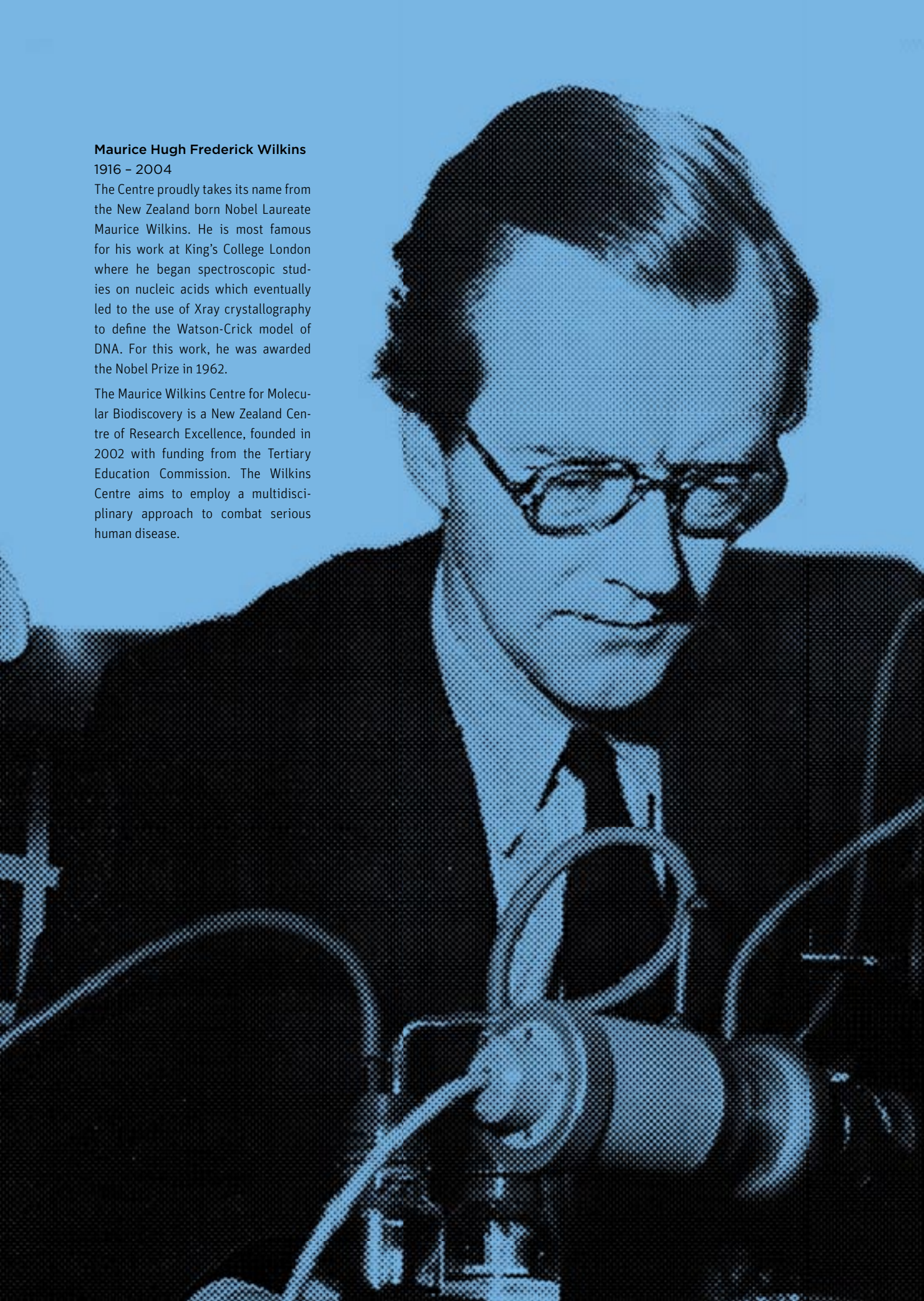
ISSUE 2 | DECEMBER 2007



# seek

MAURICE WILKINS CENTRE
FOR MOLECULAR BIODISCOVERY

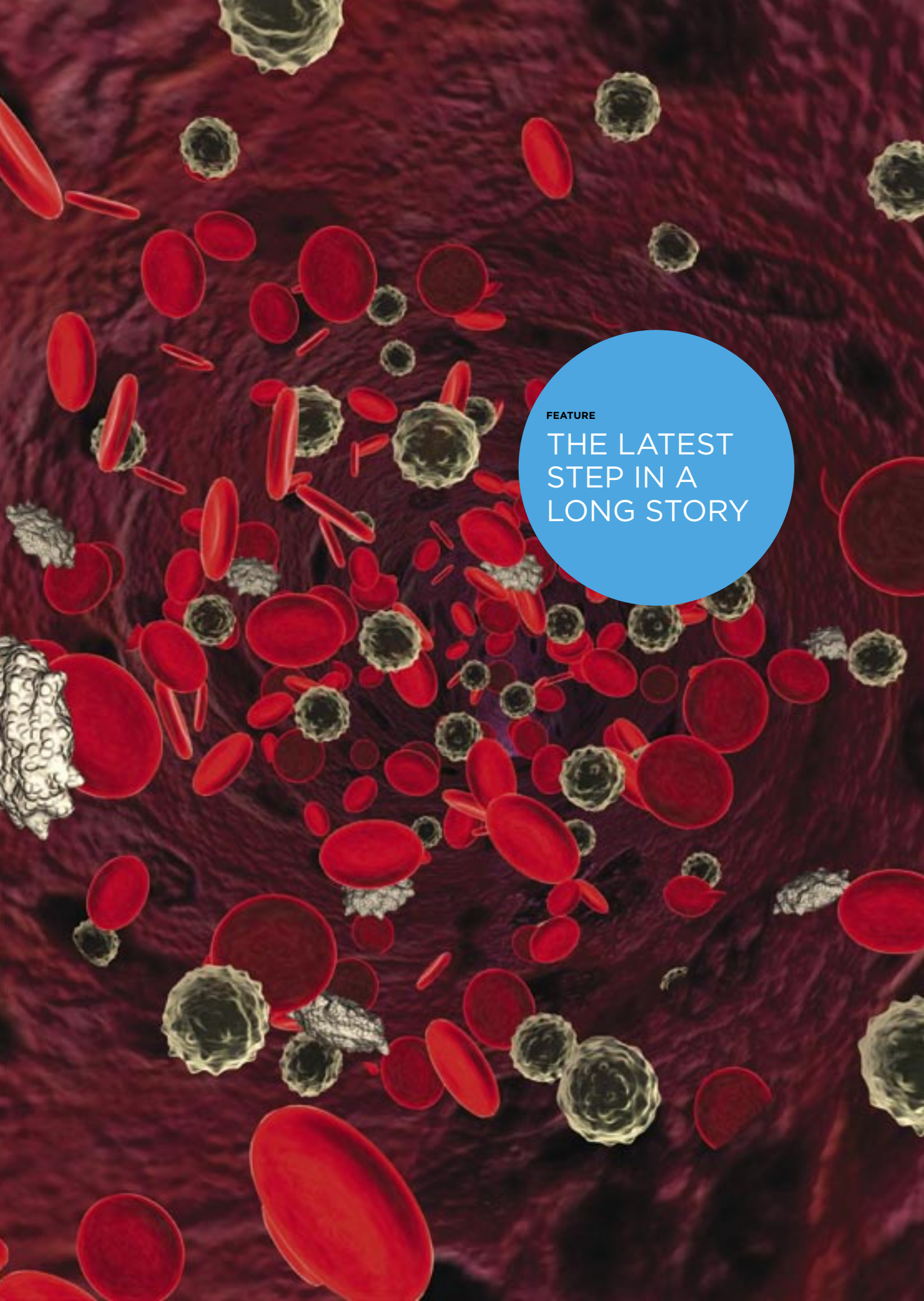


**Maurice Hugh Frederick Wilkins**
1916 – 2004

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 Xray crystallography to define the Watson-Crick model of DNA. For this work, he was awarded the Nobel Prize in 1962.

The Maurice Wilkins Centre for Molecular Biodiscovery is a New Zealand Centre of Research Excellence, founded in 2002 with funding from the Tertiary Education Commission. The Wilkins Centre aims to employ a multidisciplinary approach to combat serious human disease.

MAURICE WILKINS CENTRE
FOR MOLECULAR BIODISCOVERY



FEATURE

# THE LATEST STEP IN A LONG STORY

# BIG STEP FOR CANCER DRUG

The recent news that the global pharmaceutical company Novartis has acquired the Auckland-developed drug DMXAA illustrates both the long-term nature of drug development and the potential rewards to be gained. DMXAA (now designated ASA404) was developed in the period 1985–1997, by groups in the Auckland Cancer Society Research Centre led by Professors Bruce Baguley, Bill Denny and Bill Wilson, currently Investigators in the Maurice Wilkins Centre, and Associate Professor Lai-Ming Ching.

DMXAA is a vascular disrupting agent which selectively damages the blood vessels in tumours, causing shut-down of tumour blood flow and subsequently killing the tumour cells by oxygen and nutrient deprivation. Years of study of the mechanism of action of DMXAA, allowed the building of a case for human studies and initial Phase I trials were conducted in Auckland and the UK under the auspices of the UK cancer charity (now called Cancer Research UK), using drug manufactured in the Auckland Cancer Society Research Centre.

Following these trials, the drug was licensed to the UK biotech company Antisoma in 2001 for further development. Antisoma underwrote a series of Phase II trials, which were coordinated from Auckland by Associate Professor Mark McKeage and conducted mainly in NZ, Australia and Germany. The results of these trials, in which DMXAA was added to standard chemotherapy for non-small-cell lung cancer, ovarian cancer and prostate cancer, became available in mid-2006. In non-small-cell lung cancer, the addition of DMXAA was shown to nearly double the survival time of patients compared with those given the standard therapy, without causing any additional toxicity. The drug also appears to be useful in the treatment of prostate cancers.

On April 19th 2007, Novartis and Antisoma signed an agreement for Novartis to undertake extensive Phase III clinical trials of DMXAA, which, if successful, will lead to its registration as a medicine. The agreement included upfront fees to Antisoma of US$ 100M, and additional milestone fees of up to US$ 850M, if all the agreed milestones are met. There will be additional royalty payments to Antisoma if the drug is eventually marketed.

There will be significant financial return to New Zealand from this agreement. However, the real success here is that the drug will progress to the next step on the long road to registration and availability to patients who might ultimately benefit from it. In addition, it is another affirmation that research into human therapeutics can be conducted successfully in NZ, all the way from the initial design ideas, through subsequent scientific and medical development, to commercial engagement.

FEATURE

# TARGETING TUMOURS

# YOUNG SCIENTISTS ATTACK CANCER

Four young Maurice Wilkins Centre Associate Investigators have combined their scientific talents to create a team that is making exciting progress in the development of the next generation of cancer therapeutics.

Most current cancer chemotherapy treatments lack selectivity for cancer cells and affect healthy cells as well, which causes many side-effects. There is a large global effort towards developing a new generation of drugs, called prodrugs, which are only activated in cancer cells, thereby minimising side-effects. A particular feature of many tumours is that they contain hypoxic areas, where there are few blood vessels and therefore a lack of adequate oxygen supply. These hypoxic regions are often resistant to current radiation and chemotherapy treatments; however they can also be exploited to selectively activate prodrugs into cancer cell killing drugs. This is the basis behind the development of the hypoxia-activated prodrug PR-104 by researchers at the Auckland Cancer Society Research Centre (ACSRC, University of Auckland), led by Professors Bill Denny and Bill Wilson. PR-104 is currently being taken through clinical trials by Proacta Inc.

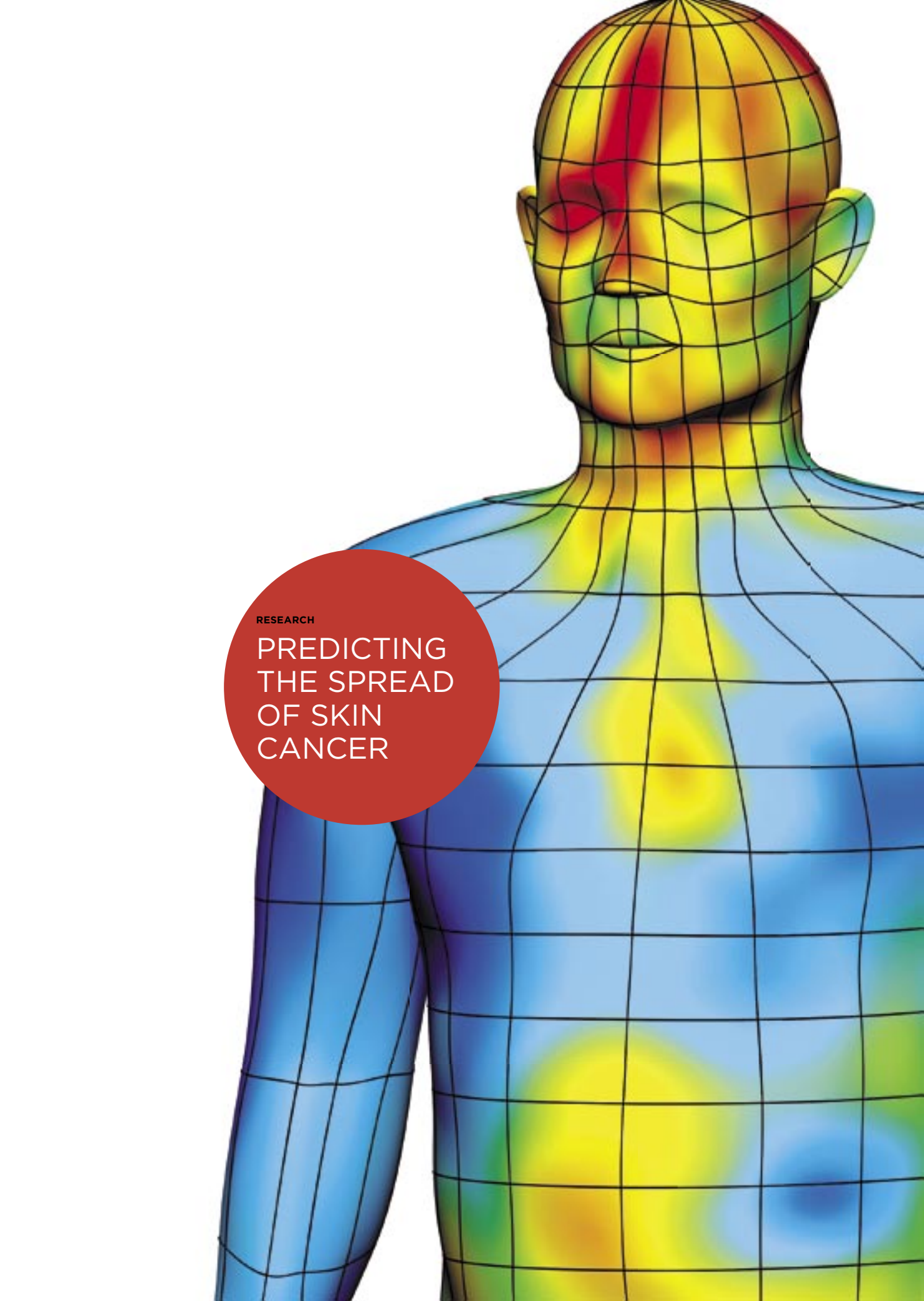
Three members of the ACSRC team, Dr Adam Patterson, Dr Jeff Smaill and Dr Michael Hay are now collaborating with Dr David Ackerley (Victoria University) with the aim of further increasing the efficacy of PR-104 by developing a complementary method of prodrug activation in oxygenated areas of tumours known as Virus Directed Enzyme Prodrug Therapy (VDEPT).

The first step in a VDEPT strategy is to identify bacterial enzymes capable of converting PR-104 to the active drug even in the presence of oxygen. These enzymes will then be modified by a powerful technique called 'directed evolution' to maximise PR-104 activation. An optimised enzyme will then be introduced to tumours using a specially modified virus that is capable of selectively replicating only in tumour cells. When the clinician has confirmed that the virus has only targeted tumour cells, PR-104 can be administered safely. The resulting dual activation of PR-104 by oxygen-inhibited cellular enzymes in hypoxic areas and by bacterial enzymes in virus infected areas of the tumour is anticipated to improve treatment outcome.

The success of this strategy requires a coordinated approach with chemists and biologists working together. Exciting progress is now being made by combining the skills and experience of Dr Smaill and Dr Hay in chemical synthesis, Dr Ackerley in molecular biology and directed evolution of enzymes and Dr Patterson in conditionally replicating viruses and cancer biology, along with their colleagues at the ACSRC and Victoria University[1]. The researchers have recently secured funding for many of the multi-disciplinary aspects of the project from the Health Research Council of New Zealand, the Foundation for Research Science and Technology, the Marsden Fund and the Cancer Society of New Zealand.

1 Singleton D.C., Li D., Bai S. Y., Syddall S.P., Smaill J.B., Shen Y., Denny W. A., Wilson W. R., Patterson A. V. (2007). The nitroreductase prodrug SN 28343 enhances the potency of systemically administered armed oncolytic adenovirus ONYX-411NTR. *Cancer Gene Therapy* 14(12):953-967

**YOUNG SCIENTISTS**
(TOP TO BOTTOM)
DR ADAM PATTERSON
DR JEFF SMAILL
DR MIKE HAY
DR DAVID ACKERLEY



RESEARCH

# PREDICTING THE SPREAD OF SKIN CANCER

# MAPPING MELANOMA

In a world first, Maurice Wilkins Centre PhD student Hayley Reynolds has created 3-dimensional maps of the human body that will help doctors predict where skin cancer is most likely to spread. A paper describing this work has just been published in *Lancet Oncology*[1], one of the world's leading cancer journals, where it inspired both an editorial and cover art based on Hayley's three-dimensional (3D) images. A website[2] has been established to allow doctors and patients to refer to Hayley's maps, and it is already receiving "hits" from around the world. Hayley has also been invited to present her work at an international conference of cancer clinicians in Sydney in February 2008.

**PREDICTING SKIN CANCER**
PHD STUDENT
HAYLEY REYNOLDS

(OPPOSITE) A "HEATMAP" SHOWING THE LIKELIHOOD THAT AN AREA OF SKIN WILL DRAIN TO MORE THAN ONE LYMPH NODE FIELD, WITH RED AREAS BEING HIGHLY LIKELY AND DARK BLUE AREAS BEING HIGHLY UNLIKELY

The project looked at patients with melanoma, the most deadly form of skin cancer. New Zealand has one of the highest rates of melanoma in the world, and early detection and treatment is an important part of managing this disease burden. When patients are diagnosed with a melanoma, doctors often trace where it is likely to spread by injecting the melanoma site with a radioactive tracer. The tracer spreads to the lymph glands, following the same path that cancer cells take when they spread beyond the skin, which allows doctors to check the correct lymph glands for any sign of disease, and schedule further surgery if necessary.

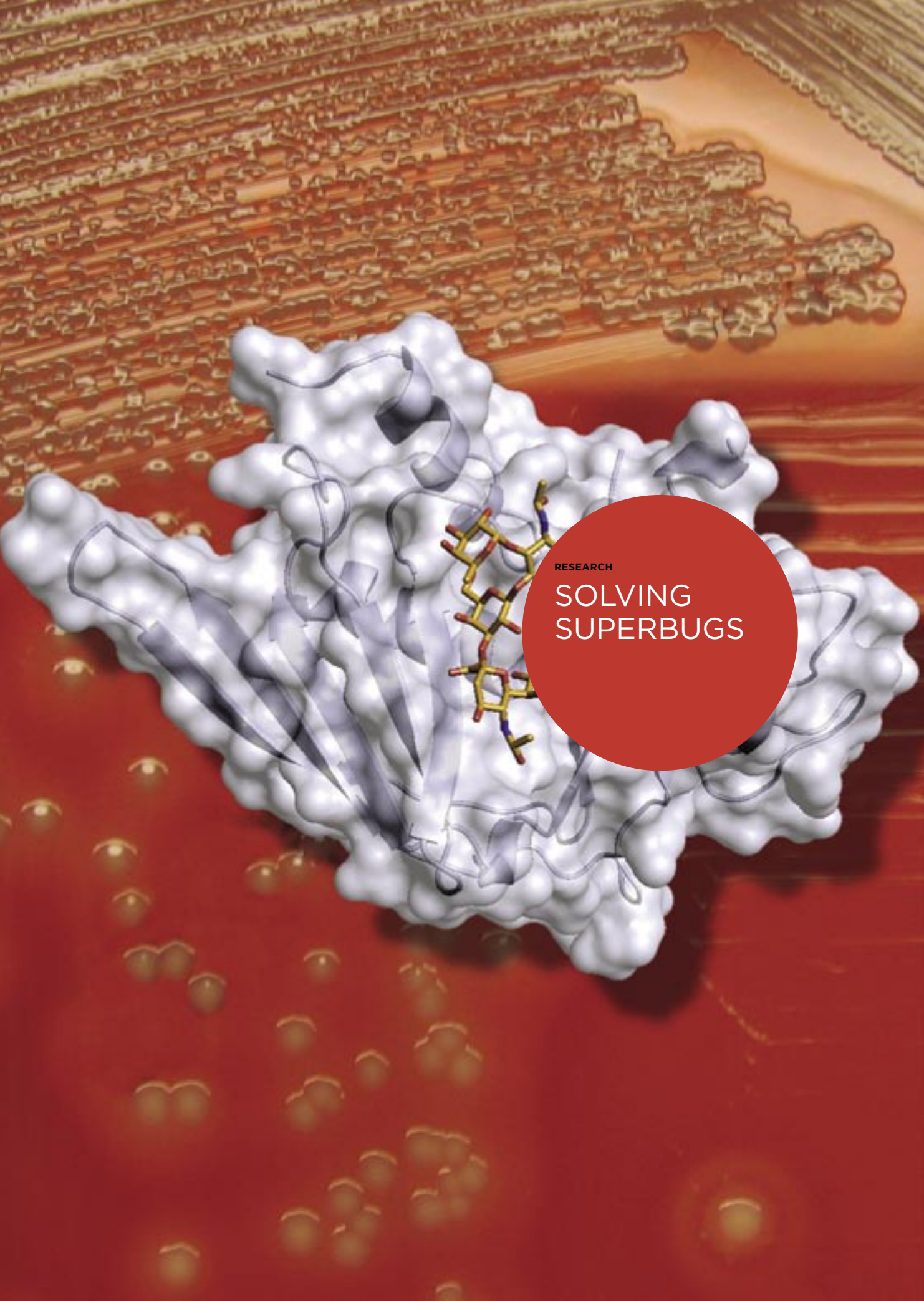
In the *Lancet Oncology* paper, Hayley combined the results of more than 4000 of these procedures (formally called *lymphoscintigraphy*), performed at the Sydney Melanoma Unit. Each procedure involved injection of a different site on the skin (depending on where the melanoma was found in that patient) and tracing the lymph glands that "drained" that skin site. By combining the results of all of these procedures, Hayley built a unique 3D map of human skin, showing which areas are drained by each group of lymph glands. These maps show that earlier models of this "lymphatic drainage" were incorrect. To make this information particularly accessible, Hayley developed an on-line software tool[2] that allows patients and their doctors to click on the area of skin where their melanoma occurred. The software tool then displays the likely lymphatic drainage patterns from that skin site.

Hayley's work reflects a multi-disciplinary approach to advance human health which is enabled by the Wilkins Centre. This approach is personified by the collaboration between her supervisors, Dr Nic Smith and Associate Professor Rod Dunbar. Dr Dunbar, an immunologist with a strong research interest in melanoma, has provided the clinical focus for the unique bioengineering tools and computational models developed by Hayley and Dr Smith.

"The success of this project underlines the potential of computer-based modelling applied to medicine and the importance of collaboration across quantitative and clinical disciplines," say the scientists. "The modern reality is that we are now generating such an avalanche of biological data that we need sophisticated computational tools to make sense of it. Hayley's project is a classic example – she's been able to take a large amount of patient data that was previously very hard to understand, and present it in ways that doctors and patients can use immediately."

1 Reynolds H.M., Dunbar P.R., Uren R.F., Thompson J.F., Smith N.P. (2007) Three dimensional visualisation of lymphatic drainage patterns in patients with cutaneous melanoma. *Lancet Oncology* 8(9):806-812

2 http://www.bioeng.auckland.ac.nz/melanoma



RESEARCH

# SOLVING SUPERBUGS

# INVADING THE IMMUNE SYSTEM

MRSA and similar infections may soon be treatable, as scientists have discovered how the bacterium evades the immune system's first line of defence.

*Staphylococcus aureus* causes a wide range of conditions, from superficial skin infections to life-threatening syndromes including sepsis, toxic shock syndrome, and heart inflammation. Antibiotic-resistant strains are becoming increasingly more common, but the development of an effective therapeutic has been hindered because the bacterium is not well understood.

Scientists at the Maurice Wilkins Centre, along with Australian collaborators, have analysed proteins produced by the bacteria *S. aureus*. The scientists have developed a detailed picture of how *Staphylococcus* avoids recognition by the human immune system, moving one step closer to developing a treatment for *Staphylococcus* infections, particularly those resistant to existing drugs, such as MRSA.

In recent work, PhD student Natasha Willoughby, Professor John Fraser and collaborators led by Drs Bruce Wines and Paul Ramsland (Burnet Institute for Medical Research, Melbourne) have determined the structure of the *S. aureus* protein toxin SSL7 bound to part of the human antibody, IgA.

Prof Fraser comments that "the research has shown in a dramatic 3 Dimensional rendition how a simple bacterial protein called SSL7 binds tightly to IgA; the antibody that coats bacteria in our gut and lung to trigger phagocytes. With SSL7 present, the phagocytes are quite blind to the presence of antibody-coated bacteria, giving the organism enough time to slip past before they're destroyed. The bacteria are then able to infiltrate our tissue and cause infection." This research was published in September in the *Proceedings of the National Academy of Science*[1].

Continuing on the same theme, Matthew Chung, Heather Baker and Indira Basu have shown how two other staphylococcal proteins, SSL5 and SSL11, use a different strategy to attack the immune system. These proteins attach themselves to human sugars on cell surfaces and disrupt the mechanisms the body uses to respond to infection. Again, these studies, one published in *Molecular Microbiology* and the other in the *Journal of Molecular Biology,* show in beautiful atomic-level detail how these processes work.

By understanding the simple but elegant mechanisms used by *S. aureus* to block immune recognition, scientists can develop ways of neutralising proteins like the SSLs to improve human resistance to diseases like MRSA strains that are currently difficult to treat with antibiotics.

The progress that has been made shows the value of combining the skills of scientists both within the Wilkins Centre and with their international collaborators. The research was supported by grants from the National Health and Medical Research Council (NHMRC) of Australia, the Health Research Council of New Zealand and the Maurice Wilkins Centre.

**SOLVING SUPERBUGS**
PROF JOHN FRASER AND PHD STUDENT NATASHA WILLOUGHBY

1 Ramsland P. A., Willoughby N., Trist H.M., Farrugia W., Hogarth P.M., Fraser J.D., and Wines B.D. (2007) Structural basis for evasionof IgA immunity by *Staphylococcus aureus* revealed in the complex of SSL7 with Fc human IgA1. *Proc. Natl. Acad. Sci. USA* 104:15051-15056.

RESEARCH

# NEW CANCER COMPANY

# THE CHEMISTRY TO COMBAT CANCER

Recently a great deal of evidence has accumulated to indicate that an enzyme called PI 3-kinase plays a key role in the development of a range of cancers. This gene is often mutated in tumours and as a result of this PI 3-kinase is considered one of the most promising targets for small molecule based therapies for cancer.

Maurice Wilkins Centre research groups led by Professor Peter Shepherd and Professor Bill Denny have had extensive experience in the area of PI 3-kinase biology and in the development of small molecule kinase inhibitors, respectively. Two years ago it was decided to begin a collaborative project between these two labs within the Wilkins Centre to develop novel inhibitors of PI 3-kinase. This project has been funded by the Wilkins Centre since the inception and a large part of the chemistry effort has been undertaken by Wilkins Centre Associate Investigator, Associate Professor Gordon Rewcastle, together with Dr Jackie Kendall. Wilkins Centre Associate Investigator Professor Bruce Baguley and researcher Dr Claire Chaussade have played a key role in the biological characterisation of the compounds.

**CLOSER LOOK**
(LEFT TO RIGHT)
ASSOC PROF
GORDON REWCASTLE
PROF PETER SHEPHERD
DR JACKIE KENDALL
PROF BILL DENNY
PROF BRUCE BAGULEY
DR CLAIRE CHAUSSADE

The programme has resulted in the development of a range of novel small molecule inhibitors and a particular feature of the work has been the use of structure based design in guiding the chemistry effort. The rapid progress made in the first year of the project resulted in a successful HRC project grant application which has helped to increase the momentum of the research.

The project has reached a stage where it has generated significant novel intellectual property and the focus is now on selecting lead molecules with the aim of developing compounds that can be tested in phase one human clinical trials. This has formed the basis of a new spinout biotech company, to be called Pathway Therapeutics.

While there is obvious commercial potential in the compounds developed in this project, the availability of novel inhibitors of PI 3-kinase has also allowed the group to create a significant body of new knowledge about how PI 3-kinase functions. Some of this was recently published in the *Biochemical Journal*[1].

Overall this project highlights how the Wilkins Centres multidisciplinary approach, here combining chemistry and biology, can rapidly pay dividends, both in terms of benefits for the economy and improvements in health care.

1. Chaussade C., Rewcastle G.W., Kendall J.A., Denny W.A., Cho K., Gronning L.M., Chong M.L., Anagnostou .S, Jackson S.P., Daniele N., Shepherd P.R.(2007) Evidence for functional redundancy of class-IA PI 3-kinase isoforms in insulin signalling. *Biochem J.* 409: 449-458.

NEWS

# RECENT AWARDS & HONOURS

## QUEEN'S BIRTHDAY HONOUR

### Professor Ted Baker

Professor Ted Baker, Director of the Maurice Wilkins Centre, was made a Companion of the New Zealand Order of Merit (CNZM) in June 2007, for services to science. Prof Baker established structural biology in New Zealand with his pioneering work on the proteins actinidin and lactoferrin, and has continued to lead the development of this key technology. He currently heads a group of more than 40 researchers working on the analysis of protein structure

## STUDENT AWARDS

### PhD Student Peter Brown

Maurice Wilkins Centre PhD student, Peter Brown has been given two awards for his research on the protein MIOX, an enzyme that breaks down the sugar inositol and is a potential target for the development of drugs to prevent diabetes.

Peter's PhD involved solving and analysing the structure of MIOX. By understanding this structure, biologists can undertake rational drug design to create a molecule that blocks the activity of MIOX. Based on Peter's structure work, Wilkins Centre scientists are now working with IRL to design such compounds and a selection of these will then be analysed for suitability as a new diabetes drug.

In June Peter was named as runner up in the Advancing Human Health category of the 2007 MacDiarmid Young Scientist of the Year Awards. These prestigious awards, presented by the Foundation for Research, Science and Technology, recognise excellence and the innovative spirit of New Zealand's top young researchers.

At the Wilkins Centre Symposium in August, Peter was also named as the inaugural winner of the Maurice Wilkins Centre Prize for the 'Best Interdisciplinary Paper' for a paper published in the journal *PNAS* on the MIOX research.

**Brown, P. M.**, Caradoc-Davies, T. T., Dickson, J. M., Cooper, G. J. S., Loomes, K. M. and Baker, E. N. (2006). Crystal structure of a substrate complex of myo-inositol oxygenase, a novel di-iron oxygenase with a key role in inositol metabolism. *Proc. Natl. Acad. Sci. USA* 103: 15032-15037.

## 2007 HATHERTON AWARD

### Dr Celia Webby

The 2007 Hatherton Award, presented by the Royal Society of New Zealand, for the best scientific paper by a PhD student at any New Zealand university in physical sciences, earth sciences, and mathematical and information sciences has been awarded to Dr Celia Webby, formerly of Massey University and now of Oxford University. In 2005, Ceila and co-authors published a paper in the prestigious journal, the *Journal of Molecular Biology*, on the structure and function of an enzyme from the Mycobacterium tuberculosis. Dr Webby carried out her PhD under the supervision of Assoc Prof Emily Parker and travelled to Auckland many times during the course of her PhD to make use of Maurice Wilkins Centre equipment and resources. The Wilkins Centre also provided partial financial support for Celia's PhD research.

**Webby, C.J.**, Baker, H.M., Lott, J.S., Baker, E.N. and Parker, E.J. (2005). The structure of 3-deoxy-D-arabino-heptulosonate synthase from *Mycobacterium tuberculosis* reveals a common catalytic scaffold and ancestry for Type I and Type II enzymes. *J. Mol. Biol.* 354: 927-939.

## INTERNATIONAL EDITORIAL ROLE

### Professor Peter Shepherd

Professor Peter Shepherd has been appointed Editor in Chief of the *Biochemical* Journal. This highly respected London based journal is the official journal of the British Biochemical Society. It has been publishing for 101 years and Peter will be the first editor in chief from outside the UK. The part time role will involve some travel to London but due to the wonders of modern communication most of the work involved can now be performed over the internet.

NEWS

# SCIENTIFIC NETWORKING AND EVENTS

## 2007 MAURICE WILKINS LECTURE

### Professor Sir John Walker

Professor Sir John Walker was the Nobel Prize winner for Chemistry in 1997, with Paul Boyer, for their work in understanding the mechanisms of ATP synthesis. Since then, Prof Walker has extended our knowledge of how cells convert sunlight, carbohydrates, fats or proteins into energy for biological processes. This work was summarised during the 2007 Maurice Wilkins Lecture, the finale of the Maurice Wilkins Centre Annual Symposium. Prof Walker showed that even with the huge amount of work that has been done to date, there is still an incomplete picture of the complex mechanism of energy conversion. Prof Walker, along with numerous collaborators, will continue trying to answer the questions as they arise.

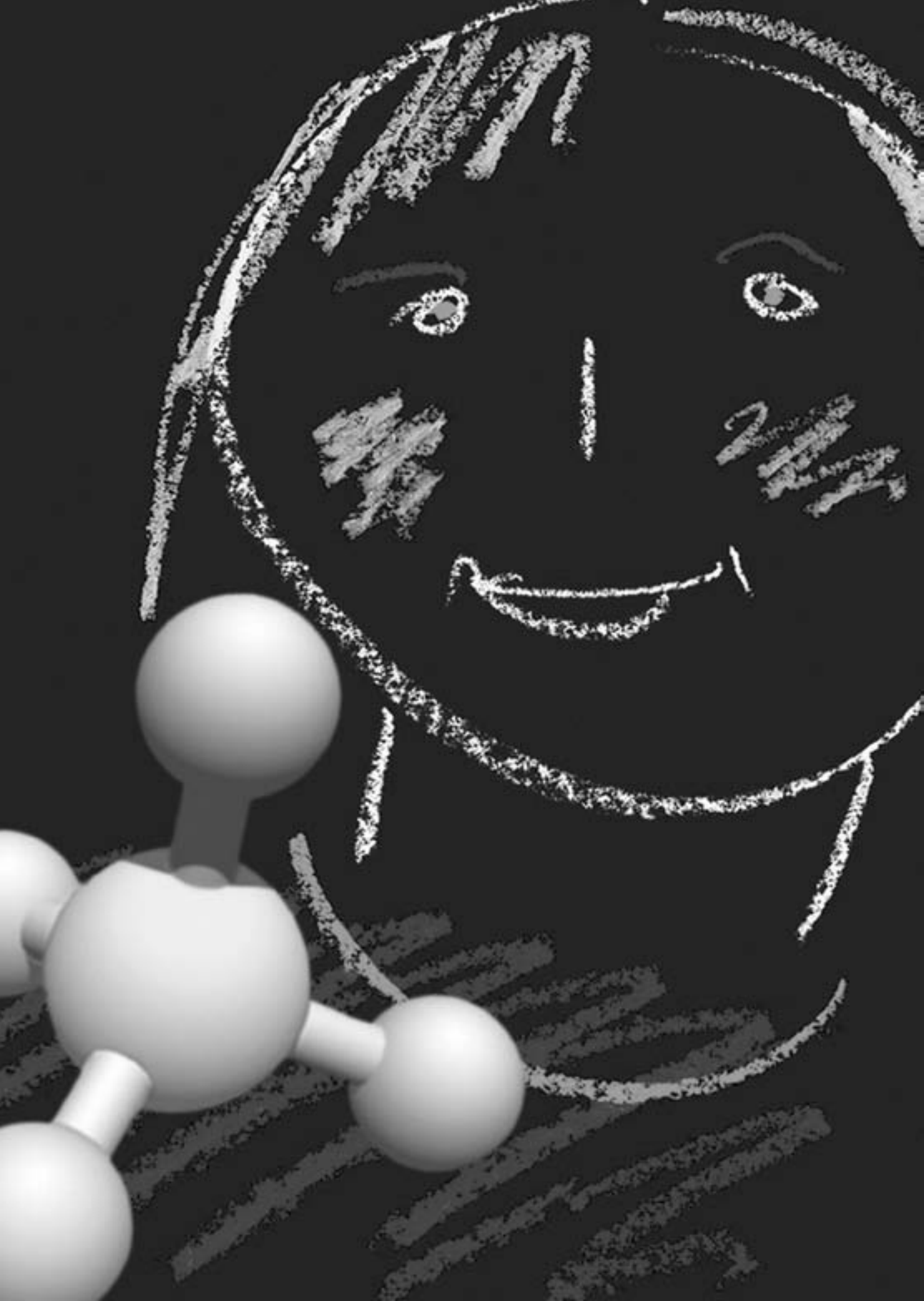
Prof Sir John Walker is Director of the MRC Dunn Human Nutrition Unit in Cambridge, UK. During his visit to New Zealand, he also gave the EMBO Lecture at the Queenstown Molecular Biology Conference.

## MAURICE WILKINS CENTRE SEMINAR

### Professor Jack Strominger

Professor Jack Strominger MD, is the Higgins Professor of Biochemistry, Harvard University. In October 2007 it was 20 years since the structure of the Major Histocompatability Complex antigen A2 was published by Pamela Bjorkman, then a graduate student with Jack Strominger and Don Wiley at Harvard. To celebrate this major event in science, the Maurice Wilkins Centre was delighted to have Prof Jack Strominger visit New Zealand and present a special seminar on the history and recent work around MHC and MHC targeted therapy.

Prof Strominger has had a remarkable science career spanning over five decades. He has published more than 1000 papers on subjects ranging from bacterial cell wall synthesis and the mechanism of penicillin, to the biochemistry, structure, function and genetics of immune recognition. He is one of the world's most respected scientists and his contribution to science training is without parallel. He is the recipient of 30 major international awards inrecognition of his discoveries.



## MOLECULES AND ME

In July, the Maurice Wilkins Centre joined with other members of the Faculty of Science, to promote science to school children as part of 'Incredible Science'.

The Wilkins Centre display, called 'Molecules and Me' was designed to help children and their families understand why DNA, proteins and cells are important for all living organisms. Potential future scientists especially enjoyed looking at their own epithelial cells under the microscope, aided by some food colouring, and Wilkins Centre research staff and students.

The display was very successful, with several hundreds of children and caregivers taking part.

'Incredible Science' is an annual one-day event, held by the Faculty of Science at the University of Auckland. It is aimed at primary and intermediate aged children along with their families and teachers and is a fun, free day of interactive activities, lectures and shows highlighting the fun and diversity that science offers.

## MAURICE WILKINS CENTRE SYMPOSIUM

The 2007 Maurice Wilkins Centre Symposium was held in Auckland on the 23rd August. This year's symposium was attended by a record 180 registrants with a significant number of Wilkins Centre Associate Investigators from outside Auckland also attending. The first half of the symposium reviewed some of the recent highlights from the Wilkins Centre research portfolio. There were several excellent presentations given by PhD students and Research Fellows that show-classed the excellent science being carried out by Wilkins Centre researchers.

The afternoon sessions were focused on looking to the future of the Wilkins Centre, learning more about the research interests and specific capabilities of investigators and how future collaborations could be built within the Wilkins Centre.

The symposium provided an excellent opportunity for Wilkins Centre investigators and research staff and students to network. The final event of the day was the 2007 Maurice Wilkins Lecture, given by Prof Sir John Walker.

## PROTEOMICS SYMPOSIUM

In March the Maurice Wilkins Centre ran a Proteomics Symposium that was attended by 70 participants in Auckland and, broadcast to Waikato, Victoria and Canterbury Universities over the KAREN network. The focus of the symposium was to inform researchers from a diverse range of scientific backgrounds about both the current and new technologies available through The Centre for Genomic and Proteomics at The University of Auckland.

## WILKINS SUPPORTS MEETINGS & AWARDS

In 2007 Maurice the Wilkins Centre has continued to provide support for international and national scientific meetings held in New Zealand. The Queenstown Molecular Biology meeting continues to be a very successful international meeting and the Wilkins Centre once again provided significant financial support for this meeting held in August 2007. The Wilkins Centre is a major sponsor of the 2007 MedSci Congress, also held in Queenstown, at the end of November.

The Wilkins Centre also provides support for smaller local scientific meetings and symposia, such as Crosstalk and the annual Auckland Neurological Network (ANN) meeting, held at Leigh Marine Laboratory. The 2007 ANN meeting was held in May and attended by 100 research staff and students from the Auckland region. Crosstalk is a young researcher led interdisciplinary forum to facilitate inter-actions between researchers involved in the broad area of signal transduction in Auckland, with the aim of providing an avenue for the exchange of ideas, reagents and expertise. In 2007 the Wilkins Centre provided financial support for Crosstalk to run seminars and a one-day Signal Transduction Symposium.

NEWS

# RESEARCH FUNDING UPDATE

## FRST FUNDING FOR CANCER RESEARCH

In July Maurice Wilkins Centre Investigators at the Auckland Cancer Society Research Centre were successful in gaining funding for four years from the Foundation for Research, Science and Technology to develop two new classes of pro-drugs to fight cancer. The focus will be on targeting cells in malignant solid tumours that are starved of oxygen (hypoxic) and how this can be exploited to treat the tumour without harming healthy cells **Dr Moana Tercel**, **Dr Adam Patterson**, **Dr Jeff Smaill**, Dr Frederik Pruijn, **Prof William Wilson**, **Prof William Denny** (Auckland Cancer Society Research Centre, The University of Auckland). *'Exploiting Tumour Hypoxia in Cancer Treatment.'*

## HRC FUNDS COLLABORATIVE RESEARCH

The results of the 2007 HRC funding round once again showed the value of the Maurice Wilkins Centre support for developing projects. A three year grant was awarded for the project *'Targeting vaccines to human antigen-presenting cells with synthetic glycopeptides.'* This project is a collaboration between three Wilkins Centre research groups and involves **Assoc Prof Rod Dunbar**, **Prof Margaret Brimble**, **Prof Ted Baker**, Dr Chris Squire, Dr Catherine Angel and Dr Paul Harris. The Wilkins Centre has provided significant support for this project over the last two years, along with other funding sources, to develop it to the point where it has been successful in securing competitive funding.

Several other Wilkins Centre associated investigators were also successful in obtaining funding:

- Assoc Prof Robert Anderson, **Prof William Denny** and Dr Sujata Shinde (Department of Chemistry and Auckland Cancer Society Research Centre, The University of Auckland) to study *'Free radical studies and disease.'*
- **Assoc Prof Vickery Arcus**, Dr Ray Cursons (Biological Sciences, University of Waikato), Dr Noel Karalus (Waikato Hospital), **Assoc Prof Greg Cook** (Microbiology, University of Otago) and Prof Kenn Gerdes (Newcastle University, UK) to study *'The role of the toxin-antitoxin repertoire in pathogen survival and persistence.'*
- **Prof William Denny**, Mr Graham Atwell, Dr Kevin Hicks, **Dr Adam Patterson**, **Dr Jeff Smaill**, **Prof William Wilson**, Dr Christopher Guise, Dr Raphael Frederick (Auckland Cancer Society Research Centre, The University of Auckland) and **Dr David Ackerley** (Biological Sciences, Victoria University) to study *'Dual activation of anticancer prodrugs by hypoxia and reductase-armed adenovirus.'*
- **Prof Peter Shepherd** (Dept Molecular Medicine and Pathology, The University of Auckland) and **Assoc Prof David Greenwood** (HortResearch/ School of Biological Sciences, The University of Auckland) to study *'A new role for beta-catenin as a sensor for changes in glucose levels.'*
- **Prof William Wilson**, Dr Kevin Hicks, **Dr Adam Patterson**, **Prof William Denny** (Auckland Cancer Society Research Centre, The University of Auckland) to study *'Pharmacokinetics and pharmacodynamics of the hypoxia-activated prodrug PR-104 plasticity.'*
- **Prof Franca Ronchese**, **Dr Thomas Backstrom** and **Prof Graham Le Gros** (Malaghan Institute of Medical Research) to study *'Manipulating antigen presentation to control disease.'*

## 2007 MARSDEN GRANTS

Several Maurice Wilkins Centre associated scientists were award Marsden grants in the 2007 funding round. This year the competition was as tough as ever and from 910 initial proposals, 93 projects were funded. **Prof Margaret Brimble**, a Wilkins Centre Principal Investigator, received a three year grant to carry out work *'Using molecules from metal enriched mines for new medicines'*.

Also awarded three year grants were Wilkins Centre Associate Investigators, **Dr Andrew Dingley** (Chemistry, University of Auckland) *'Characterising the molecular and structural mechanism of antimicrobial pore-forming toxins'*, **Assoc Prof Emily Parker** (Chemistry, University of Auckland) *'Evolving enzymes: deciphering the evolutionary relationships in a family of crucial biosynthetic aldolases'* and **Dr David Ackerley** (Biological Sciences, Victoria University) together with **Drs Michael Hay** and **Adam Patterson** (ACSRC, University of Auckland) *'New and improved: anti-cancer enzymes from bacteria'*. Congratulations to you all!

## GLOBAL FUNDING FOR TB WORK

The Global Alliance for TB has approved an extension for a futher year of the project on the development of analogues of the clinical TB drug PA-824, being carried out by Maurice Wilkins Centre associated scientists at the Auckland Cancer Society Research Centre. This project is detailed on their website (see http://www.tballiance.org/new/portfolio.php). It follows a visit to the research centre in June by Dr Mel Spigelman, Director of Research and Development for the Global Alliance for TB in New York, Dr Zhenkun Ma, who is their Head of Drug Development, and Prof Scott Franzblau from the Institute for Tuberculosis Research, University of Illinois.

## CANCER SOCIETY FUNDING

Three Maurice Wilkins Centre Associate Investigators were awarded grants from the Cancer Society of New Zealand in June. **Dr Ian Hermans** (Malaghan Institute of Medical Research) was awarded three years funding to investigate a new treatment for recurrent glioblastoma, the most commom brain cancer in adults. **Dr David Ackerley** (Biological Sciences, Victoria University) and **Dr Adam Patterson** (ACSRC, University of Auckland) were also awarded three years funding to identify new enzymes that could be useful in anti-cancer gene therapy.

## WILKINS SECURES CORE FUNDING

It was announced in June that an additional six years of Centres of Research Excellence funding was awarded to the Maurice Wilkins Centre. The continued funding will allow the Wilkins Centre to further build New Zealand's strength in biotechnology and medicine and develop new collaborations both in New Zealand and internationally.

The funding will be used to support a number of lead projects in the Wilkins Centre research portfolio and the strong infrastructure for research that the Wilkins Centre has built up since its establishment for the benefit of researchers from both Universities and Crown Research Institutes across New Zealand. In addition, a major goal for the future is to provide all our associated investigators with the opportunity to develop their own innovative multidisciplinary ideas and projects. By offering support and independence for younger scientists, we hope to inspire our researchers and provide them with a strong environment in which to develop careers in New Zealand.

MAURICE WILKINS CENTRE FOR MOLECULAR BIODISCOVERY

LEVEL 4, THOMAS BUILDING
3A SYMONDS ST, AUCKLAND
**PHONE** +64 9 373 7599 **EXT.** 85533 **FAX** +64 9 373 7414
THE UNIVERSITY OF AUCKLAND, PRIVATE BAG 92019
AUCKLAND MAIL CENTRE, AUCKLAND 1142, NEW ZEALAND

WWW.MAURICEWILKINSCENTRE.ORG