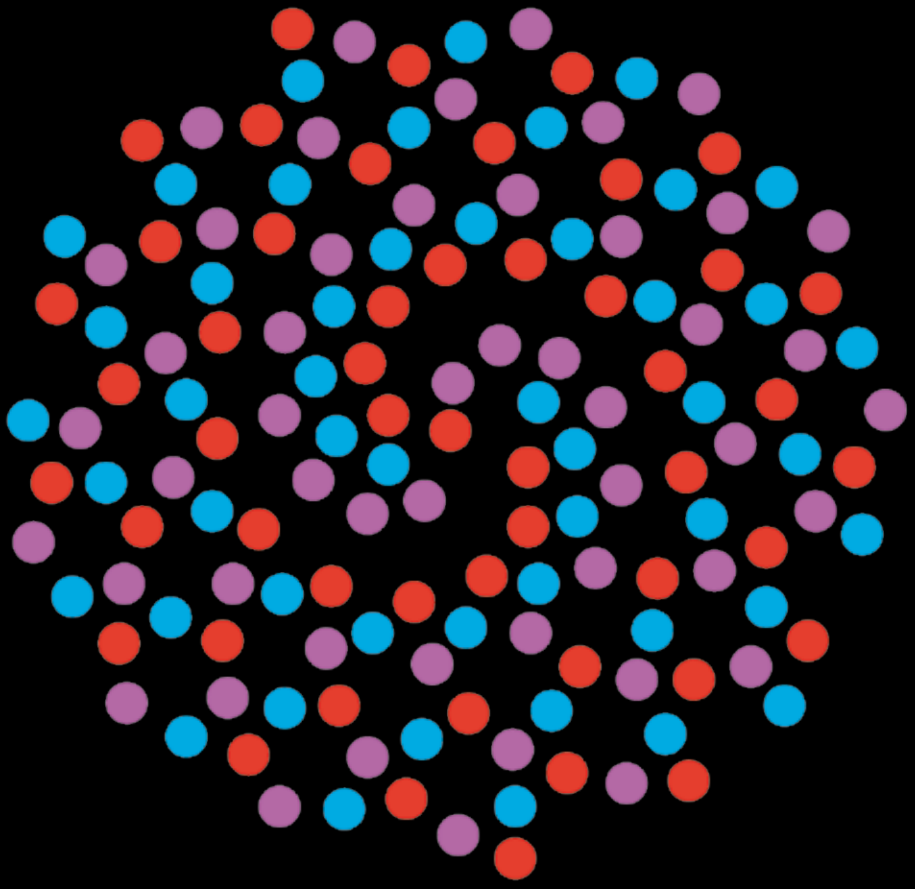

MAURICE WILKINS CENTRE

New Zealand's Centre of Research Excellence
targeting human disease

Annual Report 2011

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. By the end of 2011 it comprised 109 investigators throughout the country, and over 115 early-career affiliates, linking researchers from six Universities, three Crown Research Institutes and a private research institute. These investigators represent most of New Zealands expertise in discovering new drugs, vaccines and diagnostic tools that proceed to clinical trials.

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 research institutions and also engages with industry and the medical profession. It is committed to building the economy and building scale in the New Zealand biomedical sector.

For more information see www.mauricewilkinscentre.org

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

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MAURICE WILKINS CENTRE
FOR MOLECULAR BIODISCOVERY

Director's Report

In these pages, the Maurice Wilkins Centre reports the continuation of its mission to bring together scientists and doctors across New Zealand's research institutions to target serious disease. The stories speak for themselves, but a few developments in 2011 are worthy of particular emphasis, because they speak to the importance of the Centre's activities to New Zealand, and its place in the world.

The Maurice Wilkins Centre links all the drug discovery expertise in New Zealand, and 2011 was an exceptional year for drugs invented in this country. Four new drugs were chosen for clinical trials, and a fifth was selected for pre-clinical development. These new drugs – all invented at the Auckland Cancer Society Research Centre – join 15 other New Zealand-designed drugs that have undergone clinical trials for a range of serious diseases, with 2011 the first year that four new drugs have been slated for testing in humans.

The new drugs underscore the major contribution of New Zealand biomedical research to the global fight against cancer. As we reviewed at our annual Symposium (page 11), tremendous progress is being made in improving cancer care in general, especially with new drugs targeted at key molecules inside cancer cells. However the rate of that progress remains very uneven across different cancers, and many more of these precisely targeted medicines will be needed to bring lasting benefit to patients suffering from cancers such as melanoma, where the first drugs with strong effects on tumours are only just emerging. New Zealand cancer researchers excel in understanding the molecular basis of cancer, and designing these targeted therapies, and the Maurice Wilkins Centre aims to help bring more and more of these crucial medications to clinical trial.

It's worthwhile considering what clinical trials of new drugs mean for New Zealand. Drugs invented in New Zealand are patented internationally – a necessary step to ensure they garner the large investment needed for clinical trials – and a step that also ensures they provide economic returns to the country. Although on average only one in ten drugs entering the first stage of clinical trials will eventually reach approval for sale, the value of an individual patented drug can be enormous, with the world's most successful medicine (a treatment for high cholesterol) earning over US$100 billion during the life of its patent. New Zealand is now in the fortunate position of having a substantial portfolio of drugs entering clinical trials, backed by a pipeline of new projects, such as those initiated within

the Maurice Wilkins Centre. Indeed one of the four new drugs entering clinical trials sprang from a Maurice Wilkins Centre project that began only 5 years ago. Drug discovery is therefore one of those high-tech activities New Zealanders happen to be particularly good at, with a very large "up-side" in terms of economic returns, especially when considering our burgeoning portfolio of promising new drugs. International partners recognise this expertise, and their investment in helping take New Zealand drugs to clinical trial is the clearest possible signal of global confidence in our ability to compete in this crucial field of human endeavour.

Of course drug discovery would not be possible in this country without a wide base of scientific expertise, from biology and medicine to chemistry and computation. While inventing new drugs might be described as applied science, it depends on more fundamental investigations, from studies of the biological origins of disease to the development of new methods in medicinal chemistry. The fundamental science projects initiated within the Maurice Wilkins Centre in 2011 once again draw on skills from a wide variety of research institutions and scientific backgrounds. The active network constituted by the Centre's investigators is demonstrably encouraging rapid cross-fertilisation of ideas and transfer of technology. A good example is the cross-disciplinary collaboration to study the immune system that has now enabled a new project in cancer biology (as reported on page 13). In this particular case, imaging technology invented in New Zealand has been extended and applied in ways that were not envisaged by its inventors, due to active promotion and adaptation of the technology by the Maurice Wilkins Centre network. The Centre is increasingly able to identify new opportunities to spark cutting-edge research by bringing together investigators with complementary expertise from throughout the country, and seeding new collaborations (as described on pages 36-37) – a unique national role.

All this research and its sustainability depend on human capability, and the Maurice Wilkins Centre continues to devote substantial resources to mentoring and training. As reported on page 25, in 2011 the Centre extended its sponsorship of training programmes to include short overseas placements for early career scientists. Although the Maurice Wilkins Centre network provides world-class expertise in most technical aspects of biomedical science, such is the pace of technological advance that it is sometimes advisable to access leading laboratories and institutes overseas to acquire game-changing technical skills. The Maurice Wilkins Centre has an extensive international network that opens up such access for our early career scientists, and the new scheme will enable them to carry out brief experimental programmes in leading laboratories overseas where new techniques are under development, or to attend advanced technical workshops. Younger scientists are often more enthusiastic adopters of new technology than their mentors, so the Centre is encouraging their leadership in ensuring New Zealand retains its technical edge in biomedical science. At the same time, these talented young scientists act as superb international ambassadors for New Zealand science.

Indeed the international engagement of New Zealand biomedical science emerged as a key theme of 2011 for the Maurice Wilkins Centre. As reported on page 23, the first of our major international initiatives began to blossom, as the Centre's relationship with three leading Japanese research institutes was formalised. Strategic discussions between Maurice Wilkins Centre investigators at our annual meeting focused around international opportunities, and planning began for major initiatives in China in 2012 (to be reported in the 2012 Annual Report). International institutions have expressed enthusiasm for engaging with the Maurice Wilkins Centre as a single "shop window" for New Zealand expertise in areas such as immunology and drug discovery. This international viewpoint provides compelling support for the concept of plugging local scientific talent into larger scale national networks, able to better compete in the international science arena.

In summary this report provides a perspective on many of the key values that drive the Maurice Wilkins Centre as a national Centre of Research Excellence. The Centre is expanding New Zealand's ability to invent new drugs, with enormous potential for gains in health and in economic development. This application of our research expertise is only possible because of sustained support for fundamental science, and in particular bringing together the diverse scientific disciplines that contribute to the fight against major diseases. And bringing together investigators across different institutions as well as scientific disciplines has built a national network of sufficient scale to be attractive to international partners, opening up new opportunities for New Zealand science around the globe.

Once again it has been a pleasure and a privilege to lead the Centre, and I express my gratitude to the Management Committee and the Governing Board for their advice and support, and to all the Investigators who so energetically drive our activities. I also extend congratulations to Rochelle Ramsay and Peter Lai for their efficient management of the Centre's affairs, to Pauline Curtis for her very effective communications strategy, and to Seishi Gomibuchi for developing and pursuing our international programmes.

Rod Dunbar
Director

Delegates at the Personalised Medicine Symposium.
Photo courtesy of Godfrey Boehnke

Contribution to National Goals

The Centres of Research Excellence are collectively charged with making a contribution to national goals including fostering innovation and social and economic development. 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

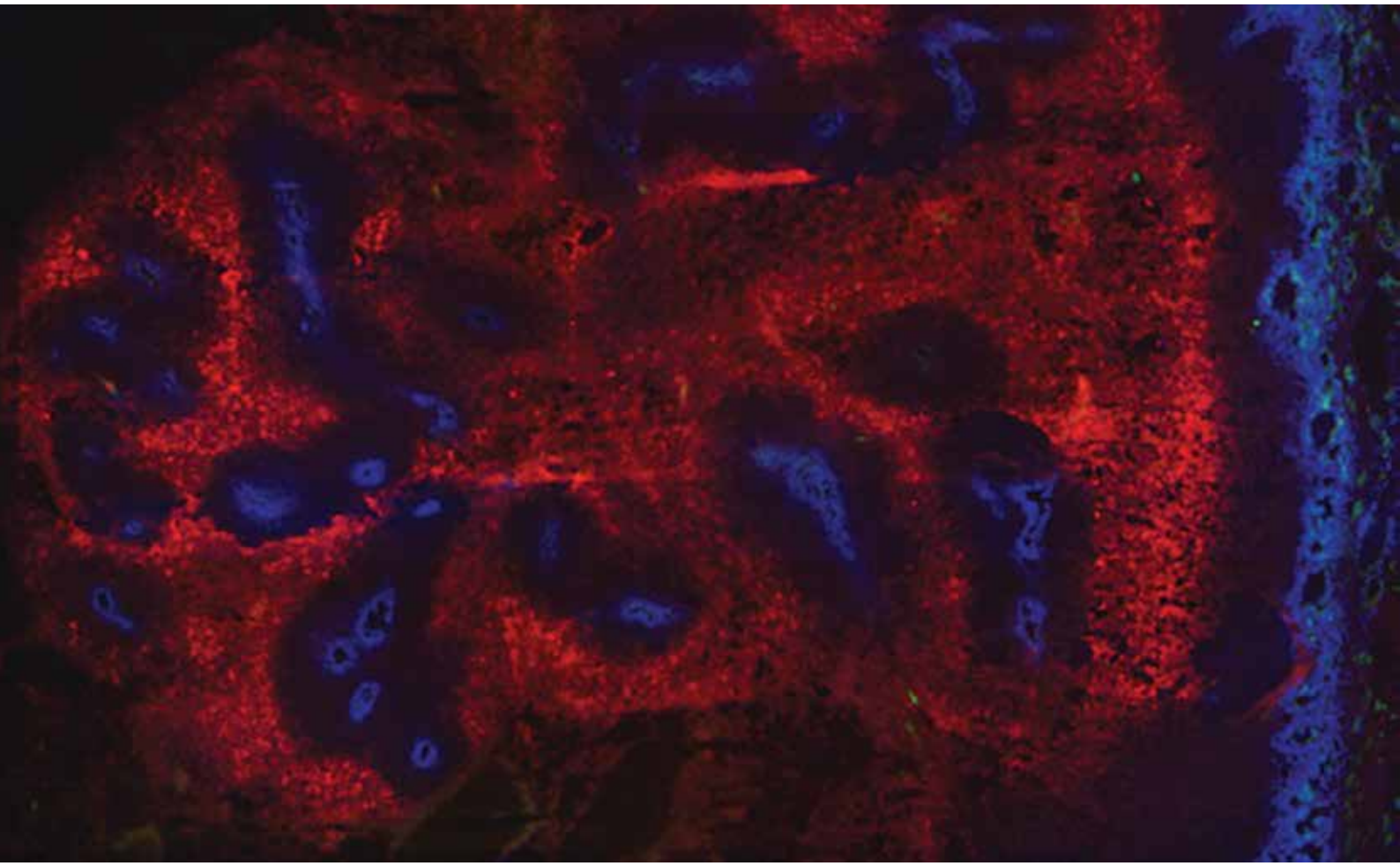
The Maurice Wilkins Centre conducts highly innovative research and enables innovation in the wider research and business sector. Its goal is to become New Zealand's engine for the discovery of new therapies and diagnostic tests. Innovation in research is often to be found at the interface between disciplines, 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 alone could address. 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, consultancy, and sharing of facilities and expertise. Fundamental scientific discoveries, novel technologies and management developed within the Centre enable new lines of research that advance understanding of human health and disease and also enable innovation in other sectors including 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. 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 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 of a tumour showing areas of hypoxic tissue (red), tissue with a normal level of oxygen (dark) and blood vessels (blue).
Image courtesy of Ms Annika Foehrenbacher, Experimental Therapeutics Group, Auckland Cancer Society Research Centre

Highlights

The following stories describe 2011 highlights in research, training and science education.

New drug targets treatment-resistant cancer

A new drug targeting an important group of cancer cells attracted international funding in 2011 and will soon enter clinical trials.

Learning how to eliminate cancer cells that are resistant to current treatments is one of the biggest challenges in cancer medicine. One of the ways cancer cells can become resistant to treatment is through low oxygen levels (hypoxia). These hypoxic cancer cells are the target of a new drug produced at the Auckland Cancer Society Research Centre (ACSRC) by Maurice Wilkins Centre investigators Associate Professor Michael Hay and Professor Bill Wilson with Drs Kevin Hicks, Frederik Pruijn and Jingli Wang. An agreement with Cancer Research UK will now allow the drug to begin clinical trials in the United Kingdom.

Tumours often have a haphazard blood supply and, as a result, zones that receive less oxygen than normal. “Hypoxia occurs in most types of solid tumours, but not necessarily in every patient with a particular tumour type,” says Michael. “Hypoxic cells in solid tumours are generally resistant to standard cancer therapies and currently there is no effective treatment for these cells.” To cope with hypoxia, the cells also undergo genetic changes that make them more aggressive, more invasive, and consequently more able to spread around the body. So once other cells have been eliminated by chemotherapy or radiation therapy, they may go on to re-establish the tumour – which may now grow even more vigorously.

The new drug, named SN30000, kills cancer cells by damaging their DNA. It is a “prodrug” designed to be given to patients in inactive form and “switch on” only when it encounters hypoxia. It is intended to be given with chemotherapy or radiation therapy, eliminating hypoxic cells that would otherwise survive those treatments. It differs from other hypoxia-targeted prodrugs under clinical evaluation in its superior ability to penetrate hypoxic tissue and efficient activation even under relatively mild hypoxia in tumours.

ACSRC scientists have pioneered the use of hypoxia as a means of selectively targeting tumours and eliminating hard-to-treat cells. SN30000 is one of the results of a broad research programme over ten years that began with a National Cancer Institute grant to support a collaboration between scientists at Stanford University and the ACSRC.

“This work has been underpinned by sustained investment in cancer research by a number of government and charitable funding agencies. It’s been a privilege for the Maurice Wilkins Centre to help fund the latter stages of this research to the point where it can potentially help patients,” says Maurice Wilkins Centre Director Professor Rod Dunbar.

Dr Mike McCrystal speaks about developments in melanoma treatment at the Personalised Medicine Symposium.
Photo courtesy of Godfrey Boehnke

The future of healthcare is already here

Tailoring a person's medical care to their genetic makeup may sound like science fiction, but "personalised medicine" is already here – as scientists and health professionals at the annual Maurice Wilkins Centre Symposium discussed.

Personalised medicine aims to deliver more effective therapies that do less harm. The greatest strides have been made in cancer medicine, making the field the natural focus for the symposium. Clinicians speaking at the event agreed that we are in a major new era of cancer medicine. No longer do all patients with a particular cancer receive the same treatment. Every patient's cancer has different characteristics, and by mapping those characteristics – in particular the genetic changes that make the cells cancerous – it is possible to select a treatment regime finely tailored to a patient's tumour. New drugs that target specific genetic changes may be part of the regime.

Oncologist and clinical researcher Professor Peter Browett described how for many years it has been standard practice to select treatments for blood cancer based on DNA analysis (both chromosomal typing and DNA sequencing), resulting in dramatically improved responses to treatment. Colleagues Professor Mark McKeage and Dr Mike McCrystal explained that personalisation is at an earlier stage for lung cancer, and for melanoma – for which the first targeted drugs are just becoming available – but even these notoriously difficult-to-treat malignancies are likely to follow suit. "I'm optimistic the advances being made in some cancers will eventually be reflected in others," Mike said.

Tumour DNA analysis is not the only way to personalise treatment, however. For instance, Associate Professor Alistair Young explained that modern medical imaging provides a detailed picture inside the patient's body before and during treatment, allowing a more tailored approach. Dr Nuala Helsby showed how a patient's genetic profile determines the rate drugs clear from their bodies – by understanding the genes involved it is possible to adjust drug dosages to maximise effectiveness and reduce side effects.

A critical factor in the rise of personalised medicine has been dramatic improvement in the speed and affordability of DNA sequencing around the world. Scientists Dr Mik Black and Associate Professor Cris Print described how sequencing technology is now readily available in New Zealand and is being used in numerous clinically-focused research programmes, both to aid diagnosis and targeting of therapy, and reveal the genetic factors behind differences in disease susceptibility for different groups of New Zealanders.

"The Maurice Wilkins Centre has a strong focus on developing high technology solutions relevant to health," says Director Professor Rod Dunbar. "The clinical insight gained at the meeting should help health professionals and administrators envision the impact of this new technology on the healthcare system. Bringing the clinical and scientific communities together also helps our investigators plan how to develop the technology for maximum impact on the health of New Zealanders."

PhD student Inken Kelch using the microscope.
Photo courtesy of Godfrey Boehnke

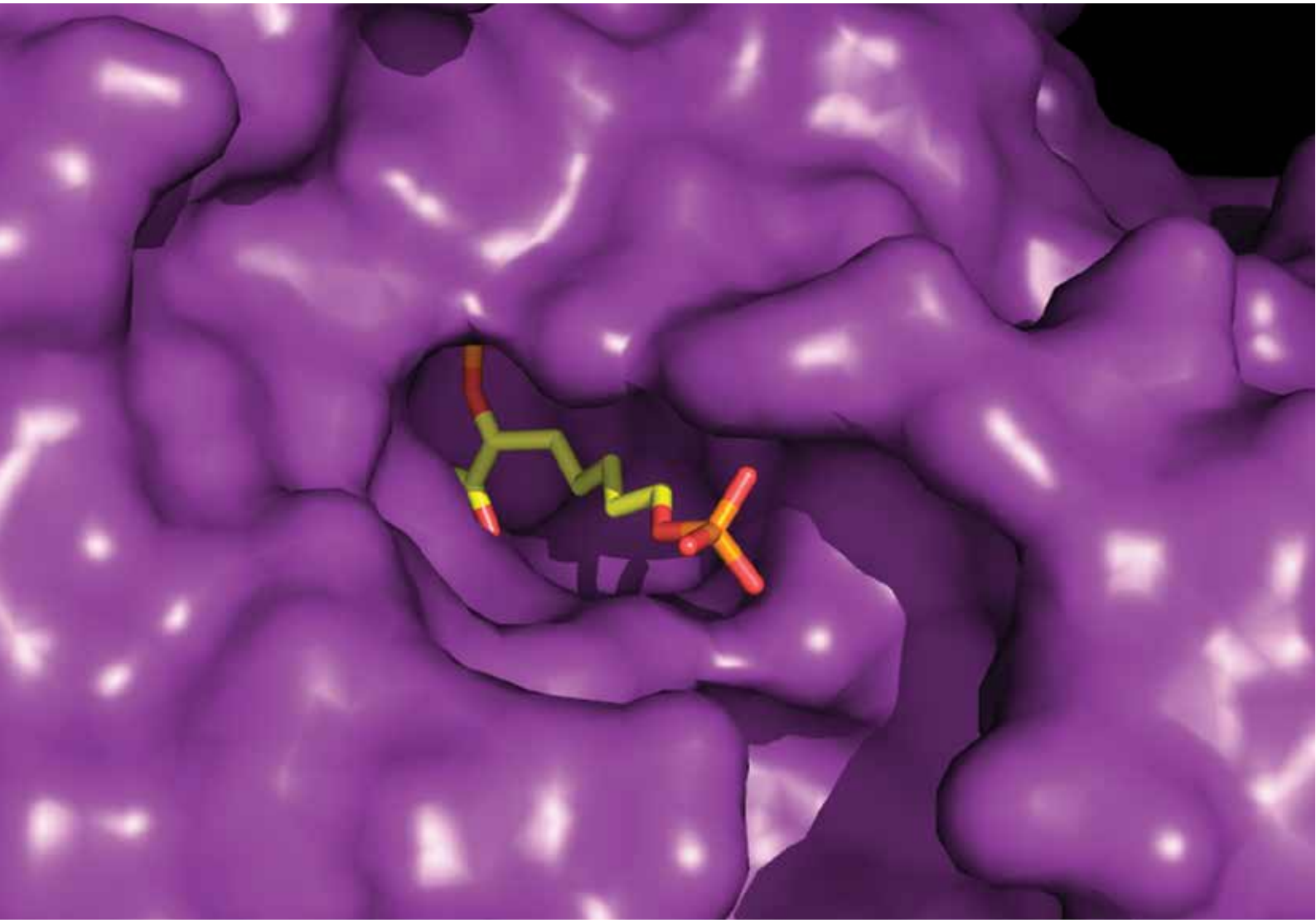
Exquisite networks

Innovative technology developed to study the heart has been adapted for a unique study of the immune system – and will now be applied to cancer, through cross-disciplinary links fostered by the Maurice Wilkins Centre.

Swollen lymph nodes (or "glands") are a sign the immune system is fighting disease. Immune cells cluster and grow in the lymph nodes, and during an immune response, they balloon in size. However, unlike a balloon, the inside of a lymph node is criss-crossed by a dense network of tubes and fibres – and it's unclear how this web of internal connections copes as the lymph node swells. To clarify this fundamental process, Inken Kelch, a Maurice Wilkins Centre PhD student in Director Professor Rod Dunbar's laboratory, is creating a 3D "road map" of the connected tubes, fibres and spaces within lymph nodes. Inken's work uses a unique microscope system that was designed and built in New Zealand.

University of Auckland physiologist Associate Professor Ian LeGrice and colleagues originally built this system so they could stitch together very large numbers of overlapping images into a single 3D picture of heart tissue. Their machine combines a powerful microscope with a precision-engineered milling platform, so it can gradually remove thin layers of tissue, taking overlapping images as it goes – all accurately aligned so they can be seamlessly combined in 3D. In a major cross-disciplinary effort within the Maurice Wilkins Centre, Inken has worked with Ian's team and surgeon Dr Anthony Phillips to adapt their imaging techniques for lymph nodes. Inken's first 3D images show the entire blood vessel network of a lymph node, and she and Dr Gib Bogle, from the Auckland Bioengineering Institute, have now turned these images into a 3D computer model. This computer model allows the blood vessel network to be measured precisely, so now the team will be able to measure how all the blood vessels change when a lymph node swells.

The cross-disciplinary links don't stop there. It became clear that the same approach to map blood vessel networks in 3D could be used by Maurice Wilkins Centre colleagues at the Auckland Cancer Society Research Centre (ACSRC). Blood vessel networks form abnormally in tumours, resulting in uneven blood supply, and zones where there is little oxygen (hypoxia). So the lymph node team is now working with Drs Frederik Pruijn and Kevin Hicks from the ACSRC to precisely map both the blood vessels and the hypoxic zones in tumours. Models of the tumour blood vessels have already been used by Kevin and ACSRC colleagues, led by Professor Bill Wilson, to help design drugs that "switch on" only in hard-to-treat hypoxic zones (see page 9). The new 3D techniques developed at the Maurice Wilkins Centre offer the opportunity to produce much better models of tumour blood vessels, with potential to improve drug design – a useful practical outcome from some very innovative fundamental research.



Representation of the new inhibitor (shown in orange and yellow) sitting in the biologically active site of the target enzyme DAH7PS (shown in purple) and blocking the enzyme's activity.
Image courtesy of Sebastian Reichau

New inhibitor for tuberculosis

A new way to shut down the bacterium responsible for tuberculosis has been devised by researchers in one of the Maurice Wilkins Centre's longest-standing collaborations.

In 2011 Maurice Wilkins Centre investigators Associate Professor Emily Parker from the University of Canterbury and Professor Ted Baker from The University of Auckland published work on a new compound with the potential to kill *Mycobacterium tuberculosis* – the bacterium that causes tuberculosis.

Emily studies enzymes and has a particular interest in DAH7PS (3-deoxy-D-arabino-heptulosonate 7-phosphate synthase), an enzyme used by bacteria to make three crucial amino acids. Amino acids are the building blocks of proteins and therefore essential to life, but humans have a different way of acquiring these particular amino acids. DAH7PS is a particularly good target for antibacterial drugs, since humans and other animals would be unaffected if DAH7PS were disabled whereas bacteria could not survive.

"I was interested in enzymes like this, and Ted was looking at targets for tuberculosis, so our interests intersected," Emily explains. Ted leads a structural biology group that examines the shape of proteins. Since its shape determines how a protein interacts with other molecules, structural analysis provides clues not only about its normal biological function but how to design drugs to block its activity. Finding new drug targets for tuberculosis is a major focus for the group.

"Ted and I began working together in 2005, with Dr Shaun Lott and Mrs Heather Baker from The University of Auckland," Emily says. "It's been one of the Maurice Wilkins Centre's longest-standing relationships." The structure of DAH7PS was solved within a year. "This showed us how the enzyme was likely to work and gave us the basis for designing molecules that might interrupt it." Now Emily's PhD student Sebastian Reichau has made a compound that does just that. By far the most potent inhibitor of DAH7PS to date, it provides a lead compound for further refinement. The Maurice Wilkins Centre has provided funding for Sebastian to visit computer modeller Dr Jack Flanagan at The University of Auckland to advance the work. The next step will be to ensure the compound can get inside *M. tuberculosis* cells and do its job there.

Meanwhile, DAH7PS is becoming an even more promising target. "Recent research shows just how critical the enzyme is, and not just in the ways we originally understood," Emily says. "It turns out that it intersects with many other enzymes and activities in *M. tuberculosis.* An inhibitor would shut down all of these processes, not just one, and it would be much harder for the bacterium to develop resistance." This is especially important for tuberculosis, which kills more than a million people each year and is becomingly increasingly resistant to current treatments.

Dissecting drug side effects offers hope

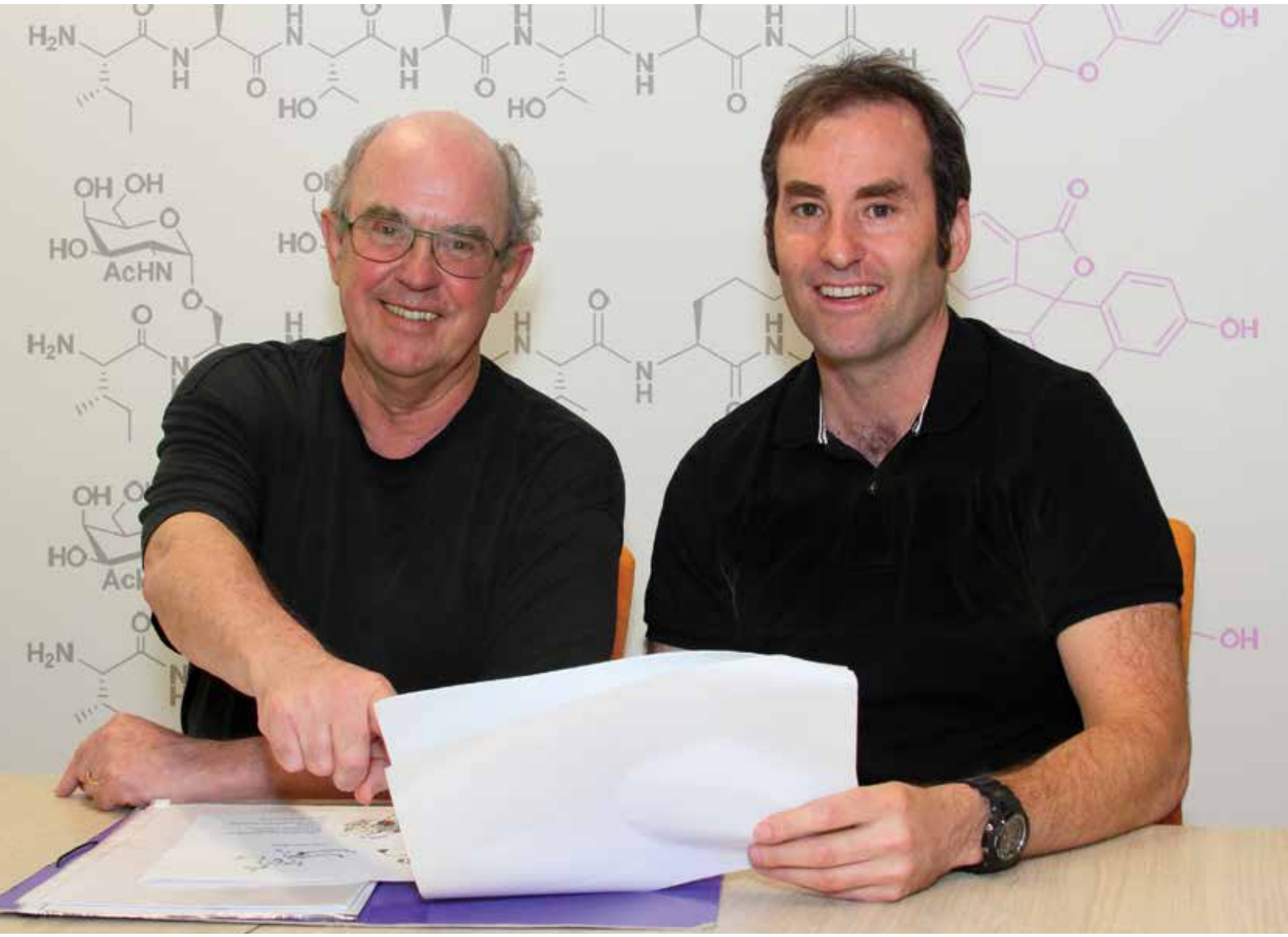
Researchers from the Maurice Wilkins Centre have discovered how a common class of medicines causes diabetes-like symptoms, and their work suggests a promising way of managing these side effects.

All medications have side effects, and studying them can point to better ways to manage disease. Professor Peter Shepherd and Dr Greg Smith at The University of Auckland investigate diabetes-like side effects associated with antipsychotic agents such as clozapine and olanzapine that are commonly used to treat schizophrenia. "Antipsychotic medications are widely prescribed internationally – in New Zealand alone around 30,000 people take these drugs – and side effects of weight gain and diabetes are a concern for many patients," says Peter. "These side effects are well recognised but affect people variably, with some people experiencing severe effects and other people none at all," says psychiatrist Dr Wayne Miles, Clinical Associate Professor at The University of Auckland. "Understanding the biochemical reasons that the side effects occur may eventually help to make treatment more tolerable."

Rates of diabetes – or "type-2 diabetes" as the most common form is more accurately known – are on the rise in New Zealand and around the world. "Most of the increase in type-2 diabetes is thought to be due to lifestyle factors, in particular obesity, but in some cases diabetes can be caused by drugs used to treat other conditions," Peter explains. Since diabetes in the wider population is most often linked with obesity, it had been assumed that weight gain over a period of time in people taking antipsychotic medications was causing their diabetes-like symptoms.

In laboratory studies published from 2008 to 2011, however, the New Zealand researchers showed that common antipsychotic medications trigger diabetes-like symptoms very rapidly, by directly altering the levels of key hormones, and that this occurs independently of any weight gain. They showed in animal studies that the medications rapidly suppressed levels of the hormone GLP-1, which in turn increased levels of a second hormone – glucagon. They went on to show that restoring GLP-1 function could overcome many of the side effects of the drugs.

The work suggests that managing diabetes-like side effects in people on antipsychotic medications may require a different approach from standard diabetes care. It also points to a possible method of reversing diabetes in this group, by correcting the hormonal imbalance caused by their medication – for example using recently-discovered drugs that activate the GLP-1 system. The researchers are now extending these studies into humans with a clinical trial funded by the Health Research Council of New Zealand. Ultimately they hope this work will not only reduce the side-effects of current antipsychotic drugs, but also open up new routes to improved drugs for both schizophrenia and diabetes.



Professor Steve Kent and Dr Paul Harris, who have successfully transferred new protein synthesis technology to The University of Auckland.
Photo courtesy of Iain McDonald

Mirror-image proteins - new biology from new chemistry

Maurice Wilkins Centre investigators are working with a pioneering international chemist to develop new methods for virus and drug research.

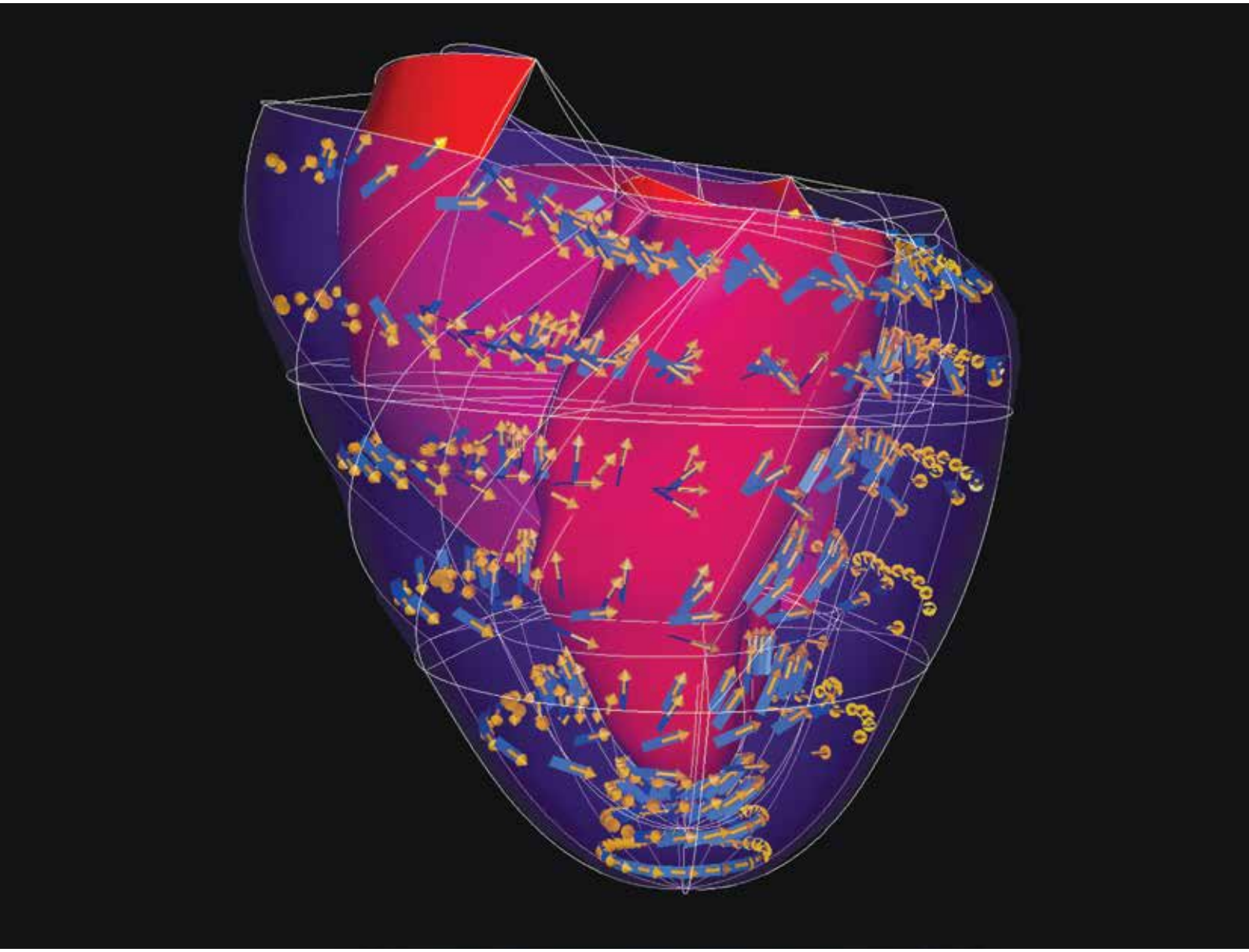
"This work is right at the cutting edge, or maybe a step or two beyond it," says Professor Steve Kent, a New Zealander based at the University of Chicago. "It relies on the unique combination of skill sets at the Maurice Wilkins Centre, and is happening nowhere else in the world." He is referring to a study of virus proteins that was granted support from the Marsden Fund in 2011. As one of the world's most eminent biochemists, Steve is well-placed to comment.

The study aims to ascertain the structure of proteins that the orf virus uses to invade cells, to learn more about the biology of such proteins and how their activity might be blocked by drugs and vaccines. The orf virus is related to the small pox virus, and affects agricultural species as well as humans. The project is highly innovative at a technical level, and will be the first to combine new techniques developed by Steve and Maurice Wilkins Centre investigators Professors Ted Baker and Margaret Brimble, relying on complementary expertise from all three groups.

One of the pioneering techniques involves chemically synthesising a protein in a mirror-image form that never occurs in nature. Mixing this mirror-image protein with its natural form helps the protein to crystallise – a critical step to allow X-ray analysis of its structure. "It increases the chance you'll get a protein to crystallise by a factor of ten," explains Dr Chris Squire who together with Ted leads the structural biology component of the orf virus research. In 2009 Steve and Ted used this new crystallisation method to determine the structure of a protein from *Mycobacterium tuberculosis* (the bacterium that causes tuberculosis) that had previously proven intractable using more conventional methods.

Making mirror-image proteins involves chemical techniques that join short chains of amino acids into longer chains. Dr Paul Harris and PhD student Danny Lee, both from Margaret's laboratory, established these techniques in New Zealand after spending time in Steve's lab in Chicago. Other methods developed in Margaret's lab have since been combined with Steve's techniques to make a synthetic analogue of erythropoietin, the protein that controls red blood cell production. All these new methods will be used in the Marsden-funded research, which will not only yield information about viral proteins that are difficult to study with traditional methods, but also test the potential of combining the techniques.

The Maurice Wilkins Centre helped to foster links with Steve, who has visited chemistry and structural biology research departments throughout New Zealand over the last three years, under the Centre's Visiting Speakers Programme. The Maurice Wilkins Centre also supported the research undertaken by Danny Lee in Steve's lab in Chicago, and was instrumental in establishing the synthetic protein facility in Auckland that will be used in the new virus protein research.



Model of muscle fibres and sheets in the heart, created by the Auckland Bioengineering Institute, and showing the kind of information that is incorporated into a comprehensive organ model.

Image courtesy of the ABI

A new toolkit for building virtual humans

The Auckland Bioengineering Institute (ABI), established by Maurice Wilkins Centre co-founder Professor Peter Hunter, is a lead player in international efforts to build comprehensive virtual models of the human body. In 2011 it published work on a new repository that makes it easier for researchers to share and use the information being gathered.

Scientists around the world are generating huge amounts of information about the human body in health and disease – from the minute scale of individual molecules through to whole organs. The European Commission-funded Virtual Physiological Human (VPH) project aims, in the long-term, to link information across all of these scales to build comprehensive mathematical computer models that simulate the human body. Auckland is playing a leading role in both the VPH project and its international counterpart, called the Physiome Project.

To explain how such models might be used, Randall Britten, leader of the ABI software team, draws analogies to the airline industry. Just as aircraft engineers use simulators to learn how design changes will affect the performance of an airplane, human models can help scientists understand how different biological conditions affect the body. And in the same way pilots learn to fly with a simulator, human models can be used by clinicians to hone their skills or trial different treatment options for their patients, or by researchers as part of the drug discovery process.

Behind all of this, however, is a massive computational challenge. Information gathered by various research methods – and addressing different aspects of human biology – must be represented in a mathematical form that can be read by computer, and stored in a central repository that allows component models to be connected and recombined.

The ABI is a global leader in the field, and has developed computer languages (FieldML and CellML) that are now the recommended standards for physiome research funded by the European Commission and National Institutes of Health. It has also successfully combined models from different fields of study into world-first organ models. For instance, its heart model successfully integrates information about the muscular structure of the heart with molecular-level detail on everything from the biochemical mechanisms that govern the heart's energy supply to channels for electrical signals that initiate the heartbeat, as well as many other cellular functions.

In 2011, researchers from the ABI published work on a new central repository that they are making freely available around the world via the Internet. In contrast to an earlier version, the new repository has almost no restrictions on file formats, so models written in almost any computer language can be stored and used alongside each other. It also has a careful process for "version control", recognising that each model is a work in progress, and that researchers combining several different models need to track when any component is updated.

The Maurice Wilkins Centre is one of several organisations that contribute funding to the VPH/Physiome Project, and it sponsors an annual event that brings the international modelling community together in Auckland.

New Zealand and Japanese immunologists at iFReC.
Front row (from left): Prof Takao Kodama, Dr Yoshihiro Baba, Dr Gavin Painter, Dr Ian Hermans, Assoc Prof Sarah Hook, Dr Cevayir Coban, Dr Anne La Flamme, Dr Diego Miranda-Savedra.
Middle row: Prof Kiyoshi Takeda, Dr Yukio Furukawa, Prof John Fraser, Prof Masayuki Miyasaka, Prof Rod Dunbar, iFReC Director Prof Shizuo Akira, Prof Masaru Ishii, Dr Gib Bogle
Back row: Prof Yoshichika Yoshioka, Dr Masao Imaizumi
Photo courtesy of iFReC

A blossoming collaboration with Japan

Formal relationships between the Maurice Wilkins Centre and high-profile Japanese research institutions were established in 2011, and exchange visits have already begun.

In 2010 a delegation of Maurice Wilkins Centre immunologists travelled to Japan, with support from the Ministry of Research Science and Technology (MoRST) and New Zealand Embassy, to discuss potential research collaborations. “The Japanese were deeply impressed with our research and keen to work with us. Both sides realised how much potential there was, and what happened completely exceeded our expectations. ” says Dr Seishi Gomibuchi who fostered the relationships while working at MoRST and now The University of Auckland.

All three institutes visited – RIKEN Research Centre for Allergy and Immunology, Chiba University Global Centre of Excellence Programme, and Osaka University Immunology Frontier Research Programme (iFReC) – initiated formal relationships with the Centre the following year. Seishi says that as a national multi-disciplinary network, the Centre is well-placed to promote New Zealand science. “By engaging with the Maurice Wilkins Centre, Japanese institutions know they’re gaining access to scientists all over New Zealand, and because the Centre has the best New Zealand researchers it is an excellent representation of what the country has to offer.”

Japan has particular strengths in immunology and the delegation focused on institutes with world-class research, the capacity for multiple collaborations, and resources complementary to New Zealand. The institutions also have Japanese government support and an international focus. Through formal agreements the Maurice Wilkins Centre can co-ordinate greater access to these institutions than individual scientists could achieve, and make personnel exchange much easier. Establishing deep institutional links also raises the Centre’s international profile and ensures enduring and productive relationships.

2011 saw the start of a collaborative programme that will include joint scientific meetings in both countries and individual exchanges. Already Maurice Wilkins Centre investigator Associate Professor Sarah Hook and PhD student Teerawan (Mo) Rattanapak from Otago University have visited Professor Masaru Ishii’s laboratory at iFReC to use advanced imaging facilities. Sarah is studying how to make vaccines that can be applied directly onto the skin, avoiding the need for sterile injections and potentially raising immunisation rates.

“We’d made several vaccines and wanted to know how well they penetrated the skin,” she explains. iFReC’s microscopes allowed them to watch as their vaccines entered the skin and immune cells responded. The next generation of vaccines will be developed based on the results, and Mo anticipates returning to Japan to evaluate them. “It was a really positive experience,” Sarah says. “We were looked after incredibly well, given a lot of access to equipment and resources, and had staff available to help us.” Sarah’s visit was supported by the Japan Society for the Promotion of Science. The Maurice Wilkins Centre provided funding for Mo to accompany her.

Julia MacDonald and Dr Anna Brooks from The University of Auckland, who will undertake specialist technical training overseas.
Photo courtesy of Iain MacDonald

International opportunity for young scientists

In 2011 the Maurice Wilkins Centre launched a new scheme to help its early-career scientists train in cutting-edge technology – and share what they have learned with New Zealand colleagues.

Maintaining New Zealand's capability in high technology areas is crucial to the Maurice Wilkins Centre's mission. As well as sponsoring technical workshops in New Zealand, the Centre now offers its early career scientists access to specialist training overseas, whether through attendance at technical workshops run by major research organisations, or short-term placements in laboratories where new technologies are being developed.

The adoption of new technology is often led by early-career scientists and it makes sense to ensure they can access the best training available. The new scheme also brings responsibility to help bring these technologies to New Zealand – applicants are required to provide a plan for how they will share their knowledge on their return. Two young scientists were successful applicants in the first round of the scheme.

Dr Anna Brooks, a flow cytometry expert from The University of Auckland, will attend an international technical congress on cytometry in Germany that includes hands-on time at workshops and tutorials. Flow cytometry allows biologists to determine what cell types are present in a tissue, and examine their attributes, then collect particular cells for further study. The applications are vast – from learning how immune cells respond to disease to isolating rare adult stem cells – and Anna's facility, equipped by the Maurice Wilkins Centre, provides access to these applications for a wide range of researchers.

"We strive to ensure that our facility is world class, and what better way to do that than to get an intensive update from the world's experts?" Anna asks. "It will be a one stop shop where I will have access to many of the leaders in the field, from the machine developers to the flow cytometry specialists pioneering new applications."

Julia MacDonald, a University of Auckland PhD student, will travel to Australia to use equipment not yet available in New Zealand. "I'm studying a newly-discovered human protein implicated in a rare form of kidney stone disease," she explains. By using a special centrifuge in Melbourne she will learn more about the protein, and how changes linked with kidney stone disease may affect its structure and function. But she will also learn how the centrifuge can help advance similar research projects and anticipates that her experience will help other scientists to access the technology in future, either through collaboration or by establishing an equivalent equipment platform in New Zealand.

By making their expertise available to the entire Maurice Wilkins Centre network, these young scientists will be instrumental in ensuring New Zealand biomedical research maintains its technical competitiveness, with the prompt adoption of useful new technology.

Secondary school biology students collect samples at Hot Water Beach.
Photo courtesy of Paul Scott, Mercury Bay Area School

School students get into hot water

With a blessing from Ngati Hei – and a polite request for tourists to move from their bathing holes – a unique experiment got underway at Hot Water Beach on the Coromandel Peninsula in early 2011.

Over a full weekend in April, around sixty secondary school students took samples from the thermal springs that well up on the beach between high and low tide, and performed genetic analyses to identify the heat-loving microorganisms that live there.

The project was spearheaded by Massey University molecular biologist and Maurice Wilkins Centre investigator Dr Justin O'Sullivan, working with Mercury Bay Area School science teacher Paul Scott, and was guided by a team of university scientists. The research – known as a metagenomic study – was the first of its kind in such an environment. It will form the basis of Massey BSc honours student Veronica Benton-Guy's dissertation and a paper for submission to a scientific journal.

Paul spotted the opportunity the previous year, when he won a Maurice Wilkins Centre scholarship to attend the Queenstown Molecular Biology meeting. "At the conference I learned about DNA sequencing and its impacts on research, and when I visited the trade centre, [biotechnology company] Roche was inviting proposals for scientists to win free use of their sequencing machine," Paul explains. "I asked whether they would consider a school using the technology and they really warmed to the idea."

A fellow conference delegate, Justin suggested that a metagenomic study would make good use of the machine's capabilities. "Since our school is based at the beach, we thought about the marine environment," Paul says, and Hot Water Beach would provide a novel setting for the research. Justin wrote up a proposal that won the Roche competition, and subsequently secured additional funding for the project from Massey University and the Maurice Wilkins Centre.

"It was a real collaboration between the scientists and teachers," Justin says. A large team from Massey brought all the equipment and supervised the students. "We streamlined the experiment as much as possible but it was still quite lengthy, and the students did really well." Paul invited students from three further schools take part, all of whom were learning about DNA technology in their Year 13 biology classes. The students extracted DNA from the samples and amplified genes that could identify the microorganisms. The material was sent to Roche for sequencing and the results will be published soon.

"We gave lectures to reinforce what the students were learning about gene amplification and DNA sequencing as part of the curriculum, and Paul really integrated it into their studies," Justin says. "The project linked well with the qualifications our students are working towards and was a very authentic learning experience," Paul adds. "It gave them access to equipment that schools cannot provide, and meeting the scientists may have challenged a few stereotypes. A survey of the students – by Rose Hipkins from the New Zealand Education Research Council – gave us very encouraging feedback," he says. The project was such a success that Justin plans to adapt it for use by schools nationwide and Paul is creating related resources for teachers.



Outreach

2011 Maurice Wilkins Centre Lecture

Renowned chemist Professor Steve Ley, the 2011 Maurice Wilkins Centre visiting lecturer, spoke to a full house about "flow chemistry", an innovative system that his research team at the University of Cambridge is developing to improve the efficiency of chemical synthesis.

"Steve's name is synonymous with synthesis, which is at the heart of all organic chemistry and drug discovery," said host Professor Margaret Brimble. "We're proud to synthesise molecules that improve health, and if we can find a good method then all chemists benefit," said Professor Ley of his research group. "Our focus is on the tools and how to do things better."

He explained that synthesis traditionally involves a series of chemical reactions performed in flasks, with purification at each step, which produces many times the volume of waste compared with the desired compound. His ground-breaking new process, modelled on how chemicals are synthesised in nature, involves immobilising all of the reagents required for a series of reactions along a cartridge and flowing the starting material through it, so that the final product emerges as though from a tap. Professor Ley is keen to train New Zealand researchers in this new technology and the Maurice Wilkins Centre will play a role in transfering the latest techniques back to New Zealand.

Sponsorship

Maurice Wilkins Centre Prize for Excellence in Chemical Research

The Maurice Wilkins Centre Prize for Excellence in Chemical Research, sponsored by the Centre in partnership with the New Zealand Institute of Chemistry (NZIC), was this year awarded to Professor David Williams from The University of Auckland. The prize is awarded annually to a member of the NZIC who has made a significant contribution to chemical science in the past five years.

Professor Williams' research in electrochemistry and corrosion science has led to a paradigm shift in the understanding of localised corrosion of stainless steels, and he has pioneered new scientific methods in the field. He also studies surfaces suitable for miniature biomedical measurement devices, aiming to maintain high activity of

biorecognition reagents whilst minimising non-specific adsorption of non-analyte. He is exploring peptides as nanoparticle growth modifiers and is investigating microfluidic devices exploiting synergies between electrochemically-active conducting polymers and ion-sensitive hydrogels. He has recently started an effort directed at microfabrication methods for studying metabolism at the single cell level.

Conferences, meetings and organisations

Scientific conferences, meetings and networks are important fora to share knowledge and form collaborative relationships. In addition to the Symposium and workshops it convenes (see pages 11 and 41), the Maurice Wilkins Centre supports international scientific meetings held in New Zealand as well as local scientific meetings and networks.

In 2011 the Maurice Wilkins Centre sponsored:

- The Queenstown Molecular Biology Meeting, this year held as part of Queenstown Research Week. This meeting attracted over 740 national and international delegates and speakers, including many from the Maurice Wilkins Centre.
- 'Crystal 27', the biannual meeting of The Society of Crystallographers in Australia and New Zealand. Held in New Zealand for the first time since 1997, the programme covered applications of crystallography in the fields of biology, chemistry and new materials.
- The Medical Sciences Congress 2011, held in association with Queenstown Research Week. The congress focused on basic research in the medical sciences and involved both experimental and clinical scientists.
- Biolive 2011. This conference brought together biology educators from the primary, seconday and tertiary education sectors and focused on sharing expertise in biology education as well as discussing how educators can work together to make students' transitions from one stage of education to the next more effective.
- ChemEd 2011. This conference brought together chemistry educators from the secondary and tertiary sectors along with researchers to share experience and expertise and celebrate the wonders of chemistry.
- AWIS 2011 Developing Women - Advancing Science. This triennial conference hosted by the Association of Women in Sciences provided opportunities for women working in science to develop their skills to benefit both their careers and personal lives and to learn from other women working in science.
- 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 acting as an advocate for the industry, 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 sector by providing companies with the expertise and facilities that their research and development programmes require. Centre investigators also provide consultancy to industry as described on page 60-61. In 2011 the Centre provided expertise and/or facilities to:

- Bayer New Zealand Limited. This company is part of the global Bayer Group which has major businesses in health care, nutrition and high-tech materials. Maurice Wilkins Centre investigator Professor Margaret Brimble has continued to work with Bayer New Zealand's Healthcare sub group on new drugs for use in livestock. In addition Maurice Wilkins Centre investigator Dr Vinod Suresh is providing expertise to the company on 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 investigators Professor Bill Denny and Dr Steve Jamieson collaborate with the company on research into inhibitors of AKR1C3, a molecular target in cancer.

- Connovation Ltd. This company is based in Auckland and undertakes research, development and manufacture of invasive animal pest control technologies. The company aims to develop smarter pest control products which are humane, cost effective and more specifically targeted to pest species. Maurice Wilkins Centre investigator Professor Margaret Brimble is working with the company on designing and synthesizing new molecules as humane rodenticides to replace the toxin 1080.

- GlycoSyn. This is the discovery, development and manufacturing arm of Industrial Research Limited, working with biotechnology clients to develop high-value small molecules. Maurice Wilkins Centre investigator Professor Margaret Brimble trained GlycoSyn staff to make glycosylated amino acid building blocks that it now sells commercially and which allows large-scale synthesis of materials for use by Maurice Wilkins Centre researchers. Professor Brimble has also provided technical advice to the company on a commercial synthesis project.

- 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 library of Maurice Wilkins Centre investigator Professor Margaret Brimble. Professor Brimble also has a contract 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.

- 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.

- Ruga Corporation (USA).This is a private biopharmaceutical company that discovers and develops novel targeted therapeutics in oncology. Maurice Wilkins Centre investigator Associate Professor Michael Hay led research into novel agents that selectively target renal cell carcinomas which was jointly licensed by UniServices and Stanford University to the company for commercial development. This resulted in a new research contract with Ruga Corp which was completed in 2011.

- Symansis Ltd. This company, with facilities in the South Island, 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 an advisor to the company.

- Zespri International Ltd. This company is the world's largest marketer of kiwifruit and manages the majority of New Zealand grown kiwifruit export sales. The spread of the bacteria *Pseudomonas syringae pv. actinidiae* (Psa), which kills the kiwifruit vines, is a significant issue for the industry. Maurice Wilkins Centre investigators Professor Margaret Brimble and Dr Paul Harris are working with Zespri to tackle this problem, by synthesizing antimicrobial peptides from the kiwifruit genome in order to engineer a solution to the Psa bacterial infection.

In addition to these examples, 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, public lectures and presentations, and through visits by schools students.

In 2011 Centre members generated national and regional media coverage on a variety of scientific topics:

- Maurice Wilkins Centre investigators Drs Jeff Smaill, Adam Patterson, Jack Flanagan, and Professors Mark McKeage and Rod Dunbar had a 30 minute feature story on TVNZ7 programe "Ever Wondered". The story covered an exciting new class of hypoxia-activated pro-drugs that selectively targets low-oxygen (hypoxic) conditions found in many solid tumours. It can be viewed at http://tvnz.co.nz/ever-wondered/s2-e4-video-4363995.
- The anticancer drug SN30000 (also called CEN-209), developed by Associate Professor Michael Hay, received both national and international media attention throughout the year. See page 9 for more details.
- The progression of another anticancer drug, PWT33597, to clinical trials in 2011 was reported on several New Zealand websites and in the National Business Review. This drug was developed by UniServices spin-out company, Pathway Therapeutics, Inc., based on research from the Auckland Cancer Society Research Centre.
- Professor Peter Shepherd featured in an interview on Nights with Bryan Crump, Radio New Zealand, about his research on anticancer drugs and the challenges of drug discovery in New Zealand.
- Professor Margaret Brimble was named "Ultimate Scientist" in Next magazine's feature on eight women who "inspire us because of the wonders they work with their time".
- Three Maurice Wilkins Centre investigators were invited to take part in The Marie Curie Lecture Series 2011, organised by the Royal Society of New Zealand as part of the International Year of Chemistry. The series was a year-long national tour of public talks by female New Zealand chemists in honour of Curie's Nobel Prize in Chemistry. Professor Margaret Brimble gave a lecture in Wellington on "Exploring nature's medicine chest", Professor Juliet Gerrard spoke in Timaru about "Promiscuous proteins" and Associate Professor Emily Parker gave a lecture at the Auckland Museum on "The wonderful world of enzymes".
- Professor Brimble also gave invited public lectures to the Hamilton Alumni and Friends Luncheon and at the L'Oreal Citizen Day.
- The Radio New Zealand programme "Our Changing World" featured Maurice Wilkins Centre investigator Siouxsie Wiles. Dr Wiles discussed the role of "glow in the dark" bacteria in a novel rapid screening technique for finding new drugs to combat superbugs. With funding from the Auckland Medical Research Foundation, The University of Auckland and the Maurice Wilkins Centre, Dr Wiles has also produced a short animated film explaining her research. The clip is currently posted on YouTube where it has received over 2000 views and a large number of positive comments.

Centre investigators also participate in visits from school students, give public presentations about their research and write on the New Zealand science blog site Sciblogs (www.sciblogs.co.nz).

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 2011 Maurice Wilkins Centre investigators were involved in many science education initiatives, including:

- Maurice Wilkins Centre biology teacher development scholarships. For the second year the Centre sponsored scholarships for high-school biology teachers to attend the Queenstown Research Week. The aim of the 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 awards were Chris Clay from Botany Downs Secondary College, David Clare from Christchurch Girls' High School, Alison Purdie from Birkenhead College and Katherine Lefever from St Andrew's College.
- Biolive 2011 conference. The Maurice Wilkins Centre provided sponsorship for this conference aimed at biology educators from the primary, secondary, and tertiary sectors, and Rochelle Ramsay, the Centre's Research Manager, was a member of the organising committee. The conference provided a chance for educators to network and share expertise in teaching biology. On the opening day of the conference posters describing the research of Maurice Wilkins Centre PhD students Paul Haseler and Inken Kelch and research fellow Dr Anna Brooks were displayed in a poster session. Anna and Paul attended the session and talked to the conference delegates about their research.
- 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 2011 many 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 fourth consecutive year, Maurice Wilkins Centre scientists Drs 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.
- The Maurice Wilkins Centre also provided support for an innovative teaching programme for Year 13 biology students using DNA technology to complement their classroom learning (see page 27).

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

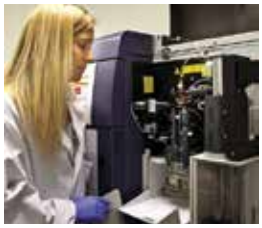
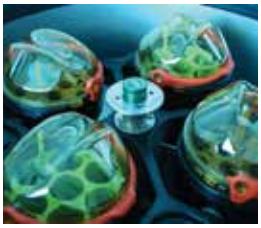
In 2011 Maurice Wilkins Centre investigators served in advisory and governance roles in many New Zealand organisations including:

- Auckland Medical Research Foundation
- Bioinformatics Institute New Zealand
- Biomolecular Interaction Centre (University of Canterbury)
- Cancer Society of New Zealand
- Canterbury Medical Research Foundation
- Diabetes NZ Auckland
- Health Research Council of New Zealand
- Institute of Environmental Science and Research
- Landcare Research New Zealand Ltd
- Marsden Fund Council and Panels
- Ministry of Science and Innovation
- National Institute of Water and Atmospheric Research Ltd
- National Institutional Biosafety Committee Board, ERMA
- New Zealand Genomics Ltd
- New Zealand Institute for Rare Disease Research Ltd
- New Zealand Society for Biochemistry and Molecular Biology
- New Zealand Society for Oncology
- New Zealand Synchrotron Group Ltd
- Nutrigenomics New Zealand
- NZBIO
- Rutherford Foundation
- Scientific Committee of the National Heart Foundation
- The Melanoma Network of New Zealand

- The New Zealand Institute of Chemistry Inc
- The Queenstown Molecular Biology Meetings Society Inc
- The Royal Society of New Zealand
- Wellington Division Cancer Society

International roles

In 2011 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, Denmark, Canada, France, Sweden, Malaysia and Egypt.


Organisational Development

Research seeding programme

One of the Maurice Wilkins Centre's main objectives is to encourage early-stage research collaborations between investigators from different scientific disciplines, achieved through its contestable research seeding programme. Three rounds of the programme were held in 2011 and 23 new projects were approved, including support for three 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 initiated in 2011:

- Identifying novel inhibitors of a crucial biosynthetic enzyme from *Mycobacterium tuberculosis:* Parker, University of Canterbury; Flanagan and Baker, The University of Auckland.
- Understanding the quarternary structure of peroxiredoxins – towards therapeutic strategies to combat tuberculosis: Gerrard, University of Canterbury; Lott, The University of Auckland.
- Imaging the endothelial cell glycocalyx: Brimble, Hall and Long, The University of Auckland.
- Induction of multifunctional T-cells by ovine adenovirus (OvAd) vectors: Taylor, Brooks and Dunbar, The University of Auckland.
- Understanding the role of GTP hydrolysis in powering the anti-viral Mx proteins: Kingston, Bulloch and Sneyd, The University of Auckland.
- Drug candidates from high throughput screening of chiral compound libraries: Furneaux, Industrial Research Limited; Atkinson and Ackerley, Victoria University of Wellington; Ching and Crosier, The University of Auckland.
- Investigating trans-generational effects of oxidative stress: Horsfield and Hampton, University of Otago.

- Synthesis and biological testing of acetylated mutant adrenocorticotropin: Mountjoy, Harris and Brimble, The University of Auckland.
- A model system for fluid and ion transport in lung epithelium: Suresh and Sneyd, The University of Auckland.
- Mixed signals: spatio-temporal decoding of calcium signalling pathways in the heart: Crampin, Soeller and Sneyd, The University of Auckland; in collaboration with Dr Llewelyn Roderick, Cambridge University (UK).
- Imaging and modelling of vasculature and hypoxia in human tumour xenografts: Pruijn, Kelch, Bogle, Hicks, Sands, Dunbar, LeGrice and Wilson; in collaboration with Dr Gregory Sands and Associate Professor Ian LeGrice, The University of Auckland.
- AKR1C3: a potential therapeutic target for ER-positive breast cancer: Jamieson and Denny; in collaboration with Dr Jo Perry, The University of Auckland.
- Management of type 2 diabetes in obese patients: gut hormone and microbiota study: Murphy, Wiles, Smith, The University of Auckland; Black, University of Otago; in collaboration with Mr Michael Booth, Waitemata District Health Board.
- Development of a new microparticle vaccine adjuvant with the ability to deliver siRNA to dendritic cells and monocytes: Mainini, Eccles, Young and Larsen, The University of Otago.

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 initiate exciting new projects.

Projects initiated in 2011:

- Investigating inhibition of anthranilate phosphoribosyl transferase: Cookson and Parker, University of Canterbury; Lott, The University of Auckland.
- Investigation of ligand binding in mutant *N. Meningitidis* α-IPMS: Huisman and Parker, University of Canterbury; Baker, Baker and Evans, The University of Auckland.
- Quantification of the S1P metabolic product hexadecenal using the QSTAR XL hybrid MS/MS system: McIntosh, Angel, Middleditch and Dunbar, The University of Auckland.
- Quantitative proteomic profiling of ob/ob mouse lung tissue: Jullig and Phillips, The University of Auckland.
- Identification and use of neovascularisation promoting cell populations from human adipose tissue for human skin tissue engineering: Brooks and Feisst, The University of Auckland.
- Deciphering adrenomedullin peptide binding: towards novel therapeutics for vascular diseases: Watkins, Hay, Brimble and Harris, The University of Auckland.

Multidisciplinary training

A major focus of the Maurice Wilkins Centre is developing the next generation of scientists to be confident working across different scientific disciplines. The Centre supports multidisciplinary PhD projects that involve collaboration between Centre investigators and research in more than one scientific discipline. The projects inititated in 2011 are the last of 23 new training fellowships offered since 2009.

Projects initiated in 2011:

- Development of multi-target antimicrobials using ancestral sequence reconstruction: Newton and Patrick, Massey University; Arcus and Hobbs, University of Waikato.
- Novel click chemistry probes to target hypoxic tumour cells and characterise their gene expression: Hou, Pruijn, Tercel, Print and Wilson, The University of Auckland.
- Role of DHPDSL in kidney stone disease: Huang, Loomes and Baker, The University of Auckland.

New investigators

In 2011, the Maurice Wilkins Centre continued to strengthen its national network of investigators and twelve new associate investigators were invited to join the Centre:

- Dr David Baddeley, Department of Physiology, The University of Auckland
- Dr Mike Cooling, Auckland Bioengineering Institute, The University of Auckland
- Dr Gabriele Dachs, Department of Pathology, University of Otago, Christchurch
- Dr Andrew Fidler, Cawthron Institute
- Dr Julia Horsfield, Department of Pathology, University of Otago
- Dr Stephen Jamieson, Auckland Cancer Society Research Centre, The University of Auckland
- Dr Mia Jullig, School of Biological Sciences, The University of Auckland
- Dr Melanie McConnell, Malaghan Institute of Medical Research
- Dr Frederik Pruijn, Auckland Cancer Society Research Centre, The University of Auckland
- Dr Vijay Rajagopal, Auckland Bioengineering Institute, The University of Auckland
- Assoc Prof Christian Soeller, Department of Physiology, The University of Auckland
- Dr Geoff Williams, School of Chemical Sciences, 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 concluded in 2011, with final orders for the last 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.

The Maurice Wilkins Centre was also awarded $4.3 million of capital equipment funding in 2002. Much of the equipment purchased with this funding is now reaching the end of its usable lifetime and some of this equipment was updated in 2011:

- In 2011 the Centre purchased a new microfluidizer cell disruptor to replace the existing cell disruptor purchased in 2003 and located at the School of Biological Sciences, The University of Auckland. This updated equipment will be used as part of the process for harvesting proteins for research purposes. It has significantly more capability than the existing equipment and will increase productivity in the laboratory.
- The Centre upgraded the ProteinPilot software package that is used to analyse data from the QSTAR mass spectrometer and is crucial for the continuing analysis of iTRAQ experiments.

In 2011 Maurice Wilkins Centre investigators also implemented new technology platforms:

- The University of Auckland provided funding to upgrade the FACS Aria II flow cytometer purchased in 2008 by the Maurice Wilkins Centre. The addition of a violet laser to the cell sorter allows the detection of 14 colours simultaneously. This new capacity has advanced the development of multicolour panels for characterising complex tissues such as human fat, skin, lymph nodes and liver.
- Centre investigators led by Professors Ted Baker and Margaret Brimble at The University of Auckland have worked together over 2011 to establish a platform for racemic protein crystallography in New Zealand. This multidisciplinary technology increases the chances of researchers getting structural information for important proteins that do not behave well in standard conditions (see page 19 for more details).

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 Crown Reseach Institutes and Health Boards. In 2011 the Centre's client list included:

- Pathway Therapeutics Ltd
- Proacta Ltd
- Plant & Food Research Ltd
- University of Waikato
- Massey University
- University of Canterbury
- AgResearch Ltd
- Somnaceutics Ltd
- Auckland District Health Board

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 2011 the Centre provided full or partial stipends for 29 PhD students and one MSc student from this cohort. Eleven Maurice Wilkins Centre-associated PhD students completed their studies in 2011.

In 2011 the Centre completed the recruitment of PhD students as part of the "multidisciplinary training" category of the research seeding programme that began in 2009. Two new PhD candidates began their studies in 2011 funded under this programme with the last PhD candidate due to start in early 2012. Two of the new students are based at The University of Auckland and one at Massey University.

In November, the Centre once again convened a successful Future Science Day providing career advice for young scientists, and challenging PhD students to communicate their research in a manner suitable for a non-specialist audience in three minutes or less. Twenty-six students participated, speaking on a diverse range of topics, and the winner was University of Auckland student Ms Donna Montesclaros who spoke about her research on the role of casein kinase-1 (CK-1) in beta catenin signalling.

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 Centre provides support for staff and students to travel to conferences, technical workshops and to visit other laboratories in New Zealand and overseas to acquire new skills and techniques.

In November 2011 the Centre initiated a new contestable programme to which affiliate investigators can apply for support to travel to international workshops and laboratories to learn new technical skills. A criterion for a successful application is that the investigator must present a plan for how they will disseminate their new knowledge and skills to other members of the New Zealand science community on their return. Two applications were approved in December 2011 for uptake in 2012 (see page 25).

During 2011 the movement of PhD students between the laboratories of Maurice Wilkins Centre investigators across New Zealand has continued. 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.

In 2011 the Centre also provided support for the following international exchanges:

- Associate Professor Sarah Hook and PhD student Terrawan (Mo) Rattanapak (School of Pharmacy, University of Otago) travelled to Japan to carry out collaborative research in the imaging laboratory of Dr Masaru Ishii at the Immunology Frontier Research Centre (iFReC) at Osaka University (see page 23).
- Maurice Wilkins Centre scientist Mr Martin Middleditch visited the Centre for Advanced Discovery and Experimental Therapeutics at the Manchester Biomedical Research Centre in the United Kingdom to learn about the cutting-edge mass spectrometry technology platforms that are being used there to perform proteomic and metabolomic analyses. While in the United Kingdom, Martin also attended the British Mass Spectrometry Society Meeting 2011 and presented a poster describing work using mass spectrometry to characterise amyloid deposits for clinical diagnosis.
- Maurice Wilkins Centre scientist Mr Ivan Ivanovic, who runs the Centre's robotic crystallisation facility at The University of Auckland, travelled to the European Lab Automation conference in Germany. This conference involved presentations, workshops, and training sessions with a core focus on automated techniques, equipment and applications. Mr Ivanovic won an award for his poster presentation "Analysis of overall success of robotic crystallisation".

Maurice Wilkins Centre workshops

Members of the Maurice Wilkins Centre ran four technology-based academic workshops in 2011. 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 David Nickerson from the Auckland Bioengineering Institute organised the annual CellML workshop in April. CellML is an open standard language being developed by the Auckland Bioengineering Institute to store and exchange computer-based mathematical models of biological processes (see page 21). The CellML workshop provides an opportunity to update users on recent developments and discuss future work with the language. Delegates included visitors from the United Kingdom, Poland, and India as well as staff and students from the Auckland Bioengineering Institute.
- Maurice Wilkins Centre investigator Dr Jack Flanagan convened the Auckland Cancer Research Network's 2011 Winter School, a one day event focussing intensively on current hot topics in cancer research. This year the event focussed on immunotherapy, the discovery and utility of biomarkers in cancer and the importance of animal models of cancer.
- A workshop entitled "Flow Cytometry and its applications in research" was convened by the Centre in Auckland in September 2011. The workshop brought together flow cytometry experts from the Malaghan Institute of Medical Research and The University of Auckland's School of Biological Sciences and School of Medical Sciences to highlight the cytometry services available in these facilities and the various research outcomes these services may achieve. This seminar has resulted in increased use of the flow cytometry suites and new collaborations.

- The Maurice Wilkins Centre teamed up with The Bioinformatics Institute at The University of Auckland to run a "Bioinformatics Methods for Next Generation Sequencing" workshop at Queenstown Research Week. Topics included sequencing technologies, experimental design, basic data analysis concepts, and metagenomics. The Centre recorded the event and made it available on its website to those who could not attend.

Fostering collaboration in biomedical research

Through its flexible research seeding programme, the Maurice Wilkins Centre sponsors collaborative research that is interdisciplinary and inter-institutional. The Centre covened a special event in Dunedin in December 2011 to review collaborations involving Maurice Wilkins Centre investigators at the University of Otago. The Symposium was chaired by Universty of Otago Emeritus Professor George Petersen, a member of the Maurice Wilkins Centre Governing Board from 2006–2011, and allowed Centre investigators based in Otago and Auckland to outline examples of current research projects, and highlight promising research areas where they would like to establish new collaborations. It is expected that many of the ideas discussed will attract support from the Centre in 2012.

Visitors to the Maurice Wilkins Centre

International companies

In 2011 Maurice Wilkins Centre investigators hosted visits from the following company representatives:

- Dr Hiroshi Maeda, Director, Global Scientific Affairs and Dr Ronald Law, Vice President, Global Scientific Affairs,Takeda Pharmaceuticals, USA
- Dr Ming-Wei Wang, Director, Chinese National Compound Library and the National Centre for Drug Screening, Chinese Academy of Sciences, China
- Dr Jeanette Wood, Head of Biology, S*BIO Pte Ltd, Singapore
- Madam Dan Hao, Founder and President, Hainan Guo Yun Feng Investment Group, China
- Dr Daniel Grant, Head of External Research and Development Innovation, Pfizer Inc, USA
- Dr Isaac Bentwich, Founding Director, Rosetta Genomics Ltd, Israel
- Dr Thorsten Melcher, CEO, Centella Therapeutics Inc, USA
- Dr Janet Gunderson and Dr John Flygare, Genentech Inc, USA
- Dr John Gutheil, Ms Terri Melink, Mr Kevin de la Torre and Dr Kate Parker, Proacta Inc, USA
- Mr Masahiko Satomi, Mr Hiroshi Kodaira, Mr Satoshi Ikeda, Mr Hiroyuki Takahashi and Dr Ryuta Yamazaki, Yakult Honsha Co Ltd, Japan
- Dr Peter Senter, Vice President of Chemistry, Seattle Genetics Inc., USA

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 2011 were:

- Professor Ulrich Baumann, Cologne University, Germany
- Associate Professor Thomas Deisboeck, Harvard University, USA
- Dr Rob Don, Drugs for Neglected Diseases Initiative, Switzerland
- Professor Paul Freemont, Imperial College London, UK
- Dr Christian Hartinger, University of Vienna, Austria
- Associate Professor Craig Hutton, University of Melbourne, Australia
- Professor Stephen Kent, University of Chicago, USA
- Professor Steve Ley, Cambridge University, UK
- Professor Eddy FY Liew, University of Glasgow, Scotland
- Professor Edison Liu, National University of Singapore, Singapore
- Dr Ashley Mansell, Monash University, Australia
- Associate Professor Paul Monga, University of Pittsburgh, USA
- Professor Ian Orme, Colorado State University, USA
- Associate Professor Mike Perkins, Flinders University, Australia
- Professor Jennifer Potts, University of York, UK
- Professor Kiyoshi Takeda, Osaka University, Japan
- Professor John Wade, Howard Florey Institute, Australia
- Dr Yu Wang, University of Hong Kong, Hong Kong
- Professor James Whisstock, Monash University, Australia
- Professor Bryan Williams, Monash University, Australia
- Professor Todd Yeates, University of California Los Angeles, USA

The Centre also hosted numerous visits by scientists from within New Zealand.

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 2011 Maurice Wilkins Centre investigators were awarded new grants worth more than $23.4 million from New Zealand funding sources for research projects to be carried out over the next one to five years, including $14.4 million from the Health Research Council of New Zealand and $5.3 million from the Marsden Fund.

International funding

In 2011 Maurice Wilkins Centre investigators secured new funding of $3.6 million from the Wellcome Trust (UK) to support future research.

Commercial funding

In 2011 Maurice Wilkins Centre investigators secured new research funding from Proacta Inc (USA) and Zespri International Ltd.

Governance and management

Governing Board

In 2011 the board consisted of Mr Bill Falconer (Chair), Professor Grant Guilford (The University of Auckland), Professor Jane Harding (The University of Auckland), Professor Gary Raumati Hook, Professor Iain Martin (The University of Auckland), Emeritus Professor George Petersen (University of Otago) and Ms Maxine Simmons (Biocatalyst Ltd).

During the year the board met three times and monitored progress of the Maurice Wilkins Centre research programme and its compliance with its funding mandate and budget. In addition the board provided advice and direction on strategies for engaging Maori and Pacific communities and postgraduate scholars, on an update of the Centre's constitution document and on further refinement of the Centre's reporting.

Emeritus Professor George Petersen and Professor Gary Raumati Hook both ended their terms with the board in 2011.

Professor Gary Raumati Hook was a founding member of the board in 2003. He brought to the board over 30 years of experience as an environmental health scientist, an editor of scientific publications and a science educator. During his term with the board Professor Hook was a great advocate for science education and for advancing the participation of Maori and Pacific students in science. His advice and experience were invaluable in the Centre's strategic planning particularly the refinement of its communications and outreach programmes.

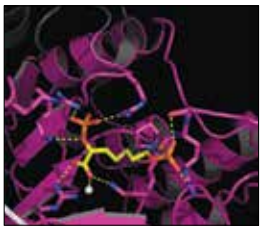
Emeritus Professor George Petersen joined the board in 2006 with over 40 years experience as an internationally renowned scientist and science leader in New Zealand. He brought a deep academic understanding to shaping the Centre's research strategy and played a key role in strengthening the Centre's links with the University of Otago. Professor Petersen initiated and chaired the Maurice Wilkins Centre workshop "Fostering collaboration in biomedical science" held in Dunedin in December 2011, which focussed on research areas where collaboration between investigators across the country was scaling up the Centre's reseach programmes.

The Centre gratefully acknowledges the input of both retiring board members during their terms.

Management Committee

The Maurice Wilkins Centre Management committee consisted 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 2011.






Research Outputs

Publications

In 2011 research outputs from Maurice Wilkins Centre investigators included more than 370 peer-reviewed scientific papers published in international journals and numerous patents. Research directly supported by the Maurice Wilkins Centre generated the following 92 scientific papers and 10 patents published or filed.

Papers and reviews:

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3. Allison, T. M., Hutton, R. D., Jiao, W., Gloyne, B. J., Nimmo, E. B., Jameson, G. B., & Parker, E. J. An extended $\beta 7\alpha 7$ substrate-binding loop is essential for efficient catalysis by 3-deoxy-d-Manno-octulosonate 8-Phosphate synthase. *Biochemistry* (2011) **50**(43): 9318-9327.

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Patents

Patents published

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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.M., Ashoorzadeh, A., Flanagan, J.U., Guise, C.P. Bacterial nitroreductase enzymes and methods relating thereto. New Zealand Patent Application PCT/NZ2011, 2011.

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4. Smaill, J.B., Patterson, A.V., Ackerley, D.F., Ashoorzadeh, A., Guise, C.P., Mowday, A.M., Williams, E.M., Copp, J.N., Anderson, R.F., Koch, C., Kachur, A., Dolbier, W.R. Nitroheterocyclic and nitroaromatic derivatives for imaging and abalation of nitroreductase expressing cells and/or biological agents. New Zealand Patent Application TIS509135NZPR, 2011.

Presentations

The international significance of the research performed by Maurice Wilkins Centre investigators and their teams is demonstrated by more than 150 invitations to give international and national presentations in 2011. The presentations included invited lectures at conferences and seminars at academic institutions in the USA, Japan, China, the United Kingdom, Germany, Australia, Singapore, Canada, Korea, United Arab Emirates, Austria, the Netherlands, Italy, Greece, Mexico, Norway, Poland, and New Zealand, as shown in the diagram below.

Presentation highlights

Significant presentations given by Maurice Wilkins Centre investigators in 2011 include:

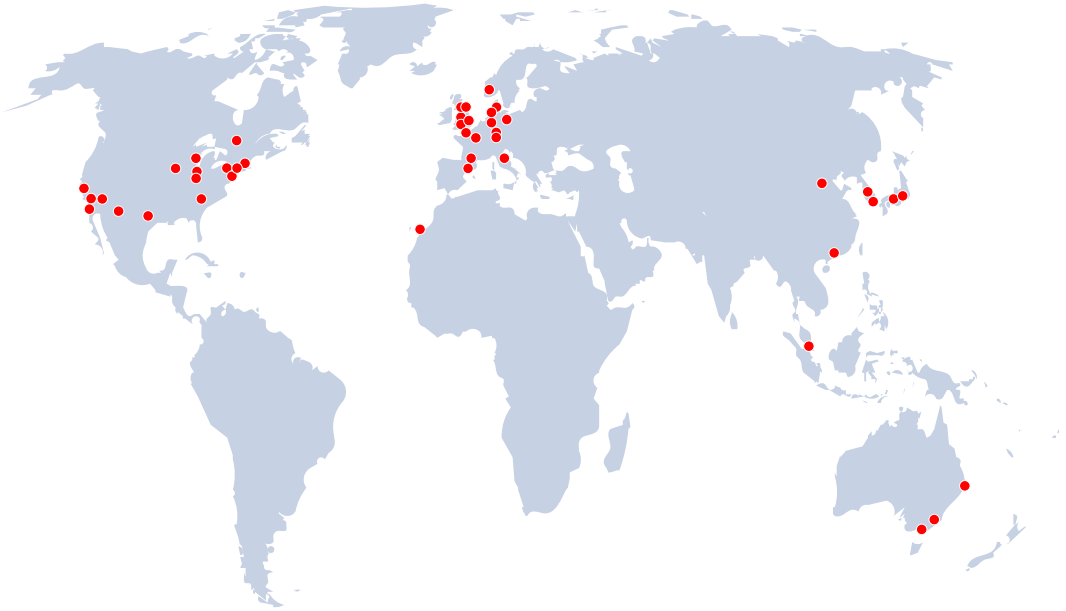
- Professor Peter Hunter was invited to give the Skalak Memorial Lecture on the 50th anniversary of Bioengineering at the University of California, San Diego. Professor Richard Skalak was a pioneer in bioengineering and biomechanics. Professor Hunter's lecture was entitled "A bioengineer's view of computational physiology".
- Professor Margaret Brimble delivered the Adrien Albert lecture at the conference of the Biomolecular Chemistry Division in Victoria, Australia, in December 2011 (see page 62).
- Professor Brimble was also invited to provide the plenary address at the 10th International Symposium "Recent Trends in Drug Discovery and Development", Yeungnam University, Gyeongsan, Korea. The lecture was entitled "Exploring Nature's Medicine Chest".

- Professor Ted Baker was invited to deliver the plenary lecture to the East Coast Protein Meeting at Coff's Harbour, NSW, Australia, in July 2011. His lecture was entitled "Seeing atoms: the rise and rise of crystallography in biology."
- Professor Peter Hunter was invited to deliver keynote lectures at the 2011 International Union of Theoretical and Applied Mechanics Symposium on Computer Models in Biomechanics held in Palo Alto, USA; the FDA / NHLBI / NSF Workshop on Computer Methods for Medical Devices: Validation of Computer with Nonclinical Models in Silver Spring , USA; and the 10th Engineering Mathematics and Applications Conference in Sydney, Australia.

Collaborations

The Maurice Wilkins Centre contributes to and benefits from an extensive network of national and international 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

McGill University (Canada)
University of British Columbia (Canada)
Medical College of Wisconsin (USA)
Pennsylvania State University (USA)
University of North Carolina (USA)
Virtual Physiological Human (VPH) Institute (Belgium)
Pierre and Marie Curie University (France)
Max Planck Institute for Molecular Genetics (Germany)
The University of Kiel (Germany)
The University of Münster (Germany)
Aston University (UK)
Bristol University (UK)
Imperial College London (UK)
Osaka University (Japan)
Riken Centre for Allergy and Inflammation (Japan)

Continuing academic collaborations

North America

Duke University North Carolina (USA)

Global Alliance for TB Drug Development (USA)

Harvard University (USA)

IUPS International Physiome Project (USA)

Ludwig Institute for Cancer Research (USA)

Massachusetts Institute of Technology (USA)

Mayo Clinic (USA)

Merck Research Laboratories (USA)

New York University (USA)

Pennsylvania State University (USA)

Proacta Inc (USA)

Stanford University (USA)

Texas Medical Center (USA)

The International TB Structural Genomics Consortium (USA)

The Scripps Research Institute (USA)

The University of Chicago (USA)

The University of Illinois (USA)

University of Iowa (USA)

Vertex Pharmaceuticals (USA)

Wake Forest University (USA)

UK and Europe

Arhus University (Denmark)

Aachen University (Germany)

Philipps University Marburg (Germany)

The Rizzoli Orthopaedic Institute (Italy)

National Institute of Occupational Health (Norway)

Norwegian University of Life Sciences (Norway)

Leiden University (The Netherlands)

Maastricht University (The Netherlands)

Hospital Universitario Nuestra Senora de Canderlaria (Spain)

Drugs for Neglected Diseases initiative (DNDi) (Switzerland)

Cancer Research Technology Ltd (UK)

European Bioinformatics Institute (UK)

John Innes Centre, Norwich (UK)

Newcastle University (UK)

Nottingham University (UK)

University of Cambridge (UK)

University of Manchester (UK)

University of Oxford (UK)

Asia Pacific

Burnett Institute, Melbourne (Australia)

Garvan Institute of Medical Research (Australia)

Mater Medical Research Institute (Australia)

Monash University (Australia)

Peter MacCallum Cancer Institute (Australia)

Queensland Institute of Medical Research (Australia)

University of Melbourne (Australia)

University of Queensland (Australia)

University of Sydney (Australia)

University of Western Sydney (Australia)

Hong Kong University of Science and Technology (China)

The Chinese Academy of Sciences (China)

RIKEN Institute Wako (Japan)

Tokyo University (Japan)

Inje University (Korea)

Seoul National University (Korea)

Novartis Institute for Tropical Diseases (Singapore)

Singapore National Imaging Institute (Singapore)

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 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 the Centre's 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 and Pathway Therapeutics 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 page 30 - 31 of this report. The Centre's investigators also act as consultants for a number of national and international companies. In 2011 the expertise of Maurice Wilkins Centre investigators was sought by:

- AFT Pharmaceuticals Ltd
- AgResearch Ltd
- Amgen Inc (USA)
- AstraZeneca (UK)
- Bayer New Zealand Ltd
- Biotech Equity Partners Pty (Australia)
- Cancer Research Technology Ltd (UK)
- Canterbury Scientific Ltd
- Centella Therapeutics Inc (USA)
- Coda Therapeutics Inc (USA)
- Comvita Ltd
- Connovation Ltd
- Douglas Pharmaceuticals Ltd
- EBonz Ltd
- Electrospinz
- Enzymatics Inc (USA)
- FB Rice (Australia)
- Fonterra Co-Operative Group Ltd
- Glycosyn
- Gene Networks International Ltd (Japan)
- Industrial Research Ltd
- Innate Therapeutics Ltd
- Insygen Therapeutics Ltd
- Integrated BioTherapeutics (USA)
- L2 Pharmaceuticals (USA)
- Landcare Research New Zealand Ltd
- Lanzatech NZ Ltd
- Merck & Co Inc (USA)
- Mesynthes Ltd

- Neuren Pharmaceuticals Ltd
- New Zealand Institute for Rare Disease Ltd
- Novartis International AG (Switzerland)
- Oxford Biomaterials Ltd (UK)
- Pacific Edge Biotechnology Ltd
- Paraco Technologies Ltd
- Pathway Therapeutics Inc (USA)
- PharmaZen Ltd
- Plant and Food Research Ltd
- Proacta Inc (USA)
- Ruga Corp (USA)
- Sanofi (France)
- Sirtex Medical Ltd (USA)
- Symansis Ltd
- VQ Orthocare (USA)
- Waitaki Bioscience-PharmaZen Ltd
- Zespri International Ltd

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 and the TB Structural Genomics Consortium.

Awards and honours

- **James Cook Research Fellowship**

  Professor Gregory Cook, a microbiologist from the University of Otago and a Maurice Wilkins Centre investigator, was one of four recipients of a prestigious 2011 James Cook Fellowship. The fellowships, administered by the Royal Society of New Zealand on behalf of the Government, are awarded to top researchers who have achieved national and international recognition in their area of scientific research. They provide two years of funding to allow the recipients to undertake concentrated work in their area of expertise.

- **Adrien Albert Award**

  Maurice Wilkins Centre investigator, Professor Margaret Brimble, from The University of Auckland, received the 2011 Adrien Albert Award. The premier award of the Biomolecular Chemistry Division of the Royal Australian Chemical Institute, the Adrien Albert Award recognises sustained and outstanding research in the field of medicinal or agricultural chemistry, related to biomolecular chemistry. Professor Brimble's research focuses on synthesising complex natural products with important biological activity, including new drug candidates. She presented the Adrien Albert lecture at the conference of the Biomolecular Chemistry Division in Victoria, December 2011.

- **Distinguished Professors**

  Maurice Wilkins Centre investigators Professors Bruce Baguley, Margaret Brimble, Bill Denny and Ian Reid, have been appointed to the rank of Distinguished Professor at The University of Auckland. The title recognises professors who have achieved international eminence of the highest order in their fields of research.

- **International leader**

  Professor Peter Hunter, a Maurice Wilkins Centre investigator, was elected Acting Vice President of the International Union of Physiological Sciences (IUPS) in 2011. The IUPS brings together physiologists from throughout the world with the aim to increase mankind's understanding of the functions of cells, tissues, organs and organ systems of animals and humans and has members from 51 countries.

- **National Animal Ethics Advisory Committee 3Rs Award**

  Maurice Wilkins Centre investigator Dr Siouxsie Wiles was awarded the 2011 National Animal Ethics Advisory Committee Three Rs award, sponsored by the Royal New Zealand SPCA. The concept of the Three Rs is to replace live animal subjects, reduce the number of animals used and refine experimental techniques to minimise pain and distress. Dr Wiles' work embodies all three techniques, and reflects the underpinning philosophy that the use of animals in science is only acceptable if all efforts are made to minimise harm or suffering.

- **Rutherford Discovery Fellowship**

  Dr Wayne Patrick, a Maurice Wilkins Centre investigator from Massey University was awarded a Rutherford Discovery Fellowship in 2011. These fellowships support New Zealand's most talented early- to mid-career researchers. This new Fellowship scheme also aims to attract top researchers, with international research experience, back to New Zealand.

- **Marsden Medal**

  Maurice Wilkins Centre investigator Professor Geoffrey Jameson, from Massey University was awarded the 2011 Marsden Medal by the New Zealand Association of Scientists. This annual award was presented to Professor Jameson "in recognition of his sustained record of leadership and service to New Zealand science and his outstanding contribution to the chemical sciences."

- **JSPS Invitation Fellowship**

  Maurice Wilkins Centre investigator Associate Professor Sarah Hook, from the University of Otago was awarded an "Invitation Fellowship" from the Japan Society for the Promotion of Science. This fellowship, funded by the Japanese Government, enabled Associate Professor Hook to travel to Japan and carry out collaborative work with Dr Masaru Ishii at Osaka University (see page 23).

- **Wellingtonian of the Year**

  Maurice Wilkins Centre investigator Professor Graham Le Gros won the Science and Technology category of the 2011 Wellingtonian of the Year Awards. Lower Hutt Mayor Ray Wallace, who presented Graham with his award, said that Professor Le Gros "is an excellent example of the science, research and technology professionals who add vibrancy and innovation to our region and make a positive contribution to society."

- **Student success**

  PhD students associated with the Maurice Wilkins Centre have received awards in 2011 including: Ms Maggie Au won first prize in a faculty wide poster competition run by the Faculty of Science at The University of Auckland. Mr Peter Bircham was awarded the Victoria University of Wellington silver medal for "best graduate student paper". Dr Michael Chu won the Amgen Young Investigator book prize at the Transplantation Society of Australia and New Zealand meeting. Ms Inken Kelch won the best image modelling competition in the annual Biomedical Imaging Research Unit awards at The University of Auckland. Ms Emma Scaletti and Sylvia Luckner together won a Webster Centre Poster Award in September 2011 for their work on the alanine racemase enzyme from *Staphylococcus aureus*.

Financial Report 2011

Operating Fund[a]

	$ 2011	$ 2010
Income		
CoRE grant	3,994,871	3,972,800
Equipment User charges[b]	227,149	364,074
Other income[c]	36,059	
Balance from previous year[d]	2,454,596	2,346,245
Total Income	**6,712,675**	**6,683,119**
Expenditure		
Salaries[e]	996,073	1,124,853
Overheads	906,270	994,045
Project costs[f]	978,246	1,001,726
Student support (PhD and other)[f]	667,679	395,799
Travel	62,007	94,740
Depreciation	507,912	617,359
Total Expenses	**4,118,186**	**4,228,520**
Income less expenditure[g]	**2,594,489**	**2,454,599**

Capital Expenditure Fund

Income	
Balance of TEC grant 2002	10,596
Balance of TEC grant 2008	10,707
Total Income	**21,303**
Expenditure	
Capital expenditure 2011	1,185
Funds carried forward to 2012[h]	**20,118**

Notes

a) This financial report is for the period 1st January to 31st December 2011 and covers the second six months of the Maurice Wilkins Centre Year 9 and the first six months of Maurice Wilkins Centre Year 10 (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. This figure includes an adjustment of -$5,698 due to the undereporting of income by this amount in the 2010 financial report.

c) This income is from the University of Auckland Foundation and UniServices and has been used to balance costs incurred by the Maurice Wilkins Centre in 2011 for student support ($18,200) and salaries ($17,859).

d) This brought forward balance is unspent funding from previous years of the Centre that will be used to fund research initiatives from 2012 to 2014.

e) Summary: Maurice Wilkins Centre supported research staff FTEs 2011

Principal Investigators	0.50
Research Fellows	7.10
Research Technicians	4.73
Total	12.33

f) These costs include the costs of subcontracts for associate investigator's research projects during 2011.

g) This balance of funding will be used to fund initiatives supporting the Maurice Wilkins Centre research programme in the period 2012 to 2014.

h) This balance will be used to complete the Centre's capital equipment purchase programme in 2012. As of the 31st December 2011 the Centre had outstanding purchase order commitments of $19,888.

Directory

Governing Board members

Mr Bill Falconer (Chair)

Prof Grant Guilford

Prof Jane Harding

Prof Gary Raumati Hook

Prof Iain Martin

Emeritus 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
Dr David Baddeley	Department of Physiology	The University of Auckland
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
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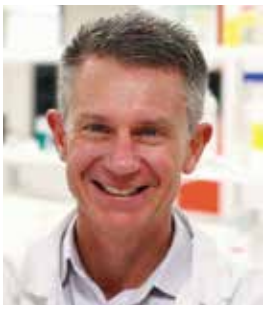

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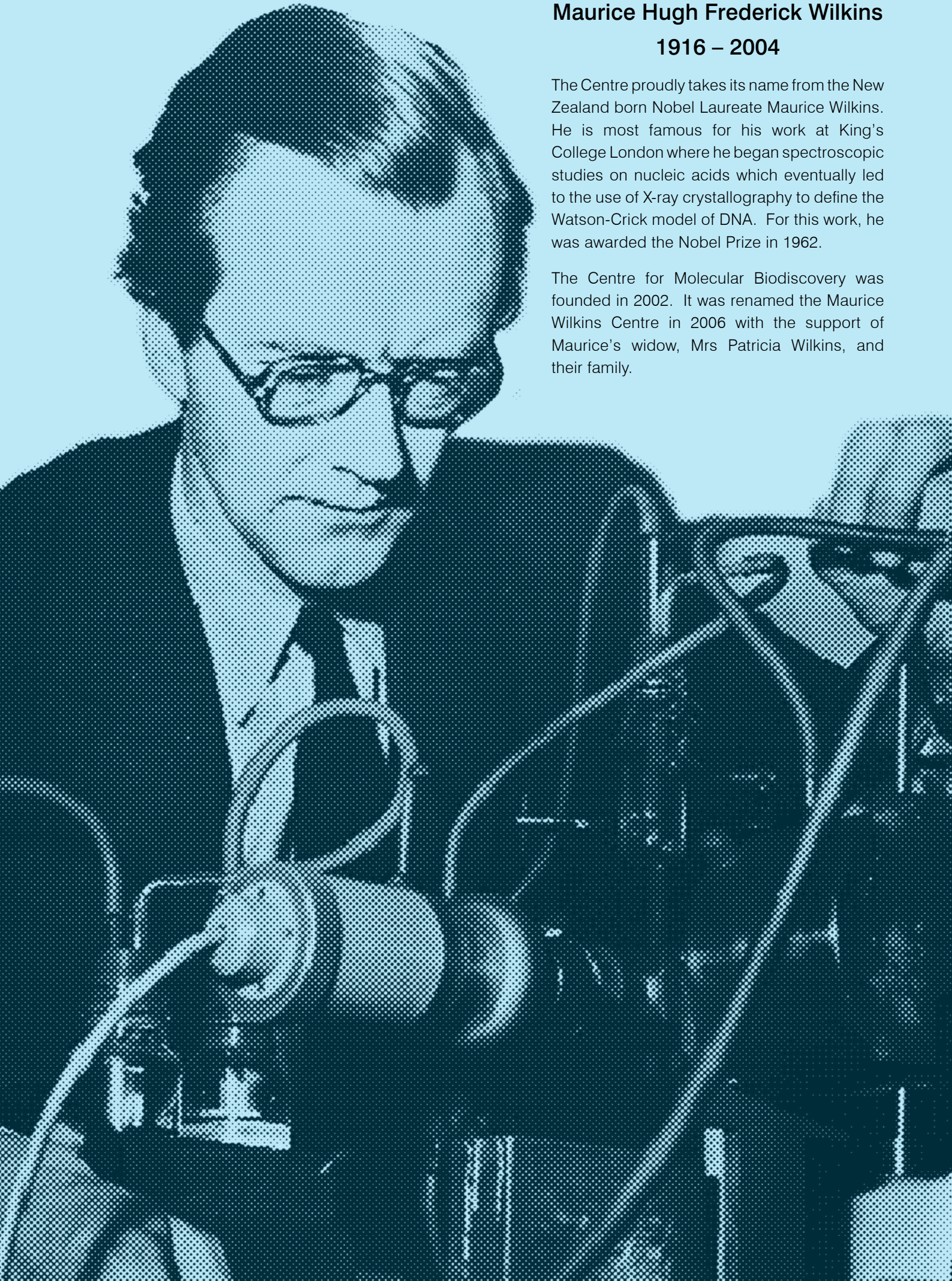

Maurice Hugh Frederick Wilkins
1916 – 2004

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.