisciplinary, collaborative research that involves Centre investigators by providing working expenses to initiate work on ground-breaking projects. The aim is to spark projects that will grow into highly innovative and sustainable research programmes.

Projects awarded funding in 2010:

- *Characterisation of Kupffer cells from human liver*: Phillips, Bartlett, Hickey and Dunbar, The University of Auckland.
- *Development of in-house expertise for chemical synthesis of 13C/15N labelled peptide hormones for NMR*: Hay, Harris, Dingley, Brimble and Au, The University of Auckland.
- *Can molecular docking combine productively with biophysical and biochemical methods inside a flexible multi-cavity active site?*: Flanagan, Squire and Jamieson, The University of Auckland.
- *Identifying the metabolites of resveratrol that activate sirtuin activity and promote mitochondrial capacity*: Loomes, Phillips, Greenwood and Hickey, The University of Auckland.
- *Characterising ligand interactions with the novel anti-asthma target hematopoietic prostaglandin D2 synthase*: Flanagan, Squire and Hay, The University of Auckland.
- *The role of the host environment in driving the evolution of pathogenic bacteria*: Wiles and Print, The University of Auckland.

Access to advanced equipment

The cost of accessing advanced equipment can be a barrier to scientific discovery. Through this category, Maurice Wilkins Centre investigators can access the Centre's advanced equipment anywhere in New Zealand to inititate exciting new projects

Projects awarded funding in 2010:

- *Lipodomic analysis - exploring mitochondrial functions in liver*: Hickey, Phillips and Bartlett, The University of Auckland.
- *Immune response to a novel virus vaccine*: Taylor, Brooks and Tang, The University of Auckland.
- *Isolation of bacterial proteins expressed in vivo*: Wiles, Holtfreter and Middleditch, The University of Auckland.
- *Proteomic characterisation of a new melanocyte-specific protein*: Sheppard, Feisst, Middleditch and Dunbar, The University of Auckland.
- *Identification of F420-ome of Mycobacterium tuberculosis using mass spectrometry*: Bashiri and Baker, The University of Auckland.

Multidisciplinary training

Developing the next generation of scientists who are confident in working across different scientific disciplines is a major focus of the Maurice Wilkins Centre. The Centre supports multidisciplinary PhD projects that involve collaboration between Centre investigators and research in more than one scientific discipline.

Projects awarded funding in 2010:

- *Structural and functional studies of the inhibition of Mycobacterium tuberculosis DAH7PS by aromatic amino acids*: Blackmore and Parker, University of Canterbury; Baker, The University of Auckland.

- *Biological mechanisms that underly rotavirus disease*: Ge, Taylor, Dunbar and Shepherd, The University of Auckland; von Itzstein, Griffith University; Coulson, University of Melbourne.
- *Identification and characterization of the regulatory system controlling oxygen utilization in Mycobacterium tuberculosis in response to hypoxia*: Aung, Cook and Berney, University of Otago; Baker and Lott, The University of Auckland.
- *The rescue of the unfolded protein response (UPR) in yeast*: Low and Atkinson, Victoria University of Wellington; Furneaux, IRL Ltd.
- *Synthesis and characterisation of native caenopore-5 and carbon bridge caenopore-5 analogues*: Medini, Dingley, Brimble, Fraser and Harris, The University of Auckland
- *COMMD proteins*: Ojeda, Lott and Ching, The University of Auckland.
- *Studies of DHDPSL*: MacDonald, Loomes, Baker, Hickey and Phillips, The University of Auckland.

New Investigators

In 2010 the Maurice Wilkins Centre continued to strengthen its national network of investigators and eighteen new Associate Investigators were invited to join the Centre:

- Professor Mike Eccles, Dept of Pathology, University of Otago
- Associate Professor Catherine Day, Dept of Biochemistry, University of Otago
- Dr Sarah Young, Dept of Pathology, University of Otago
- Dr Joel Tyndall, School of Pharmacy, University of Otago
- Dr Anne La Flamme, School of Biological Sciences, Victoria University of Wellington
- Dr Joanna Kirman, The Malaghan Institute for Medical Research
- Professor Antony Fairbanks, Dept of Chemistry, University of Canterbury
- Dr Justin O'Sullivan, Institute of Natural Sciences, Massey University Albany
- Dr David Long, Auckland Bioengineering Institute, The University of Auckland
- Dr Vinod Suresh, Auckland Bioengineering Institute, The University of Auckland
- Dr Iain Anderson, Auckland Bioengineering Institute, The University of Auckland
- Dr Rinki Murphy, Dept of Medicine, The University of Auckland
- Mr Adam Bartlett, Dept of Surgery, The University of Auckland
- Associate Professor Mark McKeage, Dept of Pharmacology, The University of Auckland

- Dr Johannes Reynisson, Dept of Chemistry, The University of Auckland
- Dr Siouxsie Wiles, Dept of Molecular Medicine and Pathology, The University of Auckland
- Professor Kathryn Crosier, Dept of Molecular Medicine and Pathology, The University of Auckland
- Professor Phil Crosier, Dept of Molecular Medicine and Pathology, The University of Auckland

Equipment & facilities

In 2007 the Maurice Wilkins Centre was awarded $2.6 million to purchase capital equipment for the CoRE, as part of its government funding. Equipment purchases from this funding allocation continued in 2010, with final orders for 16 of the 17 items on the equipment list placed by the end of the year. The investment in capital equipment through CoRE funding has enabled new research to be carried out, fostered national collaborations and contributed to many research publications.

An example is the cutting-edge LSRII flow cytometer, purchased in 2008 by the Malaghan Institute with funding from the Maurice Wilkins Centre. The technology has been invaluable, providing data for eight high-impact publications involving Malaghan Institute researchers in 2010 and contributing to a promising new cancer vaccine research programme involving Maurice Wilkins Centre investigators at the Malaghan Institute, IRL and The University of Auckland (see highlights story page 21). It has enabled the Institute to make significant progress in identifying cells critical for immunity to tuberculosis, and key immune cell targets for the development of cancer immunotherapies. In addition to supporting leading biomedical research programmes in cancer, allergy, asthma and parasitic diseases, the technology has allowed the establishment of several new research platforms, including the characterisation of unknown viruses in Antarctic sea ice in collaboration with the University of Tasmania and studies of marine sponges and bacteria with Victoria University of Wellington. It is anticipated that the number of publications resulting from use of the LSRII will continue to grow as New Zealand researchers become more familiar with its full capabilities and applications.

In 2010 Maurice Wilkins Centre investigators also implemented new technology platforms:

- The Structural Biology group at The University of Auckland implemented technology that can characterise interactions between proteins and small molecules. Using an RT-PCR machine purchased with Maurice Wilkins Centre funding, the researchers can screen proteins of interest against a library of 400 molecular fragments. When a fragment is found to bind to a protein target, it can be used to help develop lead compounds for drug discovery. The machine can also be used to carry out ligand and inhibitor binding studies.

- Maurice Wilkins Centre scientist Mr Martin Middleditch and Associate Professor Anthony Phillips established a new technology platform to analyse lipids using the Centre's QSTAR mass spectrometer. This new technology has been developed in collaboration with the School of Biological Sciences at The University of Auckland, which enabled the purchase of specialised software for analysis of the data generated by the QSTAR.
- Maurice Wilkins Centre investigator Dr. Siouxsie Wiles received Maurice Wilkins Centre support for the development of the Xenogen Caliper system for live animal imaging. This system allows users to track the movement of bioluminescent or fluorescent compounds such as drugs, vaccines or live bacteria in mice over time. It can even track the progress of transmission of an infectious agent in a group of animals showing the path of transmission.

While primarily used by Maurice 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 2010 the Centre client list included:

- Androgenix Ltd
- Pathway Therapeutics Ltd
- Proacta Ltd
- Somnaceutics Ltd
- MidCentral District Health Board
- Auckland District Health Board
- Counties Manukau District Health Board
- Waitamata District Health Board
- Waikato District Health Board
- Plant & Food Research Ltd
- AgResearch Ltd
- The University of Waikato
- Massey University
- University of Canterbury

Human capability

The multidisciplinary and collaborative nature of Maurice Wilkins Centre research provides an excellent training environment for the young scientists and students who are our future science leaders.

PhD student support

The Maurice Wilkins Centre supports a large cohort of PhD and MSc students within its associated research groups by providing funds for stipends, working expenses and travel, as well as opportunities to access specialised research equipment and facilities. In 2010 the Maurice Wilkins Centre provided full or partial stipends for 30 PhD students and one MSc student from this cohort. Fourteen Maurice Wilkins Centre-associated PhD students completed their studies in 2010.

In 2010 the number of Maurice Wilkins Centre PhD students increased dramatically as part of the Centre's research seeding programme that began funding PhD students in 2009. Fourteen new PhD candidates began their studies with funding under the programme's multidisciplinary training category. The new students are spread across New Zealand with seven based at The University of Auckland, four at the University of Otago, two at the University of Canterbury and one at Victoria University of Wellington.

In November, the Centre ran a successful Future Science Day incorporating career advice for young scientists and challenging PhD students to communicate their research in a manner suitable for a non-specialist audience (see page 27).

Personnel Exchanges

In order to maintain a world class research programme it is important that Maurice Wilkins Centre investigators and students keep up to date with international developments in their fields. The Maurice Wilkins Centre provides support for staff and students to travel to conferences and to visit other laboratories in New Zealand and overseas to acquire new skills and techniques.

During 2010 there has been an increase in movement of PhD students between the laboratories of Maurice Wilkins Centre investigators across New Zealand. This has largely been due to the requirement that PhD students funded through the multidisciplinary training category of the Centre's research seeding programme spend time working in more than one scientific discipline.

The Centre provided support for Dr Stephanie Dawes and PhD student Ms Hanna Kwon from the Structural Biology group at The University of Auckland to attend the 2010 Australasian Crystallography School. The week-long programme at The University of Queensland, Australia, combined lectures by expert crystallographers with intensive hands-on computer-based practical sessions, to provide a thorough overview of the latest techniques and software used to determine the X-ray crystal structures of proteins.

Dr Geoff Williams, a member of the peptide chemistry team in Professor Margaret Brimble's group travelled with Margaret to the University of Leiden in The Netherlands to exchange expertise in peptide synthesis. The University of Leiden has developed facilities and protocols to manufacture peptides that meet regulatory requirements for use in human clinical trials. The aim of the trip was to learn how to create a similar facility in New Zealand, as part of the cancer vaccine research programme involving Maurice Wilkins Centre researchers that began in 2010 (see page 21).

In 2010 structural biologists from New Zealand once again had good access to the Australian Synchrotron Facility. The Maurice Wilkins Centre, along with the New Zealand Synchrotron User Group, facilitated trips by research staff and students to the Australian Synchrotron to collect experimental data. The trips typically involve both experienced synchrotron users and new users who are trained during the trip. Those who travelled to the synchrotron in 2010 were research fellows Dr Chris Squire, Dr Paul Young, Dr Alina Castell, Dr Ghader Bashiri, Dr Neil Patterson, Dr Esther Bullock, Dr Shaun Lott and PhD students Richard Bunker, Jason Busby, Manuela Hospenthal, Mathew Cumming and Marisa Till.

Maurice Wilkins Centre workshops

Members of the Maurice Wilkins Centre ran four technology-based academic workshops in 2010. These workshops are designed to inform and educate attendees in the latest techniques and the technology available in New Zealand. They also provide an opportunity to discuss potential collaborative projects.

- Maurice Wilkins Centre research fellow Dr Catherine Lloyd from the Auckland Bioengineering Institute organised the annual CellML workshop in February. CellML is an open standard language being developed by the Auckland Bioengineering Institute to store and exchange computer-based mathematical models of biological processes. The CellML workshop provides an opportunity to update users on recent developments and discuss future work with the language. Thirty delegates attended the meeting, including visitors from the United Kingdom, Japan, Canada, Germany, and India.
- Professor Margaret Brimble organised a one day workshop on peptide chemistry in February, to coincide with a visit to New Zealand by Professor Steve Kent, a renowned peptide chemist from the University of Chicago. Thirteen research fellows and students presented their research over the day.
- A workshop on "Technology platforms for drug screening" was held in June, highlighting some of the technology platforms and equipment available for drug screening in New Zealand.
- The Maurice Wilkins Centre teamed up with The Bioinformatics Institute at The University of Auckland to run an "Introduction to Bioinformatics, microarrays and next generation sequencing" workshop in October. Topics included microarray and sequencing technologies, experimental design, basic data analysis concepts, pathway analysis and ideas for writing successful grant applications and scientific papers in the field. The workshop was very well attended, emphasising the demand for more training in the area.

Vistiors to the Maurice Wilkins Centre

National and international officials

In 2010 the Maurice Wilkins Centre hosted visits from the following officials, who were given an overview of its strategies and research activities:

- Hon Dr Wayne Mapp, Minister of Research, Science and Technology.
- United States Ambassador to New Zealand, Mr David Huebner and United States Consul General to New Zealand, Mr Randy W. Berry.
- German Ambassador to New Zealand, Mr Thomas Meister.
- Dr Robert Hickson and Dr Amanda Wiggins from the Emerging Technologies section of the Science Group at the Ministry of Research, Science and Technology.
- Delegation from the Chinese Academy of Sciences. This delegation of nine members from the Chinese Academy of Sciences and the National Development and Reform Commission of China was led by Professor Zhibin Zhang, Director-General of the Bureau of Life Sciences & Biotechnology, Chinese Academy of Sciences.
- Delegation from Wuhan Biolake Science Park, Wuhan, China. This delegation of five members from Wuhan Biolake was led by Mr Ling Hongshun, Vice President of the Wuhan Agriculture Biotechnology Development Ltd Co.

International Scientists

The Maurice Wilkins Centre hosts visits from international scientists so that they can share their knowledge and research experiences with the New Zealand research community and establish research links.

Visitors to the Centre in 2010 were:

- Professor Nancy Ip (Hong Kong University of Science and Technology, China)
- Professor Steve Kent (University of Chicago, USA)
- Professor Helen Hailes (University College London, UK)
- Professor Peter Scott (University of Warwick, UK)
- Professor Ekke Hahn (University of Munster, Ireland)
- Dr Chris Cooper (Global Alliance for TB, New York, USA)
- Professor Carole Robinson (Oxford University, UK)
- Professor David Patterson (Oxford University, UK)
- Dr Alison Thorburn (Monash University, Australia)
- Professor John Collier (Harvard University, USA)
- Professor James Naismith (University of St. Andrews, UK)
- Dr Elad Binshtein (Ben-Gurion University, Israel)

External funding

Many of the projects within the Maurice 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 become successful in securing competitive funding.

New Zealand funding

In 2010 Maurice Wilkins Centre investigators were awarded new grants worth more than $12 million from New Zealand funding sources for research projects to be carried out over the next one to five years:

- Health Research Council of New Zealand (2 grants, $5.3 million)
- Foundation for Science, Research and Technology (1 grant, $6.0 million)
- Other New Zealand funding sources (9 grants, $0.7 million)

International funding

In 2010 Maurice Wilkins Centre investigators secured new funding of over $2.7 million from the following international sources to support future research:

- National Institute for Health Research (UK)
- Global Alliance for TB (USA)
- Drugs for Neglected Diseases Initiative (Switzerland)
- Wellcome Trust (UK)

Commercial funding

In 2010 Maurice Wilkins Centre investigators secured new research funding of $0.8 million from the following commercial sources:

- Proacta Inc (USA)
- Ruga Corp (USA)

Governance and management

International Science Advisory Board

The Maurice Wilkins Centre International Scientific Advisory Board met in Auckland from 21–23 April 2010. The board consisted of: Dr Jim Watson (Chair) (CEO Caldera Health Limited, Auckland), Professor Peter Andrews (Queensland Chief Scientist), Professor Suzanne Cory (Walter and Eliza Hall Institute, Melbourne), Dr Jilly Evans (Amira Pharmaceuticals, USA), Professor Shankar Subramaniam (University of California, San Diego) and Professor Richard Wettenhall (Bio21 Institute, Melbourne).

The board was briefed on Maurice Wilkins Centre strategies and goals as well as the Centre's progress since the last meeting of the board. Presentations on Maurice Wilkins Centre research were given to the board by principal and associate investigators and a young scientist poster session was also held. At the board's request, the Prime Minister's Chief Science Advisor, Professor Sir Peter Gluckman, also attended part of the meeting to confer with the board.

The final report from the board reaffirmed that the Maurice Wilkins Centre is "unquestionably, a world class science group" and supported an expanded vision for the future of the Centre. The board stated that development of such a strategy for expansion had "major implications for the future of science and the commercialisation of science in New Zealand". In response, the Maurice Wilkins Centre began preparing a strategy for its expansion in the second half of 2010. This strategy will be reported in the 2011 Annual Report, once consultation has been completed.

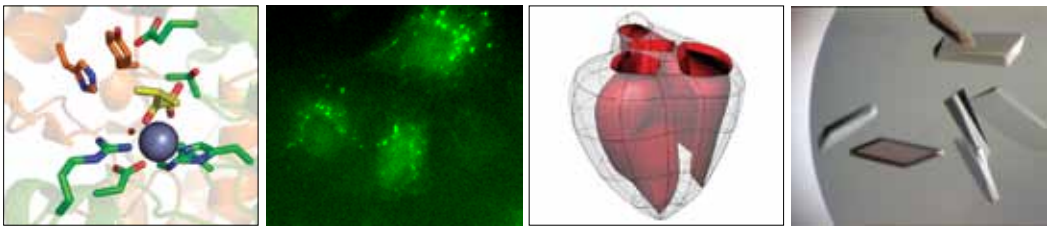
Governing Board

In 2010 the board consisted of: Mr Bill Falconer (Chair), Professor Grant Guilford (The University of Auckland), Professor Gary Hook, Professor Iain Martin (The University of Auckland), Professor Emeritus George Petersen (University of Otago) and Ms Maxine Simmons (Biocatalyst Ltd). Mr John Loof (Cancer Society Auckland) resigned from the board in 2010 after a three year term and the Centre gratefully acknowledges his input over that time.

During the year the board continued to monitor progress of the Maurice Wilkins Centre research programme and its compliance with its funding mandate and budget. In addition the board provide input and advice to the Management Committee on responses to the recommendations of the Report of the Science Advisory Board, and on specific issues including the development of the national network of investigators, strategies for international engagement, and improvements to the Centre's Annual Report and Annual Plan documents.

Management Committee

The Maurice Wilkins Centre Management Committee consists of the Maurice Wilkins Centre principal investigators; Professors Rod Dunbar (Director), John Fraser (Deputy Director), Ted Baker, Margaret Brimble, Garth Cooper, Bill Denny, Peter Hunter and Peter Shepherd. The committee controls the operation of the Centre, under the guidance of the Governing Board and the Scientific Advisory Board and met six times during 2010.



Research Outputs

Publications

In 2010 research outputs from Maurice Wilkins Centre investigators included more than 340 peer-reviewed scientific papers published in international journals, and 26 patents granted, published or filed. Research directly supported by the Maurice Wilkins Centre generated the following 77 scientific papers.

Papers and Reviews:

1. Aitken, J. F., Loomes, K. M., Scott, D. W., Reddy, S., Phillips, A. R. J., Prijic, G., Fernando, C., Zhang, S., Broadhurst, R., L'Huillier, P., & Cooper, G. J. S. Tetracycline treatment retards the onset and slows the progression of diabetes in human amylin/islet amyloid polypeptide transgenic mice. *Diabetes* (2010) **59**(1): 161-171.

2. Atkinson, D. J., Sperry, J., & Brimble, M. A. Improved synthesis of the benzyne precursor 2-(trimethylsilyl) phenyl trifluoromethane sulfonate. *Synthesis* (2010) (6): 911-913.

3. Bashiri, G., Rehan, A. M., Greenwood, D. R., Dickson, J. M. J., & Baker, E. N. Metabolic engineering of cofactor F420 production in mycobacterium smegmatis. *PLoS ONE* (2010) **5**(12).

4. Brauer, R., Wang, L. C., Woon, S. T., Bridewell, D. J., Henare, K., Malinger, D., Palmer, B. D., Vogel, S. N., Kieda, C., Tijono, S. M., & Ching, L. M. Labeling of oxidizable proteins with a photoactivatable analog of the antitumor agent DMXAA: evidence for redox signaling in its mode of action. *Neoplasia* (2010) **12**(9): 755-765.

5. Bogle, G., & Dunbar, P. R. Agent-based simulation of T-cell activation and proliferation within a lymph node. *Immunology and Cell Biology* (2010) **88**(2): 172-179.

6. Bogle, G. & Dunbar, P. R. T cell responses in lymph nodes. *Wiley Interdisciplinary Reviews: Systems Biology & Medicine* (2010) **2**: 107-116.

7. Buchanan, C. M., Phillips, A. R. J., & Cooper, G. J. S. A novel two-chain IGF-II-derived peptide from purified β-cell granules. *Growth Hormone and IGF Research* (2010) **20**(5): 360-366.

8. Chan, Y., Balle, J., Kevin Sparrow, J., Boyd, P. D. W., Brimble, M. A., & Barker, D. A double Mannich approach to the synthesis of substituted piperidones - Application to the synthesis of substituted E-ring analogues of methyllycaconitine. *Tetrahedron* (2010) **66**(35): 7179-7191.

9. Chang, J. Y. C., Stevenson, R. J., Lu, G. L., Brothers, P. J., Clark, G. R., Denny, W. A., & Ware, D. C. Syntheses of 8-quinolinolatocobalt(III) complexes containing cyclen based auxiliary ligands as models for hypoxia-activated prodrugs. *Dalton Transactions* (2010) **39**(48): 11535-11550.

10. Chen, J. L. Y., & Brimble, M. A. Synthesis of the bis-spiroacetal C25-C40 moiety of the antimitotic agent spirastrellolide B using a bis-dithiane deprotection/spiroacetalisation sequence. *Chemical Communications* (2010) **46**(22): 3967-3969.

11. Chien, V., Aitken, J. F., Zhang, S., Buchanan, C. M., Hickey, A., Brittain, T., Cooper, G. J. S., & Loomes, K. M. The chaperone proteins HSP70, HSP40/DnaJ and GRP78/BiP suppress misfolding and formation of β-sheet-containing aggregates by human amylin: A potential role for defective chaperone biology in Type 2 diabetes. *Biochemical Journal* (2010) **432**(1): 113-121.

12. Choi, P. J., Sperry, J., & Brimble, M. A. Heteroatom-directed reverse Wacker oxidations. Synthesis of the reported structure of (-)-herbaric acid. *Journal of Organic Chemistry* (2010) **75**(21): 7388-7392.

13. Cooper, G. J. S., Aitken, J. F., & Zhang, S. Is type 2 diabetes an amyloidosis and does it really matter (to patients)? *Diabetologia* (2010) **53**(6): 1011-1016.

14. Denny, W. A. Hypoxia-activated prodrugs in cancer therapy: Progress to the clinic. *Future Oncology* (2010) **6**(3): 419-428.

15. Denny, W. A., & Palmer, B. D. The nitroimidazooxazines (PA-824 and analogs): Structure-activity relationship and mechanistic studies. *Future Medicinal Chemistry* (2010) **2**(8): 1295-1304.

16. Garny, A., Cooper, J., & Hunter, P. J. Toward a VPH/Physiome ToolKit. *Wiley interdisciplinary reviews. Systems biology and medicine* (2010) **2**(2): 134-147.

17. Gianni, D., McKeever, S., Yu, T., Britten, R., Delingette, H., Frangi, A., Hunter, P., & Smith, N. Sharing and reusing cardiovascular anatomical models over the Web: A step towards the implementation of the virtual physiological human project. *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences* (2010) **368**(1921): 3039-3056.

18. Graham, E. S., Angel, C. E., Schwarcz, L. E., Dunbar, P. R., & Glass, M. Detailed characterisation of CB2 receptor protein expression in peripheral blood immune cells from healthy human volunteers using flow cytometry. *International Journal of Immunopathology and Pharmacology* (2010) **23**(1): 25-34.

19. Grey, A., Chaussade, C., Empson, V., Lin, J. M., Watson, M., O'Sullivan, S., Rewcastle, G., Naot, D., Cornish, J., & Shepherd, P. Evidence for a role for the p110-alpha isoform of PI3K in skeletal function. *Biochemical and Biophysical Research Communications* (2010) **391**(1): 564-569.

20. Guéret, S. M., Boyd, P. D. W., & Brimble, M. A. (1R,6R,13R,18R)-(Z,Z)-1,18-Bis[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]-3, 16-dimethylene-8,20-diazadispiro-[5.6.5.6]tetracosa-7,19-diene. *Acta Crystallographica Section E: Structure Reports Online* (2010) **66**(7).

21. Guéret, S. M., & Brimble, M. A. Spiroimine shellfish poisoning (SSP) and the spirolide family of shellfish toxins: Isolation, structure, biological activity and synthesis. *Natural Product Reports* (2010) **27**(9): 1350-1366.

22. Guéret, S. M., Furkert, D. P., & Brimble, M. A. Synthesis of a functionalized 7,6-bicyclic spiroimine ring fragment of the spirolides. *Organic Letters* (2010) **12**(22): 5226-5229.

23. Harris, P. W., & Brimble, M. A. Toward the total chemical synthesis of the cancer protein NY-ESO-1. *Biopolymers* (2010) **94**(4): 542-550.

24. Hay, M. P., Turcotte, S., Flanagan, J. U., Bonnet, M., Chan, D. A., Sutphin, P. D., Nguyen, P., Giaccia, A. J., & Denny, W. A. 4-Pyridylanilinothiazoles that selectively target von Hippel - Lindau deficient renal cell carcinoma cells by inducing autophagic cell death. *Journal of Medicinal Chemistry* (2010) **53**(2): 787-797.

25. Heapy, A. M., & Brimble, M. A. Synthesis of the FG ring fragment of pectenotoxins 1-9. *Tetrahedron* (2010) **66**(29): 5424-5431.

26. Hicks, K. O., Siim, B. G., Jaiswal, J. K., Pruijn, F. B., Fraser, A. M., Patel, R., Hogg, A., Liyanage, H. D. S., Dorie, M. J., Brown, J. M., Denny, W. A., Hay, M. P., & Wilson, W. R. Pharmacokinetic/pharmacodynamic modeling identifies SN30000 and SN29751 as tirapazamine analogues with improved tissue penetration and hypoxic cell killing in tumors. *Clinical Cancer Research* (2010) **16**(20): 4946-4957.

27. Ho, H., Mithraratne, K., Schmid, H., Sands, G., & Hunter, P. Computer simulation of vertebral artery occlusion in endovascular procedures. *International Journal of Computer Assisted Radiology and Surgery* (2010) **5**(1): 29-37.

28. Hung, K. Y., Harris, P. W. R., & Brimble, M. A. Synthesis of methyl N-Boc-(2 S,4 R)-4-methylpipecolate. *Journal of Organic Chemistry* (2010) **75**(24): 8728-8731.

29. Hunter, P., Coveney, P. V., De Bono, B., Diaz, V., Fenner, J., Frangi, A. F., Harris, P., Hose, R., Kohl, P., Lawford, P., McCormack, K., Mendes, M., Omholt, S., Quarteroni, A., Skår, J., Tegner, J., Thomas, S. R., Tollis, I., Tsamardinos, I., Van Beek, J. H. G. M., & Viceconti, M. A vision and strategy for the virtual physiological human in 2010 and beyond. P*hilosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences* (2010) **368**(1920): 2595-2614.

30. Jameson, M. B., Rischin, D., Pegram, M., Gutheil, J., Patterson, A. V., Denny, W. A., & Wilson, W. R. A phase I trial of PR-104, a nitrogen mustard prodrug activated by both hypoxia and aldo-keto reductase 1C3, in patients with solid tumors. *Cancer Chemotherapy and Pharmacology* (2010) **65**(4): 791-801.

31. Johnston, J. M., Jiang, M., Guo, Z., & Baker, E. N. Structural and functional analysis of Rv0554 from Mycobacterium tuberculosis: Testing a putative role in menaquinone biosynthesis. *Acta Crystallographica Section D: Biological Crystallography* (2010) **66**(8): 909-917.

32. Jongbloed, S. L., Kassianos, A. J., McDonald, K. J., Clark, G. J., Ju, X., Angel, C. E., Chen, C. J. J., Dunbar, P. R., Wadley, R. B., Jeet, V., Vulink, A. J. E., Hart, D. N. J., & Radford, K. J. Human CD141+ (BDCA-3)+ dendritic cells (DCs) represent a unique myeloid DC subset that cross-presents necrotic cell antigens. *Journal of Experimental Medicine* (2010) **207**(6): 1247-1260.

33. Jor, J. W. Y., Nash, M. P., Nielsen, P. M. F., & Hunter, P. J. Estimating material parameters of a structurally based constitutive relation for skin mechanics. *Biomechanics and Modeling in Mechanobiology* (2010): 1-12.

34. Jüllig, M., Chen, X., Middleditch, M. J., Vazhoor, G., Hickey, A. J., Gong, D., Lu, J., Zhang, S., Phillips, A. R. J., & Cooper, G. J. S. Illuminating the molecular basis of diabetic arteriopathy: A proteomic comparison of aortic tissue from diabetic and healthy rats. *Proteomics* (2010) **10**(18): 3367-3378.

35. Kenny, L. C., Broadhurst, D. I., Dunn, W., Brown, M., North, R. A., McCowan, L., Roberts, C., Cooper, G. J. S., Kell, D. B., & Baker, P. N. Robust early pregnancy prediction of later preeclampsia using metabolomic biomarkers. *Hypertension* (2010) **56**(4): 741-749.

36. Kim, N., Cannell, M. B., & Hunter, P. J. Changes in the calcium current among different transmural regions contributes to action potential heterogeneity in rat heart. *Progress in Biophysics and Molecular Biology* (2010) **103**(1): 28-34.

37. Kmentova, I., Sutherland, H. S., Palmer, B. D., Blaser, A., Franzblau, S. G., Wan, B., Wang, Y., Ma, Z., Denny, W. A., & Thompson, A. M. Synthesis and structure-activity relationships of aza- and diazabiphenyl analogues of the antitubercular drug (6 S)-2-nitro-6-{[4-(trifluoromethoxy) benzyl]oxy}-6,7-dihydro-5 H-imidazo[2,1-b][1,3]oxazine (PA-824). *Journal of Medicinal Chemistry* (2010) **53**(23): 8421-8439.

38. Koch, C., Augustine, R. A., Steger, J., Ganjam, G. K., Benzler, J., Pracht, C., Lowe, C., Schwartz, M. W., Shepherd, P. R., Anderson, G. M., Grattan, D. R., & Tups, A. Leptin rapidly improves glucose homeostasis in obese mice by increasing hypothalamic insulin sensitivity. *Journal of Neuroscience* (2010) **30**(48): 16180-16187.

39. Kolnes, A. J., Ingvaldsen, A., Bolling, A., Stuenæs, J. T., Kreft, M., Zorec, R., Shepherd, P. R., & Jensen, J. Caffeine and theophylline block insulin-stimulated glucose uptake and PKB phosphorylation in rat skeletal muscles. *Acta Physiologica* (2010) **200**(1): 65-74.

40. Langley, R., Patel, D., Jackson, N., Clow, F., & Fraser, J. D. Staphylococcal superantigen super-domains in immune evasion. *Critical Reviews in Immunology* (2010) **30**(2): 149-165.

41. Laursen, N. S., Gordon, N., Hermans, S., Lorenz, N., Jackson, N., Wines, B., Spillner, E., Christensen, J. B., Jensen, M., Fredslund, F., Bjerre, M., Sottrup-Jensen, L., Fraser, J. D., & Andersen, G. R. Structural basis for inhibition of complement C5 by the SSL7 protein from Staphylococcus aureus. *Proceedings of the National Academy of Sciences of the United States of America* (2010) **107**(8): 3681-3686.

42. Lee, D. J., Harris, P. W. R., Kowalczyk, R., Dunbar, P. R., & Brimble, M. A. Microwave-assisted synthesis of fluorescein-labelled GalNAcα1-O-Ser/ Thr (Tn) glycopeptides as immunological probes. *Synthesis* (2010) **5**: 763-769.

43. Linke, C., Young, P. G., Kang, H. J., Bunker, R. D., Middleditch, M. J., Caradoc-Davies, T. T., Proft, T., & Baker, E. N. Crystal structure of the minor pilin FctB reveals determinants of group A streptococcal pilus anchoring. *Journal of Biological Chemistry* (2010) **285**(26): 20381-20389.

44. Linke, C., Young, P. G., Kang, H. J., Proft, T., & Baker, E. N. Purification, crystallization and preliminary crystallographic analysis of the minor pilin FctB from Streptococcus pyogenes. *Acta Crystallographica Section F: Structural Biology and Crystallization Communications* (2010) **66**(2): 177-179.

45. Lu, J., Gong, D., Choong, S. Y., Xu, H., Chan, Y. K., Chen, X., Fitzpatrick, S., Glyn-Jones, S., Zhang, S., Nakamura, T., Ruggiero, K., Obolonkin, V., Poppitt, S. D., Phillips, A. R. J., & Cooper, G. J. S. Copper(II)-selective chelation improves function and antioxidant defences in cardiovascular tissues of rats as a model of diabetes: Comparisons between triethylenetetramine and three less copper-selective transition-metal-targeted treatments. *Diabetologia* (2010) **53**(6): 1217-1226.

46. Lu, J., Poppitt, S. D., Othman, A. A., Sunderland, T., Ruggiero, K., Willett, M. S., Diamond, L. E., Garcia, W. D., Roesch, B. G., & Cooper, G. J. S. Pharmacokinetics, pharmacodynamics, and metabolism of triethylenetetramine in healthy human participants: An open-label trial. *Journal of Clinical Pharmacology* (2010) **50**(6): 647-658.

47. Manos-Turvey, A., Bulloch, E. M. M., Rutledge, P. J., Baker, E. N., Lott, J. S., & Payne, R. J. Inhibition studies of Mycobacterium tuberculosis salicylate synthase (MbtI). *ChemMedChem* (2010) **5**(7): 1067-1079.

48. Maroz, A., Shinde, S. S., Franzblau, S. G., Ma, Z., Denny, W. A., Palmer, B. D., & Anderson, R. F. Release of nitrite from the antitubercular nitroimidazole drug PA-824 and analogues upon one-electron reduction in protic, non-aqueous solvent. *Organic and Biomolecular Chemistry* (2010) **8**(2): 413-418.

49. Martin, S. K., Fitter, S., Bong, L. F., Drew, J. J., Gronthos, S., Shepherd, P. R., & Zannettino, A. C. W. NVP-BEZ235, a dual pan class I PI3 kinase and mTOR inhibitor, promotes osteogenic differentiation in human mesenchymal stromal cells. *Journal of Bone and Mineral Research* (2010) **25**(10): 2126-2137.

50. McKay, V. A., Thompson, S. J., Tran, P. M., Goodall, K. J., Brimble, M. A., & Barker, D. Stereoselective synthesis of 4-substituted 4-hydroxypiperidines via epoxidation-ring opening of 4-methylenepiperidines. *Synlett* (2010) **17**: 2631-2635.

51. Miller, N., Williams, G. M., & Brimble, M. A. Synthesis of Neoglycopeptides via Click Chemistry. *International Journal of Peptide Research and Therapeutics* (2010): 1-8.

52. Mittal, A., Göke, F., Flint, R., Loveday, B. P. T., Thompson, N., Delahunt, B., Kilmartin, P. A., Cooper, G. J. S., MacDonald, J., Hickey, A., Windsor, J. A., & Phillips, A. R. J. The redox status of experimental hemorrhagic shock as measured by cyclic voltammetry. *Shock* (2010) **33**(5): 460-466.

53. Mittal, A., Middleditch, M., Ruggiero, K., Loveday, B., Delahunt, B., Jüllig, M., Cooper, G. J. S., Windsor, J. A., & Phillips, A. R. J. Changes in the mesenteric lymph proteome induced by hemorrhagic shock. *Shock* (2010) **34**(2): 140-149.

54. Nikac, M., Brimble, M. A., Crumbie, R. L., & Bailey, T. D. Metal binding studies using spiroacetal thiacrown ethers. *Tetrahedron Letters* (2010) **51**(7): 1072-1074.

55. Palmer, B. D., Thompson, A. M., Sutherland, H. S., Blaser, A., Kmentova, I., Franzblau, S. G., Wan, B., Wang, Y., Ma, Z., & Denny, W. A. Synthesis and structure-activity studies of biphenyl analogues of the tuberculosis drug (6S)-2-nitro-6-{[4-(trifluoromethoxy) benzyl]oxy}-6,7-dihydro- 5H-imidazo[2,1-b][1,3]oxazine (PA-824). *Journal of Medicinal Chemistry* (2010) **53**(1): 282-294.

56. Patel, D., Wines, B. D., Langley, R. J., & Fraser, J. D. Specificity of staphylococcal superantigen-like protein 10 toward the human IgG1 Fc domain. *Journal of Immunology (*2010) **184**(11): 6283-6292.

57. Peltier, R., Brimble, M. A., Wojnar, J. M., Williams, D. E., Evans, C. W., & DeVries, A. L. Synthesis and antifreeze activity of fish antifreeze glycoproteins and their analogues. *Chemical Science* (2010) **1**(5): 538-551.

58. Peltier, R., Evans, C. W., Devries, A. L., Brimble, M. A., Dingley, A. J., & Williams, D. E. Growth habit modification of ice crystals using antifreeze glycoprotein (AFGP) analogues. *Crystal Growth and Design* (2010) **10**(12): 5066-5077.

59. Prosser, G. A., Copp, J. N., Syddall, S. P., Williams, E. M., Smaill, J. B., Wilson, W. R., Patterson, A. V., & Ackerley, D. F. Discovery and evaluation of Escherichia coli nitroreductases that activate the anti-cancer prodrug CB1954. *Biochemical Pharmacology* (2010) **79**(5): 678-687.

60. Prosser, G. A., Patterson, A. V., & Ackerley, D. F. uvrB gene deletion enhances SOS chromotest sensitivity for nitroreductases that preferentially generate the 4-hydroxylamine metabolite of the anti-cancer prodrug CB1954. *Journal of Biotechnology* (2010) **150**(1): 190-194.

61. Rathwell, K., Sperry, J., & Brimble, M. A. Synthesis of triazole analogues of the nanaomycin antibiotics using 'click chemistry'. *Tetrahedron* (2010) **66**(23): 4002-4009.

62. Reynolds, H. M., Walker, C. G., Dunbar, P. R., O'Sullivan, M. J., Uren, R. F., Thompson, J. F., & Smith, N. P. Functional anatomy of the lymphatics draining the skin: A detailed statistical analysis. *Journal of Anatomy* (2010) **216**(3): 344-355.

63. Shinde, S. S., Maroz, A., Hay, M. P., Patterson, A. V., Denny, W. A., & Anderson, R. F. Characterization of radicals formed following enzymatic reduction of 3-substituted analogues of the hypoxia-selective cytotoxin 3-amino-1,2,4- benzotriazine 1,4-dioxide (tirapazamine). *Journal of the American Chemical Society* (2010) **132**(8): 2591-2599.

64. Smith, W. D., Pointon, J. A., Abbot, E., Kang, H. J., Baker, E. N., Hirst, B. H., Wilson, J. A., Banfield, M. J., & Kehoe, M. A. Roles of minor pilin subunits Spy0125 and Spy0130 in the serotype M1 Streptococcus pyogenes strain SF370. *Journal of Bacteriology* (2010) **192**(18): 4651-4659.

65. Sperry, J., Harris, E. B. J., & Brimble, M. A. Total synthesis and absolute configuration of (-)-berkeleyamide A. *Organic Letters* (2010) **12**(3): 420-423.

66. Sperry, J., Liu, Y. C., & Brimble, M. A. Synthesis of natural products containing spiroketals via intramolecular hydrogen abstraction. *Organic and Biomolecular Chemistry* (2010) **8**(1): 29-38.

67. Sperry, J., Wilson, Z. E., Rathwell, D. C. K., & Brimble, M. A. Isolation, biological activity and synthesis of benzannulated spiroketal natural products. *Natural Product Reports* (2010) **27**(8): 1117-1137.

68. Sutherland, H. S., Blaser, A., Kmentova, I., Franzblau, S. G., Wan, B., Wang, Y., Ma, Z., Palmer, B. D., Denny, W. A., & Thompson, A. M. Synthesis and structure-activity relationships of antitubercular 2-nitroimidazooxazines bearing heterocyclic side chains. *Journal of Medicinal Chemistry* (2010) **53**(2): 855-866.

69. Tercel, M., Yang, S., Atwell, G. J., Smith, E., Gu, Y., Anderson, R. F., Denny, W. A., Wilson, W. R., & Pruijn, F. B. Hypoxic selectivity and solubility - Investigating the properties of A-ring substituted nitro seco-1,2,9,9a-tetrahydrocyclopropa[c]benz[e] indol-4-ones (nitroCBIs) as hypoxia-activated prodrugs for antitumor therapy. *Bioorganic and Medicinal Chemistry* (2010) **18**(14): 4997-5006.

70. Tups, A., Anderson, G. M., Rizwan, M., Augustine, R. A., Chaussade, C., Shepherd, P. R., & Grattan, D. R. Both p110α and p110β isoforms of phosphatidylinositol 3-OH-kinase are required for insulin signalling in the hypothalamus. *Journal of Neuroendocrinology* (2010) **22**(6): 534-542.

71. Ussher, J. E., & Taylor, J. A. Optimized transduction of human monocyte-derived dendritic cells by recombinant adeno-associated virus serotype 6. *Human Gene Therapy* (2010) **21**(12): 1675-1686.

72. Wadsworth, A. D., Sperry, J., & Brimble, M. A. Synthesis of the pyranonaphthoquinones dehydroherbarin, (+)-astropaquinone B and (+)-astropaquinone C en route to ascomycones A and B. *Synthesis* (2010) **15**: 2604-2608.

73. Walker, C. S., Li, X., Whiting, L., Glyn-Jones, S., Zhang, S., Hickey, A. J., Sewell, M. A., Ruggiero, K., Phillips, A. R. J., Kraegen, E. W., Hay, D. L., Cooper, G. J. S., & Loomes, K. M. Mice lacking the neuropeptide α-calcitonin gene-related peptide are protected against diet-induced obesity. *Endocrinology* (2010) **151**(9): 4257-4269.

74. Watkins, H. A., & Baker, E. N. Structural and functional characterization of an RNase HI domain from the bifunctional protein Rv2228c from Mycobacterium tuberculosis. *Journal of Bacteriology* (2010) **192**(11): 2878-2886.

75. Webby, C. J., Jiao, W., Hutton, R. D., Blackmore, N. J., Baker, H. M., Baker, E. N., Jameson, G. B., & Parker, E. J. Synergistic allostery, a sophisticated regulatory network for the control of aromatic amino acid biosynthesis in Mycobacterium tuberculosis. *Journal of Biological Chemistry* (2010) **285**(40): 30567-30576.

76. Wilson, Z. E., & Brimble, M. A. A flexible asymmetric synthesis of the tetracyclic core of berkelic acid using a Horner-Wadsworth-Emmons/oxa-Michael cascade. *Organic and Biomolecular Chemistry* (2010) **8**(6): 1284-1286.

77. Zhang, H., Li, B., Young, A. A., & Hunter, P. J. Recovery of myocardial kinematic function without the time history of external loads. *EURASIP Journal on Advances in Signal Processing* (2010) **2010**: 1-9.

Patents

Patents granted

1. Denny, W.A., Atwell, G.J., Yang, S., Wilson, W.R., Patterson, A.V. Nitroaniline-based alkylating agents and their use as prodrugs. *US Patent 7776924,* 2010

2. Denny, W.A., Hay, M.P., Hicks, K.O., Pruijn, F.B., Wilson, W.R., Pchalek, K. 1,2,4-Benzotriazine-1,4-dioxides. *US Patent 7816521,* 2010

3. 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. *US Patent 7718688,* 2010

4. Ding, C.Z., Lu, G., Combrink, K., Chen, D.D., Song, M., Wang, J., Ma. Z., Palmer, B.D., Blaser, A., Thompson, A.M., Kmentova, I., Sutherland, H.S., Denny, W.A. Bicyclic nitroimidazole-substituted phenyl oxazolidinones. *US Patent 7666864,* 2010

5. Hay, M.P., Blaser, A., Denny, W.A., Hicks, K.O., Lee, H.H., Pchalek, K., Pruijn, F.B., Siim, B.G., Wilson, W.R., Yang, S. Tricyclic 1,2,4-triazine oxides and compositions therefrom for therapeutic use in cancer treatments. *US Patent 24231,* 2010

6. Phiasivongsa, P., Redkar, S.G., Gamage, S., Brooke, D., Denny, W., Bearss, D.J., Vankayalapati, H. Quinoline derivatives for modulating DNA methylation. *US Patent 7790746,* 2010

Patents published

1. Atwell, G.J., Denny, W.A., Yang, S. Processes of preparing asymmetric dinitrobenzamide mustard compounds, intermediate compounds useful therein and products obta ined therefrom. *US Patent Appl. US20100121091A1,* 2010

2. Denny, W.A., Atwell, G.J., Yang, S., Wilson, W.R., Patterson, A.V., Helsby, N.A. Novel nitrophenyl mustard and nitrophenylaziridine alcohols and their corresponding phosphates and their use as targeted cytotoxic agents. *US Patent Appl. US20100010094A1,* 2010

3. Giaccia, A.J., Lai, E., Razorenova, O., Chan, D., Hay, M.P., Bonnet, M., Sun, C.L., Tabibiazar, R. Heteroaryl alkylbenzamides and their uses. *US Patent Appl. US61/391958,* 2010

4. Hay, M.P., Blaser, A., Denny, W.A., Hicks, K.O., Lee, H.H., Pchalek, K., Pruijn, F.B., Siim, B.G., Wilson, W.R., Yang, S. Tricyclic 1,2,4-triazine oxides and compositions therefrom for therapeutic use in cancer treatments. *European Patent Appl. EP1866292A4,* 2010

5. Patterson, A.V., Guise, C.P., Abbatista, M.R., Wilson, W.R., Smaill, J.B., Syddall, S., Denny, W.A., Ashoorzadeh, A. AKR1C3 as a biomarker, methods of selecting and treating patients based upon an AKR1C3 profile and compounds for use therein. *PCT Int. Appl. WO2010044686 A1,* 2010

6. Patterson, A.V., Smaill, J.B., Denny, W.A., Wilson, W.R., Syddall, S., Ashoorzadeh, A. Nitrophenyl mustard alcohols, their corresponding phosphates and their use as targeted cytotoxic agents. *PCT Int. Appl. WO2010044685 A1,* 2010

7. Rewcastle, G.W; Gamage, S.A. Preparation of pyrimidinyl and 1,3,5-triazinyl benzimidazoles and their use in cancer therapy. *PCT Int. Appl. WO10110686,* 2010

8. Rewcastle, G.W; Gamage, S.A; Flanagan, J.U; Giddens, A.C. Pyrimidinyl and 1,3,5-triazinyl benzimidazole sulfonamides and their use in cancer therapy. *PCT Int. Appl. WO10110685,* 2010

9. Rewcastle, G.W., Shepherd, P.R., Chaussade, C., Denny, W.A., Gamage, S.A. Substituted pyrimidine and triazine derivatives and their use in cancer therapy. *PCT Int. Appl. WO2009120094A3,* 2010

10. Smaill, J.B., Patterson, A.V., Denny, W.A., Wilson, W.R., Lu, G.-L., Anderson, R.F., Lee, H.H., Ashoorzadeh, A. Prodrug forms of kinase inhibitors and their use in therapy. *PCT Int. Appl. WO2010104406 A1,* 2010

Patents filed

1. Patterson, A.V., Smaill, J.B., Ackerley, D.F., Syddall, S.P., Copp, J.N., Prosser, G.A., Mowday, A.M., Williams, E., Ashoorzadeh, A., Flanagan, J.U. Bacterial nitroreductase enzymes and methods relating thereto. *NZ Provisional Patent Application 586849,* 2010

2. Owen, J.G., Ackerley, D.F., Methods for identifying and characterising natural product gene clusters. *NZ Provisional Patent Application 587972,* 2010

3. Ackerley, D.F., Owen, J.G., A method for characterising and detecting modifiers of a phosphopantetheinyl transferase. *NZ Provisional Patent Application 590002,* 2010

4. Eason, C., Brimble, M.A., Rennison, D., Conole, D., Vertebrate pest control. *NZ Patent Application 583496,* 2010

5. Turcotte, S., Chan, D.A., Sutphin, P.D., Giaccia, A.J., Hay, M.P., Denny, W.A., Bonnet, M.M. Heteroaryl compounds, compositions of matter and methods of use in cancer treatment. *PCT/US Appl. No. 12/921,767,* 2010

6. Thompson, A.M., Blaser, A., Denny, W.A., Ma, Z. Nitroimidazooxazine and nitroimidazooxazole analogues and their uses. *PCT Appl, 2010/044908,* 2010

7. Denny, W.A., Thompson, .M., Blaser, A., Ma, Z., Palmer, B.D., Sutherland, H.S., Kmentova, I. Nitroimidazooxazines and their uses in anti-tubercular therapy. *PCT Appl, 2010/043906,* 2010

8. Sutphin, P., Chan, D., Turcotte, S., Denny, W.A., Hay, M.P., Giddens, A.C., Bonnet, M., Giaccia, A. Heteroaryl benzamides; compositions and methods of use. *PCT Appl. No. PCT/US10/42742,* 2010

9. Smaill, J.B., Patterson, A.V., Lu, G-L., Lee, H.H., Ashoorzadeh, A., Anderson, R.F., Wilson, W.R., Denny, W.A., Hsu, H-L., Maroz, A., Jamieson, S.M.F., Mowday, A.M., Carlin, K.M. Kinase inhibitors, prodrug forms of kinase inhibitors and use in therapy. *PCT Int Appl,* 2010

10. Spicer. J.A., Huttunen, K.A., Lyons, D.M., Trapani, J.A., Smyth. M.J., Denny. W.A. Benzylidene-2- thioxoimidazolidinones and related compounds capable of inhibiting perforin activity. *PCT Appl. No. PCT /US/61/289,871,* 2010

Presentations

The international significance of the research carried out by Maurice Wilkins Centre investigators and their teams is demonstrated by more than 150 invitations to give international and national presentations in 2010. The presentations included invited lectures at conferences and seminars at academic institutions in the United States of America, Japan, the United Kingdom, Germany, Australia, France, Singapore, Switzerland, Canada, Korea, Austria, the Netherlands, Italy, Greece, Argentina, Belgium, Spain, Poland, Ireland, Sweden and New Zealand, as shown in the diagram below.

Presentation highlights

Significant presentations given by Maurice Wilkins Centre investigators in 2010 include:

- Professor Ted Baker gave the Leach Medal Lecture at the 35th Lorne Conference on Protein Structure and Function in Lorne, Australia, in February. The title of his lecture was “Serendipity and discovery: structure, assembly and stability of gram-positive bacterial pili”.
- Professor Margaret Brimble received the Royal Society of Chemistry (UK) Natural Products Chemistry Award in 2010 and gave four award lectures in the United Kingdom and Ireland, at the University of Reading, The University of Manchester, University College Dublin and University College Cork.
- Professor Margaret Brimble was also invited to give plenary lectures at the Royal Society of Chemistry (UK) Organic Division Chemistry Biology Interface Symposium in Dublin, Ireland; at the 1st International Conference on Molecular and Functional Catalysis in Singapore; and at the 35th RACI Victoria Annual Synthesis Symposium in Melbourne, Australia.

- Dr Michael Berney, a Maurice Wilkins Centre affiliate investigator, was awarded the 2010 Swiss Society of Microbiology Early Career Award and gave his award lecture on the survival of pathogenic bacteria in hostile environments at the society's 2010 Annual Congress. He also presented work from his collaboration with Maurice Wilkins Centre investigator Professor Greg Cook on "Adaptation of the mycobacterial cell to hypoxia: deployment of anaerobic enzymes and an unexpected role for proline metabolism" in a lecture tour with invited talks at the National Institute of Medical Research, Mill Hill, London, UK; Institute of Microbiology, ETH Zurich, Switzerland; Swiss Tropical and Public Health Institute, Basel, Switzerland; and Eawag Aquatic Research Institute, Dubendorf, Switzerland.
- Professor Peter Hunter was invited to give keynote lectures at the International Conference on Computational Science in Amsterdam, The Netherlands, and the 17th Congress of the European Society of Biomechanics in Edinburgh, Scotland.

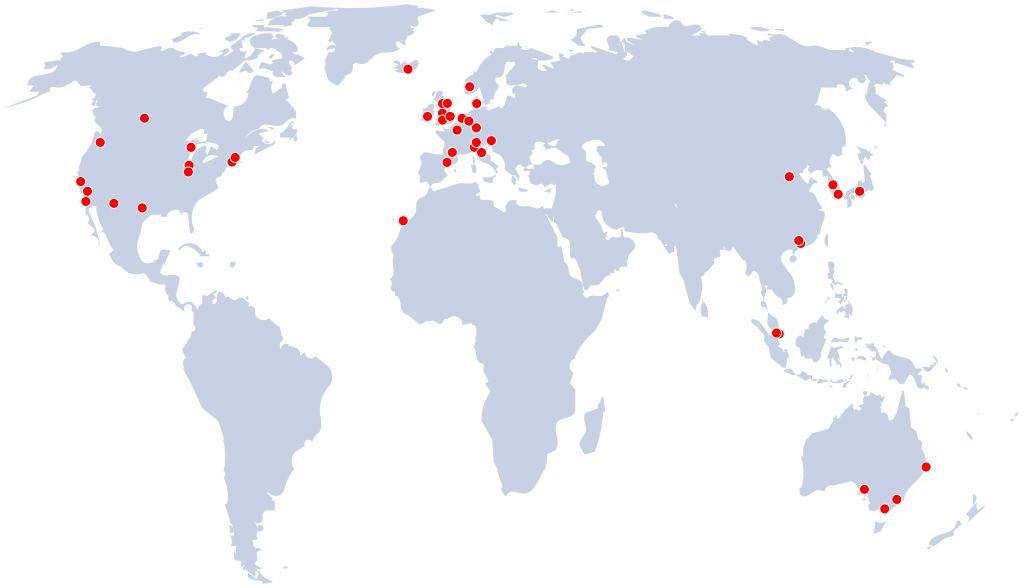
Delegation to Japan

A delegation of Maurice Maurice Wilkins Centre investigators visited three leading immunology institutes in Japan (RIKEN-RCAI in Yokohama, iFReC in Osaka, and Chiba University) in June 2010, sponsored by the Ministry of Research, Science and Technology. The delegation included investigators from five NZ institutions: Sarah Hook (University of Otago), Anne La Flamme (Victoria University of Wellington), Gavin Painter (IRL Ltd), Ian Hermans (Malaghan Institute of Medical Research) and John Fraser, Rod Dunbar and Gib Bogle from The University of Auckland. Joint symposia were held at the Japanese institutions, and individual meetings between investigators followed to develop collaborative opportunities. The Maurice Wilkins Centre is continuing to build relationships with these institutions, and a number of collaborations are already underway.

Collaborations

The Maurice Wilkins Centre contributes to and benefits from an extensive network of national and international academic collaborations that has been built up by our investigators over a number of years. The research funded through the Centre has strengthened many of these existing links and helped to establish new collaborations.

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



New academic collaborations

The University of Washington (USA)

Integrated Biotherapeutics (USA)

The University of Newcastle (UK)

Centre for Computational Science (UK)

John Innes Centre (UK)

Manchester Centre for Integrative Systems Biology (UK)

University College Cork (Ireland)

National Centre for Scientific Research (France)

Centre de Physiopathologic de Toulouse-Purpan (France)

European Synchrotron Radiation Facility (France)

Philipps University Marburg (Germany)

RWTH Aachen University (Germany)

Universitat Pompeu Fabra (Spain)

Istituto Ortopedico Rizzoli (Italy)

Norwegian University of Life Sciences (Norway)

National Institute of Occupational Health (Norway)

ShenZhen University (China)

Institute of Biophysics, Chinese Academy of Science (China)

Inje University (South Korea)

Kansai Medical University (Japan)

Singapore National Imaging Institute (Singapore)

The University of New South Wales (Australia)

The University of Sydney (Australia)

University of Western Sydney (Australia)

Royal Prince Alfred Hospital (Australia)

Continuing academic collaborations

North America

Stanford University (USA)

The University of California (USA)

The University of Chicago (USA)

The University of Illinois (USA)

New York University (USA)

The Scripps Research Institute (USA)

Global Alliance for TB Drug Development (USA)

The International TB Structural Genomics Consortium (USA)

Texas Medical Center (USA)

Ludwig Institute for Cancer Research (USA)

Advanced Biomedical Research Inc (USA)

IUPS International Physiome Project (USA)

Proacta Inc (USA)

University of Alberta (Canada)

Asia Pacific

Hong Kong University of Science and Technology (China)

Seoul National University (Korea)

Agency for Science Technology & Research (A*STAR)(Singapore)

University of Melbourne (Australia)

University of Adelaide (Australia)

Garvan Institute of Medical Research (Australia)

Queensland Institute of Medical Research (Australia)

Mater Medical Research Institute (Australia)

The Cancer Institute NSW (Australia)

Burnet Institute Melbourne (Australia)

Peter MacCallum Cancer Centre Melbourne (Australia)

UK and Europe

University of Oxford (UK)

Kings College London (UK)

University College Cork (UK)

The University of Manchester (UK)

Cancer Research Technology Ltd (UK)

European Bioinformatics Institute (UK)

Hospital Universitario Nuestra Senora de Canderlaria (Spain)

Leiden University (The Netherlands)

University of Aarhus (Denmark)

University of Oslo (Norway)

University of Iceland (Iceland)

Uptake of Maurice Wilkins Centre research and expertise

The primary focus of the Maurice Wilkins Centre is on finding new ways to effectively target human disease. The Centre drives the translation of its research and expertise from the laboratory to development phase through a variety of partnerships with commercial and non-profit organisations, in New Zealand and overseas.

The creation of spin-out companies is an important pathway for the development of Maurice Wilkins Centre research, and often brings in international partners and funds. Maurice Wilkins Centre investigators maintain close links with such companies and further work is regularly contracted back to their research groups. The Centre has close links with spin-out companies such as ProActa Inc, Pathway Therapeutics Ltd and Symansis Ltd.

The Maurice Wilkins Centre also partners with established companies, and the knowledge and expertise that its investigators have developed in scientific fields vital to the biotechnology and pharmaceutical sectors are highly sought after. Examples of contract research and the provision of facilities to industry are outlined on pages 30-31 of this report and Maurice Wilkins Centre investigators also act as consultants for a number of national and international companies. In 2010 the expertise of Maurice Wilkins Centre investigators was sought by:

- Paraco Ltd
- Landcare Research New Zealand Ltd
- Industrial Research Ltd
- AFT Pharmaceuticals Ltd
- Ruga Corp (USA)
- Proacta Inc (USA)
- Pathway Therapeutics Inc (USA)
- Bomac Laboratories Ltd
- Symansis Ltd
- Neuren Pharmaceuticals Ltd
- Androgenix Ltd
- InSyGen Therapeutics Ltd
- EBonz Ltd
- Pacific Edge Biotechnology Ltd
- Innate Therapeutics Ltd
- New Zealand Institute for Rare Disease Ltd
- Biotech Equity Partners Pty (Australia)
- Comvita Ltd
- Coda Therapeutics Inc (USA)
- GNI Ltd (Japan)
- Centella Biotechnologies Inc (USA)
- Sirtex Medical Ltd (USA)
- Novartis International AG (Switzerland)
- Amgen Inc (USA)
- Merck & Co Inc (USA)
- PharmaZen Ltd
- Alcon Laboratories Inc (USA)

The establishment of partnerships with international non-profit organisations is another way in which the Maurice Wilkins Centre achieves uptake of its research and expertise.

For example, researchers associated with the Centre and based at the Auckland Bioengineering Institute are paid to work on the "Human Physiome Project", along with European collaborators, under the European Commission Framework Programme. Maurice Wilkins Centre investigators are also involved with international organisations such as the Global Alliance for TB Drug Development (see page 17) and the TB Structural Genomics Consortium.

In 2010, in the first royalty-free license agreement between two non-profit drug developers, the Global Alliance for TB Drug Development granted rights to the Drugs for Neglected Disease Initiative (DNDi) to develop some of its anti-tuberculosis drugs for use in other neglected diseases, such as visceral leishmaniasis, human African trypanosomiasis and Chagas' disease. Amongst these are a series of compounds designed and synthesized by the Auckland Cancer Society Research Group led by Maurice Wilkins Centre investigator Professor Bill Denny.

Awards and Honours

- **Leach Medal**

  Professor Ted Baker was awarded the 2010 Leach Medal at the Lorne Conference on Protein Structure and Function (Australia) and gave the Leach Lecture at the conference, entitled "Serendipity and discovery: structure, assembly and stability of Gram-positive bacterial pili".

- **Royal Society of Chemistry Awards**

  Professor Margaret Brimble received two awards from the Royal Society of Chemistry (UK) in 2010. She was awarded the 2010 Royal Society of Chemistry Natural Products Award and the Simonsen Lectureship for her outstanding contributions to the synthesis of biologically active natural products, their derivatives and analogues. Professor Brimble also received the Royal Society of Chemistry Editorial Board Award for reviewing the most papers across all Royal Society of Chemistry editorial boards.

- **Invitrogen Life Science Award**

  Maurice Wilkins Centre investigator Dr Justin O'Sullivan received the 2010 Invitrogen Life Science Award at the Queenstown Molecular Biology meeeting in September. The award is presented annually to an emerging New Zealand-based researcher who has published excellent molecular biology based research in high-ranking international journals. Dr O'Sullivan, a Senior Lecturer in Molecular Biology at Massey University, was given the award for his pioneering work on the nano-scale labyrinth of chromosomal linkages within cells.

- **NZBIO Young Biotechnologist of the Year**

  Maurice Wilkins Centre investigator, Dr Wayne Patrick, from the Institute of Natural Sciences at Massey University, Albany, was named the NZBIO Young Biotechnologist of the Year at the NZBIO Awards Dinner in March. Dr Patrick won the award for his world-class research and development in the field of DNA ligase enzymes, which has attracted significant recognition from his peers and funding from key agencies.

- **Swiss Society of Microbiology Early Career Award**

  Maurice Wilkins Centre affiliate investigator Dr Michael Berney, from the Department of Microbiology and Immunology, University of Otago, was awarded the 2010 Swiss Society of Microbiology Early Career Award. This award is given annually to young investigators in the field of microbiology for achievements that are outstanding in terms of their originality and particular scientific value. Dr Berney presented his work on the survival of pathogenic bacteria in hostile environments at the 2010 Annual Congress of the Swiss Society of Microbiology.

- **New Zealand Science and Technology Postdoctoral Fellowships**

  Maurice Wilkins Centre affiliate investigators Dr Esther Bulloch and Dr Greg Smith were both awarded a New Zealand Science and Technology Postdoctoral Fellowship in 2010. The fellowships, which provide three years of funding, are designed to take New Zealand's emerging researchers to the next stage of their career, and help build greater national capability and knowledge. Dr Bulloch's project aims to develop new biotechnology to produce proteins for research purposes, and apply it to study the paramyxoviruses that cause acute respiratory disease in New Zealand children. Dr Smith will investigate molecular mechanisms of the metabolic side effects of drugs used to treat schizophrenia.

- **Newton International Fellowship**

  Dr Zoe Wilson, a PhD student supervised by Professor Margaret Brimble, was awarded a Newton International Fellowship in 2010 by the Royal Society of Chemistry (UK). The award recognises the very best early stage post-doctoral researchers from around the world, and offers support for two years at a research institution in the United Kingdom. Zoe will carry her post-doctoral research at the laboratory of Professor Steve Ley, Trinity College, Cambridge University (see page 15).

- **Humboldt Research Fellowship and Hatherton Award**

  Dr Dominea Rathwell, a PhD student supervised by Professor Margaret Brimble, was awarded a Humboldt Research Fellowship for Postdoctoral Researchers in 2010 by the Humboldt Foundation, Germany, to conduct research at the laboratory of Professor Peter Seeberger, Department of Biomolecular System, Max Planck Institute of Colloid and Interface (see page 15). Dominea was also awarded the 2010 Hatherton Award by the Royal Society of New Zealand, an annual award for the best scientific paper in physical, earth, or maths and information sciences by a doctoral student from a New Zealand university.

Financial Report 2010

Operating Fund[a]

	$ 2010	$ 2009
Income		
CoRE grant	-3,972,800	-3,972,800
Equipment User charges[b]	-364,074	-220,980
Balance from previous year[c]	-2,346,245	-1,781,293
Total Income	**-6,683,119**	**-5,975,074**
Expenditure		
Salaries[d]	1,124,853	1,234,620
Overheads	994,045	861,831
Project costs[e]	1,001,726	631,530
Student support (PhD and other)[e]	395,799	199,819
Travel	94,740	85,492
Depreciation	617,359	615,536
Total Expenses	**4,228,520**	**3,628,828**
Income less expenditure[f]	**-2,454,599**	**-2,346,245**

Capital Expenditure Fund

Income	
Balance of TEC grant 2002	-10,596
Balance of TEC grant 2008	-56,965
Total Income	**-67,561**
Expenditure	
Capital expenditure 2009	46,257
Funds carried forward to 2010[g]	**-21,303**

Notes

a) This financial report is for the period 1st January to 31st December 2010 and covers the second six months of the Maurice Wilkins Centre Year 8 and the first six months of Maurice Wilkins Centre Year 9 (CoRE grant 2008 to 2014). This report only details income and expenditure relating to the CoRE grant funding that the Maurice Wilkins Centre receives from the Tertiary Education Commission. It does not contain details of external operating funding to Centre investigators from other funding agencies.

b) These equipment user charges are collected by the Maurice 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 and depreciation costs of the equipment.

c) This brought forward balance is funding from previous years of the Maurice Wilkins Centre that has been committed to funding research initiatives from 2011 to 2014.

d) Summary: Maurice Wilkins Centre supported research staff FTEs 2010

Principal Investigators	0.50
Research Fellows	8.67
Research Technicians	4.33
Total	13.50

e) These costs include the costs of subcontracts for Associate Investigator's research projects during 2010.

f) This balance of funding has been committed to supporting Maurice Wilkins Centre research initiatives from 2011 to 2014.

g) This balance of funding represents savings made on the costs of Maurice Wilkins Centre capital equipment purchased from 2003 to 2011. These savings are largely due to variation in exchange rates between the time that the capital equipment budget was set and the time of equipment purchase. This funding will be used to add additional capacity to existing Maurice Wilkins Centre capital equipment.

Directory

Governing Board Members

Mr. Bill Falconer (Chair)

Prof Dick Bellamy

Prof Grant Guilford

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 Suzanne Cory

Dr Jilly Evans

Prof Shankar Subramaniam

Prof Dick Wettenhall

Principal investigators

Prof Rod Dunbar (Director)	School of Biological Sciences	The University of Auckland
Prof John Fraser (Deputy Director)	Department of Molecular Medicine and Pathology	The University of Auckland
Prof Ted Baker	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
Dr Iain Anderson	Auckland Bioengineering Institute	The University of Auckland
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
Mr Adam Bartlett	Department of Surgery	The University of Auckland
Dr Mik Black	Department of Biochemistry	University of Otago
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 Lai-Ming Ching	Auckland Cancer Society Research Centre	The University of Auckland
Prof Gregory Cook	Department of Microbiology and Immunology	University of Otago
Assoc Prof Brent Copp	Department of Chemistry	The University of Auckland
Prof Jillian Cornish	School of Medicine	The University of Auckland
Dr Edmund Crampin	Auckland Bioengineering Institute	The University of Auckland
Professor Kathryn Crosier	Department of Molecular Medicine and Pathology	The University of Auckland
Professor Phil Crosier	Department of Molecular Medicine and Pathology	The University of Auckland
Assoc Prof John Cutfield	Department of Biochemistry	University of Otago
Assoc Prof Catherine Day	Department of Biochemistry	University of Otago
Dr Andrew Dingley	Department of Chemistry	The University of Auckland
Prof Mike Eccles	Department of Pathology	University of Otago
Dr Gary Evans	Industrial Research Ltd	
Prof Antony Fairbanks	Department of Chemistry	University of Canterbury
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	
Prof Juliet Gerrard	School of Biological Sciences	University of Canterbury
Prof Dave Grattan	Department of Anatomy and Structural Biology	University of Otago
Prof Colin Green	School of Medicine	The University of Auckland
Assoc Prof David Greenwood	Plant and Food Research	
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
Dr Sarah Hook	School of Pharmacy	University of Otago
Dr Marc Jacobs	Auckland Bioengineering Institute	The University of Auckland
Prof Geoffrey Jameson	Institute of Fundamental Sciences	Massey University
Dr Richard Kingston	School of Biological Sciences	The University of Auckland

Dr Joanna Kirman	Malaghan Institute of Medical Research	
Prof Kurt Krause	Department of Biochemistry	University of Otago
Dr Anne La Flamme	School of Biological Sciences	Victoria University of Wellington
Dr David Larsen	Department of Chemistry	University of Otago
Prof Graham Le Gros	Malaghan Institute of Medical Research	
Prof Peter Lobie	The Liggins Institute	The University of Auckland
Dr Kerry Loomes	School of Biological Sciences	The University of Auckland
Dr David Long	Auckland Bioengineering Institute	The University of Auckland
Dr Shaun Lott	School of Biological Sciences	The University of Auckland
Assoc Prof Mark McKeage	Department of Pharmacology	The University of Auckland
Prof Andrew Mercer	Department of Microbiology and Immunology	University of Otago
Assoc Prof Peter Metcalf	School of Biological Sciences	The University of Auckland
Dr Kathy Mountjoy	Department of Physiology	The University of Auckland
Dr Rinki Murphy	Department of Medicine	The University of Auckland
Dr Richard Newcomb	Plant and Food Research	
Assoc Prof Poul Nielsen	Auckland Bioengineering Institute	The University of Auckland
Dr Justin O'Sullivan	Institute of Natural Sciences	Massey University, Albany
Dr Gavin Painter	Industrial Research Ltd	
Assoc Prof Brian Palmer	Auckland Cancer Society Research Centre	The University of Auckland
Assoc Prof Emily Parker	Department of Chemistry	University of Canterbury
Dr Wayne Patrick	Institute of Natural Sciences	Massey University
Dr Adam Patterson	Auckland Cancer Society Research Centre	The University of Auckland
Assoc Prof James Paxton	Department of Pharmacology and Clinical Pharmacology	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
Prof Thomas Rades	National School of Pharmacy	University of Otago
Prof Ian Reid	School of Medicine	The University of Auckland
Assoc Prof Gordon Rewcastle	Auckland Cancer Society Research Centre	The University of Auckland
Dr Johannes Reynisson	Department of Chemistry	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 Rob Smith	Department of Chemistry	University of Otago
Prof James Sneyd	Department of Mathematics	The University of Auckland
Dr Christopher Squire	School of Biological Sciences	The University of Auckland
Dr Vinod Suresh	Auckland Bioengineering Institute	The University of Auckland
Dr John Taylor	School of Biological Sciences	The University of Auckland
Dr Matt Templeton	Plant and Food Research	
Dr Moana Tercel	Auckland Cancer Society Research Centre	The University of Auckland
Dr Peter Tyler	Industrial Research Ltd	
Dr Joel Tyndall	School of Pharmacy	University of Otago
Dr Siouxsie Wiles	Department of Molecular Medicine and Pathology	The University of Auckland
Prof William Wilson	Auckland Cancer Society Research Centre	The University of Auckland
Prof John Windsor	Department of Surgery	The University of Auckland
Dr Sarah Young	Department of Pathology	University of Otago
Dr Shaoping Zhang	School of Biological Sciences	The University of Auckland

CoRE funded research fellows

Dr Gib Bogle	Auckland Bioengineering Institute	The University of Auckland
Dr Anna Brooks	School of Biological Sciences	The University of Auckland
Dr Christina Buchanan	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
Assoc Prof Michael Hay	Auckland Cancer Society Research Centre	The University of Auckland
Dr Hyun-Sun Jin	Department of Molecular Medicine and Pathology	The University of Auckland
Dr Mia Jullig	School of Biological Sciences	The University of Auckland
Dr Catherine Lloyd	Auckland Bioengineering Institute	The University of Auckland
Assoc Prof Gordon Rewcastle	Auckland Cancer Society Research Centre	The University of Auckland
Dr Jeff Smaill	Auckland Cancer Society Research Centre	The University of Auckland
Dr Hiliary Sheppard	School of Biological Sciences	The University of Auckland
Dr Greg Smith	Department of Molecular Medicine and Pathology	The University of Auckland

Dr Christopher Squire	School of Biological Sciences	The University of Auckland
Dr James Ussher	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
Ms Coralie Dargaville	Department of Molecular Medicine and Pathology	The University of Auckland
Mr Ivan Ivanovic	School of Biological Sciences	The University of Auckland
Mr James Lawson	Auckland Bioengineering Institute	The University of Auckland
Ms Alisha Malik	Department of Molecular Medicine and Pathology	The University of Auckland
Mr Martin Middleditch	School of Biological Sciences	The University of Auckland
Ms Dominea Rathwell	Department of Chemistry	The University of Auckland
Ms Zoe Wilson	Department of Chemistry	The University of Auckland
Ms Sintia Winkler	School of Biological Sciences	The University of Auckland

CoRE funded PhD students

Ms Maggie Au	School of Biological Sciences	The University of Auckland
Mr Htin Lin Aung	Department of Microbiology and Immunology	University of Otago
Ms Nicola Blackmore	Department of Chemistry	University of Canterbury
Mr Matthew Bull	Auckland Cancer Society Research Centre	The University of Auckland
Mr Richard Bunker	School of Biological Sciences	The University of Auckland
Ms Kristina Burkert	School of Biological Sciences	The University of Auckland
Ms Tammie Cookson	Department of Chemistry	Canterbury University
Ms Alicia Didsbury	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 Simon Fung	Auckland Cancer Society Research Centre	The University of Auckland
Mr Ray Ge	School of Biological Sciences	The University of Auckland
Mr Joseph Gingell	School of Biological Sciences	The University of Auckland
Mr Paul Haseler	Department of Chemistry	The University of Auckland
Ms Weilin Hou	Department of Molecular Medicine and Pathology	The University of Auckland

Mr Daniel Hurley	Auckland Bioengineering Institute	The University of Auckland
Mr Dimitri Joseph	Department of Chemistry	University of Canterbury
Mr Meder Kamalov	Department of Chemistry	The University of Auckland
Ms Wendy Kang	Auckland Bioengineering Institute	The University of Auckland
Ms Inken Kelch	School of Biological Sciences	The University of Auckland
Mr Thomas Lagautriere	School of Biological Sciences	The University of Auckland
Ms Yee Suen Low	School of Biological Sciences	Victoria University of Wellington
Mr Hayden McEwen	Department of Anatomy and Structural Biology	University of Otago
Ms Siri McKelvie	School of Biological Sciences	The University of Auckland
Ms Karima Medini	Department of Chemistry	The University of Auckland
Ms Silke Neumann	School of Pharmacy	University of Otago
Ms Saem Park	School of Biological Sciences	The University of Auckland
Ms Deepa Patel	Department of Molecular Medicine and Pathology	The University of Auckland
Mr Soroush Safaei	Auckland Bioengineering Institute	The University of Auckland
Ms Emma Scaletti	Department of Biochemistry	University of Otago
Ms Katrin Schunemann	Department of Chemistry	The University of Auckland
Ms Jennifer Sweny	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

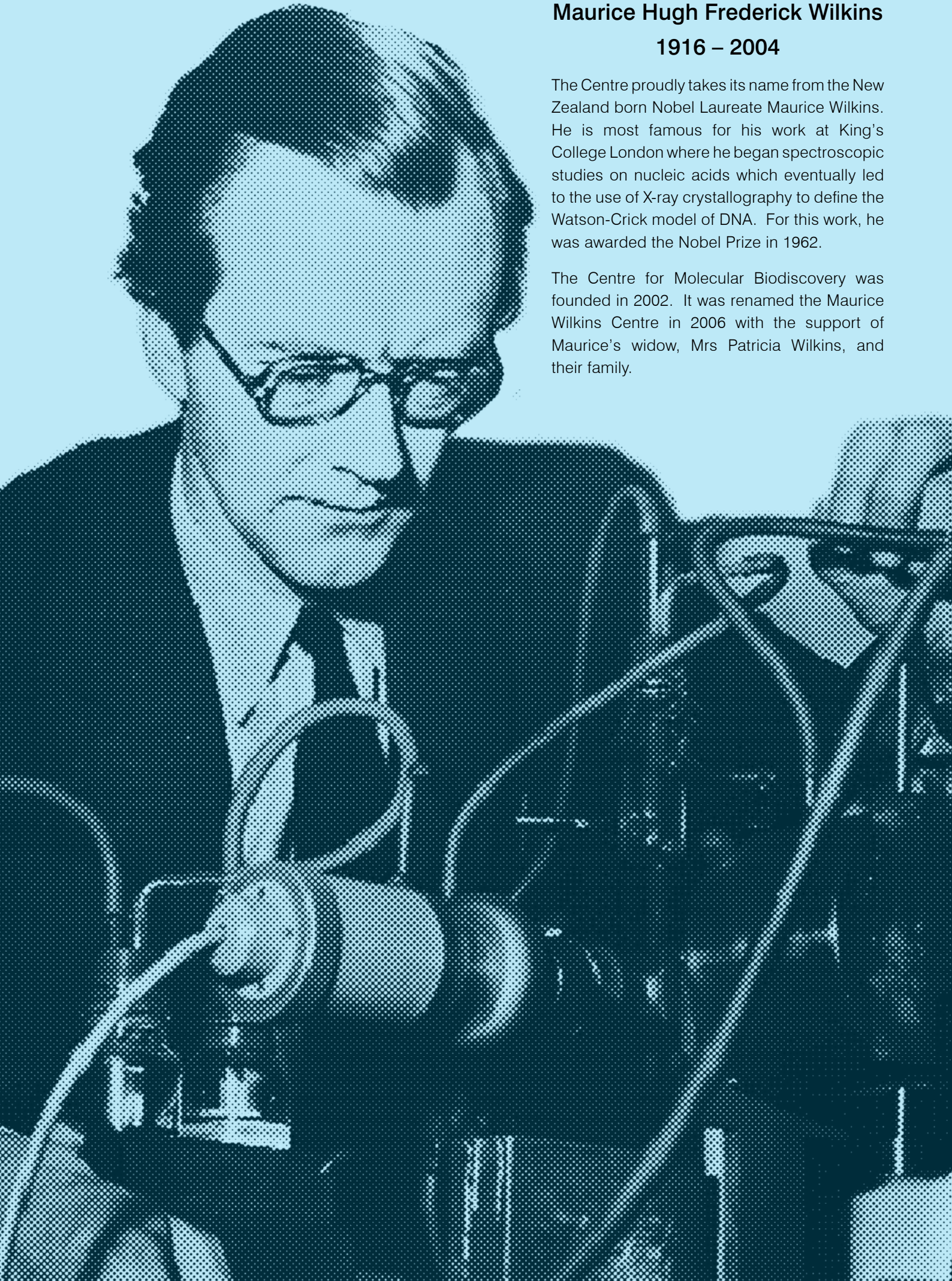
Professor Rod Dunbar
School of Biological Sciences
Faculty of Science
The University of Auckland
Private Bag 92019
Auckland 1142, New Zealand
Phone: +64 9 373 7599 ext 85765
Email: r.dunbar@auckland.ac.nz

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
Phone: + 64 9 373 7599 ext 86036
Email: jd.fraser@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
Phone: +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 their family.