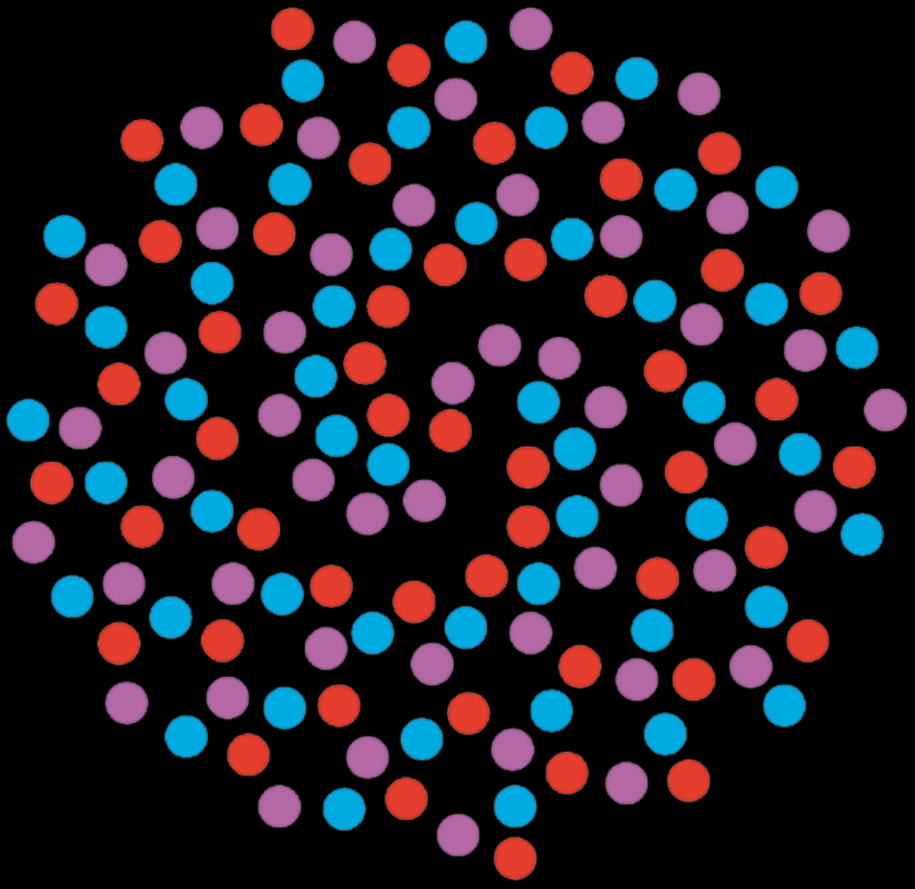

MAURICE WILKINS CENTRE

New Zealand's Centre of Research Excellence
targeting human disease

Annual Report 2016

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 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. At the end of 2016 it comprised 171 investigators throughout the country, and over 200 early-career affiliates, linking researchers from six Universities, three Crown Research Institutes and one private research institute. These investigators represent most of New Zealand's 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 national 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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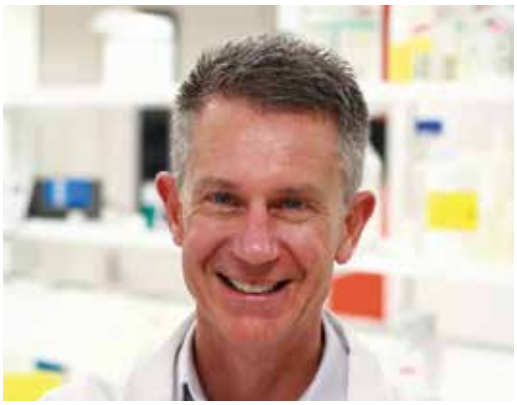
MAURICE WILKINS CENTRE
FOR MOLECULAR BIODISCOVERY

Director's Report



In November 2016, the Maurice Wilkins Centre welcomed its international Scientific Advisory Board to review progress. The SAB's report commends not only the Centre's continued "outstanding" research and fostering of new talent, but also its strong sense of focus. This focus is also evident in this year's Annual Report where it's obvious that much of the Centre's resource is converging on particular areas where our teams of investigators know they are likely to have impact on health.

In particular, immune therapy of cancer is emerging as a strong focus. This has not just been driven by those of us who work in this field. Many other investigators working in cancer biology and drug chemistry have recognised that the results from immunotherapy clinical trials are so strong that the most rapid improvements in patient care are likely to come from this field. The government's release of new funding to Pharmac (NZ's drug funding agency) to enable the new anti-PD1 drugs for melanoma to be funded from 2016 – a decision that the MWC openly advocated for – was also recognition of the unprecedented impact on patient care being achieved by immune therapy.

For MWC investigators, this recognition of the impact of immune therapy has provided the opportunity to pivot their research programmes towards accelerating its advance. As reported in the Highlights stories, our cancer drug designers have begun to target molecules on immune cells as well as cancer cells, and have patented a series of new molecules with major potential to modulate the immune system. Similarly, the realisation that low oxygen ("hypoxia") within tumours inhibits immune responses against cancer cells has led to a very exciting new programme that combines the MWC's expertise in hypoxia-activated pro-drugs with its deep experience in cancer vaccines. And our genomic and bioinformatics specialists are increasingly focused on questions of the interactions between cancer cells and the immune system, examining "immune signatures" alongside their multi-dimensional studies of cancer genomes. All of these subtle shifts in orientation underscore the Centre's ability to bring together large national multi-disciplinary teams to respond to new opportunities, and to focus NZ's biomedical research capability on areas where it can achieve the largest potential impact on health.

Of course none of this work happens in isolation, so the international connectivity we report here is not only pleasing but essential. This activity spans invited visits from international experts to collaboration with international pharmaceutical and biotech companies that is already delivering new clinical trials that NZ patients can access. In that context it's worth highlighting the excellent global reputation NZ enjoys for its early phase clinical trials

expertise, that continues to bring international partners here. However, looking to the opportunities ahead, it's obvious that substantial barriers to clinical trials still persist within our health system, so we would encourage the Ministry of Health to work on enabling many more clinical trials in NZ. Apart from benefiting patients by increasing their access to novel therapies, increasing clinical trial activity is well documented internationally as a route to lifting the overall quality of health service delivery. So a central commitment to increasing clinical trials activity across NZ, plus leadership mandates for DHBs to carry out this policy, would seem to be a "no brainer".

My own perspective on 2016 has partly been shaped by the launch of two new start-up companies, as detailed on page 9. For academic scientists, the commercial world can often seem daunting, but in biomedicine, facing the challenges of research commercialisation is a necessary part of translating your research through to clinical practice. Clinical trials are expensive, and with very few exceptions, clinical trials require private investment. MWC investigators are now quite familiar with all the routes to obtaining this investment, ably assisted by the technology transfer offices of its partner institutions.

Our lab's first start-up, SapVax LLC (sapvaxllc.com) was co-founded with Margaret Brimble's outstanding medicinal chemistry team, and has been funded from and incorporated in the USA. Previous drug development companies spun out by other MWC investigators, such as ProActa (founded by Profs Bill Denny and Bill Wilson) and Pathway Therapeutics (Profs Bill Denny and Peter Shepherd), had also been incorporated in the USA. A US base holds many advantages, from ready access to capital to fund future development, to the availability of world-leading expertise such as regulatory advice in designing and executing clinical trials. To date the experience of working with SapVax's US partners has been excellent, and it's exciting to see how the expertise they bring to bear on the project is blazing a trail direct to the clinic.

Our lab's second start-up, Upside Biotechnologies (upside.nz), was co-founded by our own post-doctoral research fellow Dr Vaughan Feisst, and has been funded almost entirely from New Zealand. While there are plenty of precedents for local funding of NZ biomedical technology, I encountered a new level of enthusiasm from the NZ investment community in backing this particular slice of home-cooked biotech. In most cases I've found this enthusiasm is not only based on a sanguine assessment of the risk/reward ratio, but also a genuine desire to be part of the story of a great new kiwi start-up. The "angel investor" community has been particularly welcoming – a wonderful network of seasoned professionals who seem to have at heart the country's need to build new engines of economic growth. So as the portfolio of projects nurtured by the Maurice Wilkins Centre matures, we intend to ensure that investors throughout New Zealand get the opportunity to back these projects. As with other high technology sectors, we see tremendous synergies working with local capital and business expertise to spin out our science into fast-growing companies, and look forward to many exciting new partnerships.

The wider investment environment is also encouraging. In 2016 the Inventors' Fund was launched by the University of Auckland's commercialisation company, Auckland UniServices. This $20M fund allows the university to invest directly in companies founded by academics and students, and has undoubtedly accelerated overall start-up activity at the university (11 start-up companies in 2016 compared with 3 in 2015). And the NZ government's contribution to the Medical Research Commercialisation Fund in Australia has opened up a deep new source of capital to take our most promising projects through into the clinic. We welcome these very progressive steps in enabling more investment into advancing MWC projects into the clinic, and look forward to the advent of other similar initiatives from other NZ institutions.

Of course one might still ask: why are academics concerned at all with investment and start-ups – isn't your job just to carry out excellent science? At the MWC we still maintain the primacy of excellent research. Breakthroughs in medicine still depend on outstanding science carried out by investigators who are driven to discover the fundamental nature of our beings. But for many of us, the reason we chose biomedicine as a field was the desire to use our science to change the fates of the human body – to learn how to manipulate our biology so we can lead healthier longer lives. So it's now routine within the MWC for investigators to overtly chart a path from the discoveries they seek to their ultimate goal of impact on health – whether that impact is proximate enough to contemplate a clinical trial or potentially decades from fruition. For many of us, research commercialisation is part of that journey to clinical impact, and learning to navigate the route from the bench to the clinic becomes an essential skillset. If these forays into the commercial domain bring with them the potential for economic growth – and especially the generation of new private sector jobs for our outstanding graduate students – then all the better. Indeed, exposing many of our graduates to the private sector through research commercialisation will help them transform the landscape of New Zealand biomedicine in the future.

None of this is possible without excellent people, and our researchers at all career stages remain at the core of everything the MWC sets out to achieve. Once again I salute my outstanding colleagues whose achievements are celebrated in these pages. Without their commitment to excellence in their fields, and their well-honed willingness to share their skills and expertise across our national network, we would not be able to achieve our scientific goals at their current scale. And of course the Centre simply would not function without our Research Operations Manager Rochelle Ramsay and her outstanding administrative team, supported by our highly constructive and efficient Board. Our sincere thanks are due to Rochelle and her colleagues for enabling MWC to achieve its increasingly ambitious goals year on year.

Rod Dunbar

Director

Mission and Strategic Outcomes

Mission

The Maurice Wilkins Centre will target major diseases affecting New Zealanders, particularly cancer, diabetes and infectious disease, by delivering world-class research that enables the discovery of new therapies, diagnostics and vaccines.

Strategic outcomes

MWC will fulfil its mission through the generation and translation of new scientific knowledge, training and outreach initiatives that will achieve:

1. Contributions to improved health and well-being of New Zealanders, and the global population, through clinically relevant world-class research
2. Contributions to the New Zealand economy through discovery of new therapies, diagnostics and vaccines and the development of new technology
3. Contributions to increased innovation across the New Zealand biomedical sector, by fostering inter-disciplinary and inter-institutional collaborations, and engagement with clinical researchers
4. A cohort of young scientists who are trained to contribute to scientific innovation and have skills valued by future employers
5. Enhanced scientific partnerships between New Zealand and other nations that leads to increased opportunities for New Zealand researchers
6. Contributions towards a greater understanding of biomedical science in the New Zealand community.

Distinguished Professor Bill Denny was inducted into the Hall of Fame of the American Chemical Society's Division of Medicinal Chemistry.

Image courtesy of Bill Denny

Highlights

Standouts on the science stage

In 2016, Maurice Wilkins Centre investigators received a number of national and international honours in recognition of their services to science.

Distinguished Professor Bill Denny was inducted into the Hall of Fame of the American Chemical Society's Division of Medicinal Chemistry. Bill is a principal investigator of the Maurice Wilkins Centre and Director of the Auckland Cancer Society Research Centre (ACSRC), and has spent more than 40 years successfully developing anti-cancer drugs. Under his leadership, the ACSRC has to date brought 12 drugs to clinical trial. Hall of Fame inductees are nominated by their peers in recognition of outstanding contributions to medicinal chemistry through research, teaching and service. Bill is the first New Zealander, and one of a very small number of non-Americans, to receive the accolade.

Distinguished Professor Ted Baker, an emeritus principal investigator, was awarded the Lawrence Bragg Medal from the Society of Crystallographers in Australia and New Zealand. The Bragg medal is the premier award of the SCANZ and honours the awardee's "distinguished contributions to science involving X-ray, neutron or electron diffractions and/or imaging" for work done primarily in Australia or New Zealand.

A number of Maurice Wilkins Centre investigators also received national honours throughout 2016. Professor Tony Merriman, Deputy Director Peter Shepherd and Director Rod Dunbar were elected as Fellows to the Royal Society of New Zealand – an honour recognising their international reputations in research and scholarship.

Principal Investigator Antony Braithwaite from the University of Otago received the Shorland Medal from the New Zealand Association of Scientists (NZAS). The medal acknowledges major and continued research that has significantly contributed to an understanding of cancer biology. Antony received the award in recognition of his work on the tumour suppressor protein p53 and other cancer associated genes.

Distinguished Professor Margaret Brimble was also honoured by the NZAS when she received the Marsden Medal for her lifetime of outstanding service to science. Margaret, a principal investigator with the Maurice Wilkins Centre, has conducted research that has led to numerous discoveries, including a new synthetic peptide drug she has developed with potential to treat the genetic disorders Rett syndrome and Fragile X syndrome.

Associate Investigator Dr Siouxsie Wiles also received national recognition when she was named a Blake Leader 2016 from the Sir Peter Blake Trust. The Blake Leader Award recognises inspirational leaders who have determination, a will to succeed and a belief in achieving extraordinary things. Dr Wiles is a microbiologist who uses bioluminescence to study infectious disease, and is also a renowned science communicator, with a regular slot on Radio NZ's Nine to Noon programme.

Maurice Wilkins Centre research attracted the support of local and international investors, leading to the establishment of three spin-outs companies.

Home-grown research attracts high investor interest

Home-grown, high-tech health research from the Maurice Wilkins Centre has attracted support from local and international investors, leading to three spin-out companies in as many months. Investors have recognised not only attractive investment opportunities in the Centre's science, but also major potential to benefit patients in New Zealand and overseas.

The first spin-out company, SapVax LLC (sapvaxllc.com), was established in the US in a partnership between drug development accelerator BioMotiv and the University of Auckland.

The new company is advancing a novel immune therapy for cancer developed at the Maurice Wilkins Centre in a long-standing collaboration between Professor Rod Dunbar's immunology group and the medicinal chemistry team led by Distinguished Professor Margaret Brimble and Dr Geoff Williams. The new company is working to progress its first product, a vaccine to stimulate cancer-killing T cells, into clinical development in a targeted subset of cancer patients. SapVax will make use of clinical trial resources available in New Zealand as well as the team's own clinical-grade laboratory – a facility that has already been used to manufacture vaccine components currently in clinical trial in partnership with the Malaghan Institute.

Professor Dunbar is also a founder of a second start-up company, Upside Biotechnologies (upside.nz), this time funded by $2.3M raised almost entirely from New Zealand investors. Upside Biotechnologies is growing human skin in the laboratory to replace skin lost in severe burns. Professor Dunbar and Affiliate Investigator Dr Vaughan Feisst have been developing the new regenerative medicine technology for five years, with support from the Maurice Wilkins Centre, the University of Auckland and the charity Cure Kids. The project was an unexpected spin-off from the cancer vaccine project. The team had been studying immune cells purified from human skin to improve vaccine targeting, and consulted colleagues in plastic surgery about potential uses for the other skin cells. They have subsequently developed a unique method that enables a sample of a patient's unburnt skin to be rapidly grown into large areas of full thickness skin for use in skin grafts.

A third company, Convert Pharmaceuticals (convertpharma.com), has been incorporated in Belgium to take a new cancer drug into clinical trials. The drug CP-506 was discovered by the Translational Therapeutics Team in the Auckland Cancer Society Research Centre, led by Associate Professor Adam Patterson and Dr Jeff Smaill. CP-506 is a cytotoxic 'prodrug' that is activated only in low oxygen environments such as those found in tumours. The new company is currently carrying out final pre-clinical studies and production of the drug for clinical trials, with Phase 1 trials anticipated to commence in Europe at the end of 2017.

"We're all absolutely delighted to see investors helping to take our discoveries forward into clinical trials," says Rod. "We're especially pleased to see local investors showing such confidence and excitement in New Zealand science."

"The Maurice Wilkins Centre is aiming to bring a portfolio of exciting medical opportunities to the local investment community over the next few years, and this should lead to even more clinical trials of treatments invented here being made available to New Zealand patients."

A team of Maurice Wilkins Centre researchers has determined the structure of an enzyme target for new anti-TB therapies. L-r: Dr Ghader Bashiri, Mr Ehab Jirqis, Dr Jodie Johnston, Ms Laura Nigon.

Image courtesy of Jodie Johnston

MenD-ing TB: early career researchers zoom in on important drug target

An estimated 1.3 million people die from tuberculosis (TB) each year, and new drugs are desperately needed, especially as resistance to existing drugs increases. In a world-first, a team of Maurice Wilkins Centre researchers has determined the structure of an enzyme that is an important target for development of new antibiotics to fight TB.

"It was just beautiful to see - I recall standing there thinking, this is amazing and exactly why I am doing science." That's how Dr Jodie Johnston describes the moment she and a team of fellow Maurice Wilkins Centre investigators managed to capture and visualise the changing structures of the enzyme as it does its job.

The enzyme, called MenD, plays a critical role in the production pathway of vitamin K, also known as menaquinone. Vitamin K is essential to the survival of the *Mycobacterium tuberculosis* bacterium responsible for TB.

"MenD sits at the start of a pathway of enzymes that help make Vitamin K, and is therefore an important drug target for treating TB," explains Jodie.

The MenD enzyme makes several intermediate molecules on its way to producing Vitamin K, Jodie continues. Together with her colleagues Dr Ghader Bashiri, Dr Esther Bulloch, Ehab Jirgis and Distinguished Professor Ted Baker, she used X-ray crystallography to "see" the 3-D structure of the MenD enzyme as it was bound to key intermediates. Ghader comments that "Capturing reaction intermediates in enzymatic reactions is not trivial. A combination of factors, including elaborate generation of an unstable substrate, and a slow enzyme – and of course perseverance and a bit of luck – led us to visualize two intermediates in our crystal structures."

The team's work appeared on the front cover of the *Structure* journal last year. Understanding the structure of MenD now opens up new possibilities in developing drugs that could kill the *Mycobacterium tuberculosis* bacterium even when it's not growing. Finding new TB treatments is the focus of one of the Maurice Wilkins Centre's Flagship Research Programmes, so a large team of researchers around the country is now poring over these results.

The research also led to a prestigious 2016 Marsden Fund grant for Jodie, Ghader, Esther and fellow Maurice Wilkins Centre investigator Dr Wanting Jiao, all of whom are at early stages in their research careers. During their investigation of MenD's structure, the team discovered that the enzyme only has two of its four active sites working at any one time. They also found that the enzyme had a regulatory site distant from the active site and captured a regulatory molecule bound in a molecular structure. The discovery has led the team to hypothesise that the control of the enzyme and its active sites assists the TB bacterium in "hiding out" in a latent state evading the body's immune defences.

The team is now using the Marsden grant to understand how the enzyme is able to turn its active sites on and off. Their research may also provide insight into a fundamental process known as protein cooperativity where molecules bind to a protein and alter the protein's activity at other binding sites – potentially allowing organisms to adapt to environmental changes.

Professor Peter Shepherd (pictured) is collaborating with several Maurice Wilkins Centre investigators on the development of a novel compound for potential use in cancer immunotherapy.

Image courtesy of Billy Wong

Chemistry, biology and immunology combine to target an immune receptor

A Maurice Wilkins Centre collaboration across several scientific disciplines has led to a patent for a new immunotherapy drug.

Maurice Wilkins Centre investigators have been collaborating to target a molecule on immune cells ("CSF1R") that can slow down the immune system's attack on cancer.

"The immune system's response against a tumour involves complex interactions between many different immune cells," explains Professor Peter Shepherd, Deputy Director of the Maurice Wilkins Centre.

While white blood cells called T cells can attack and kill cancer cells, says Peter, a second type of white blood cells called macrophages can slow the T cells down.

"CSF1R is a receptor located on the surface of macrophages, and it's crucial to the development and function of macrophages. By inhibiting CSF1R we can stop the macrophages in tumours from blocking the T cells, thereby enabling T cells to kill the cancer cells."

Peter collaborated with chemist Distinguished Professor Bill Denny from the Auckland Cancer Society Research Centre, and immunologists Professor Rod Dunbar from the University of Auckland and Professor Ian Hermans from the Malaghan Institute of Medical Research to develop a unique series of chemicals that target CSF1R's enzyme activity. Other Maurice Wilkins Centre investigators involved in the project include Jack Flanagan, Gordon Rewcastle, Stephen Jamieson and Christina Buchanan.

Peter says the ability of the Maurice Wilkins Centre to bring together the country's best biomedical scientists has enabled the research to advance rapidly: "The Centre specialises in bringing together powerful teams to tackle major projects, in this case enabling the cancer biologists and chemists to work directly with immunologists."

Rod agrees: "To date much of our immune therapy work has focused on vaccines. It's exciting to see how we can apply New Zealand's small molecule capabilities to help accelerate immune therapy for cancer."

The next stage for the researchers is to understand how this new class of drugs perform in animal models of cancer, and how they will affect macrophages in those contexts. From there the team hopes to find candidates that can go into clinical development.

"The Maurice Wilkins Centre has been involved in the development of 'molecularly-targeted' enzyme inhibitors since the mid-1990s, when it was a new paradigm in cancer drug development," says Peter.

"Our successful track record of advancing these types of drugs to clinical trials with commercial partners makes this landmark development of CSF1R inhibitors all the more exciting.

Significant research is being conducted to examine the link between Group A streptococcus skin infections and rheumatic fever.

Image courtesy of © Chansom Pantip | Dreamstime.com

Rethinking the causes of rheumatic fever

Researchers and health professionals are rethinking the causes of rheumatic fever after studies by Maurice Wilkins Centre investigators confirmed a link between skin infections and the disease. Their findings have potential implications for health prevention programmes around the world.

For decades, health professionals have believed 'strep throat' – a throat infection caused by the Group A streptococcus (GAS) bacteria – was solely responsible for the development of rheumatic fever. Growing evidence, however, suggests GAS skin infections may also be a precursor to the disease.

"A link between skin infections and rheumatic fever was first mooted by Australians around 15 years ago, based on data from Aboriginal populations," explains Nikki Moreland, an associate investigator with the Maurice Wilkins Centre.

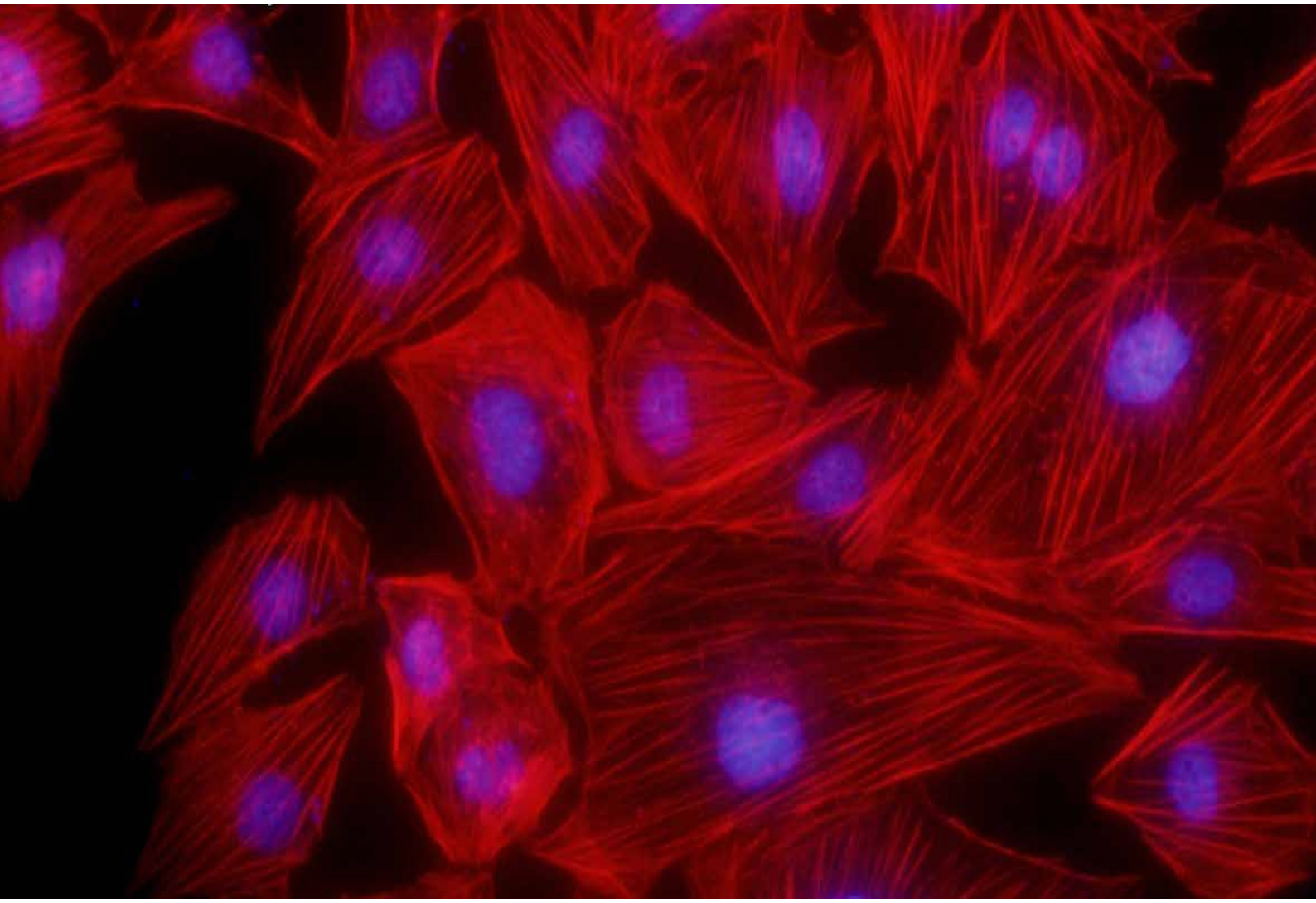
Māori and Pacific children in New Zealand, and Aboriginal children in Australia, suffer some of the highest rates of the disease in the world. Inflammation associated with rheumatic fever can lead to rheumatic heart disease and long-term damage to heart valves.

Working with fellow investigators Dr Debbie Williamson from ESR and Professor Michael Baker from the University of Otago, and several Australian collaborators, Nikki and the team sought to gather evidence to investigate the role of skin infections in rheumatic fever. The team studied GAS isolates in throat swabs collected from children with rheumatic fever in New Zealand, and found that many had characteristics normally associated with skin infection. "That was the first thing that made us go, 'How did they get there and why do they look like skin strains?'" says Nikki.

The researchers then investigated GAS throat and skins isolates from children living in South Auckland, a high-risk area for rheumatic fever, and children from Dunedin where there is no occurrence of the disease. "In the high-risk children we saw a much larger proportion of skin-type strains, in both throat and skin infections, but in low-risk children we hardly saw any of those strains at all."

Another piece of the puzzle came after Northland GP Dr Lance O'Sullivan gave a talk at the University of Auckland. Lance has been instrumental in rolling out the rheumatic fever primary prevention programme in Northland. During his visit, Lance described a case of rheumatic fever that had occurred in the absence of strep throat. After going back through his case notes, Lance discovered the patient had presented with a skin infection 4 weeks before developing rheumatic fever. The atypical presentation led to a published case report co-authored with Nikki.

The findings are initiating an important dialogue about the role of skin infections in rheumatic fever that could ultimately lead to important changes in primary health prevention programmes. Armed with evidence about a long-suspected precursor to the disease, the investigators hope to initiate new MWC research projects into the biological mechanisms and disease pathways behind GAS skin infections and rheumatic fever.



A team of MWC researchers is investigating why a specific form of a common protein promotes cancer progression.

Image courtesy of Imogen Roth and Adele Woolley

The tumour-promoting activities of a famous protein

Developing new cancer therapies and a more reliable test for prostate cancer are just some of the potential outcomes of Maurice Wilkins Centre research into the cellular mechanisms that trigger aggressive forms of cancer.

The work of PhD student Imogen Roth and her colleagues, recently published in the international cancer journal *Oncogene,* delves into how a variant of the renowned cancer biology protein called "p53" causes particularly poor survival in cancer patients.

The gene that encodes p53 is the most commonly mutated gene in cancer. p53 normally acts to suppress cancer formation, so loss of p53 makes cells susceptible to becoming cancerous. What is often less appreciated is that there are several different isoforms of the p53 protein. One of these, known as Δ133p53, promotes cancer progression. The MWC team, led by principal investigator Professor Antony Braithwaite at the University of Otago, has been studying why.

Studies in mice demonstrated that Δ133p53 is a cancer-promoting gene or "oncogene". Subsequent pathology revealed widespread inflammation and high levels of an inflammatory chemical messenger called Interleukin 6 (IL-6).

"If inflammation is sustained over a long period of time it can also be a driver of cancer," says Antony. That led to further research to ask if IL-6 could promote the spread of cancer cells through the process known as metastasis.

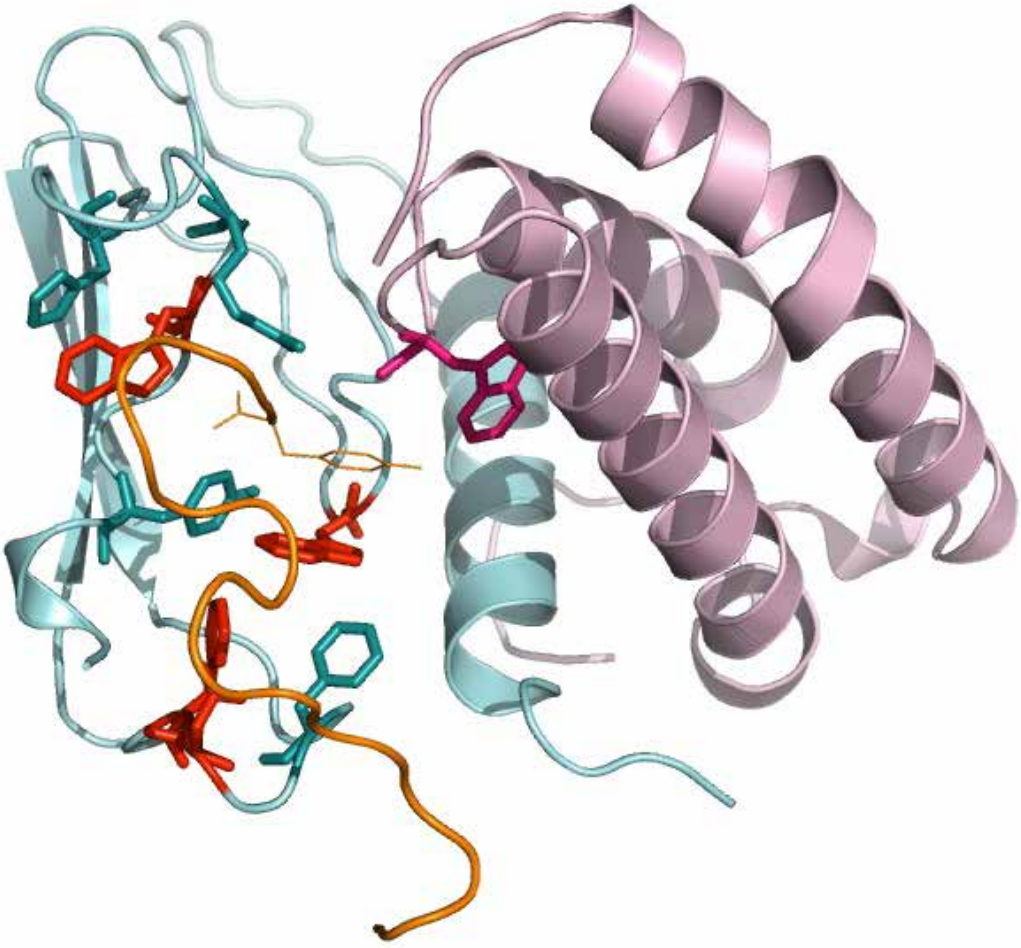
The team concluded that Δ133p53 is a driver of metastasis, and that IL-6 is a major component of the cancer cells' increased ability to invade other tissues. IL-6 also works in conjunction with CCL2, a chemical messenger responsible for making cells migrate. "So IL-6 is the switch and CCL2 is the effector of that migration," says Antony. "I think we've made the first link between the Δ133p53 isoform and inflammation that drives cancer."

Pathological examination of prostate cancers has also revealed that 30 per cent of cases have high levels of Δ133p53. The patients that have the poorest survival rates also have the highest levels of Δ133p53 and involvement of inflammatory cells, according to Antony.

As for future research, Antony hopes to "recreate" their mutant mouse within prostate cells that could answer questions about the role of Δ133p53 in prostate cancer. That, in turn, could lead to the development of specific therapies to prevent tumours.

Following completion of her PhD, Imogen was successful in obtaining a Nuffield Fellowship to Oxford where she is continuing to work on p53 and inflammation.

Thanks to the MWC, Antony says she received "really critical funding without which she would have never got to the point she is now."



A graphical representation of amylin, a naturally occurring hormone and a potential novel target for diabetes drug treatment.

Image courtesy of Debbie Hay

New insight into an established diabetes target

Facilitating the development of better medicines for diabetes, obesity and cardiovascular disease is a key driver behind some painstaking research at the Maurice Wilkins Centre to unlock a molecular blueprint.

Up to 40 per cent of marketed drugs target so-called G protein-coupled receptors (GPCRs) on the outside of their target cells. The natural hormone amylin, and an important diabetes medication called pramlintide that mimics amylin, also act through a GPCR.

Professor Debbie Hay at the University of Auckland's School of Biological Sciences, says "we've been trying to understand exactly how amylin engages with its GPCR target, so we can develop modified forms of amylin-like drugs that are more stable in the bloodstream and help people suppress their appetite, eat less, and lose weight."

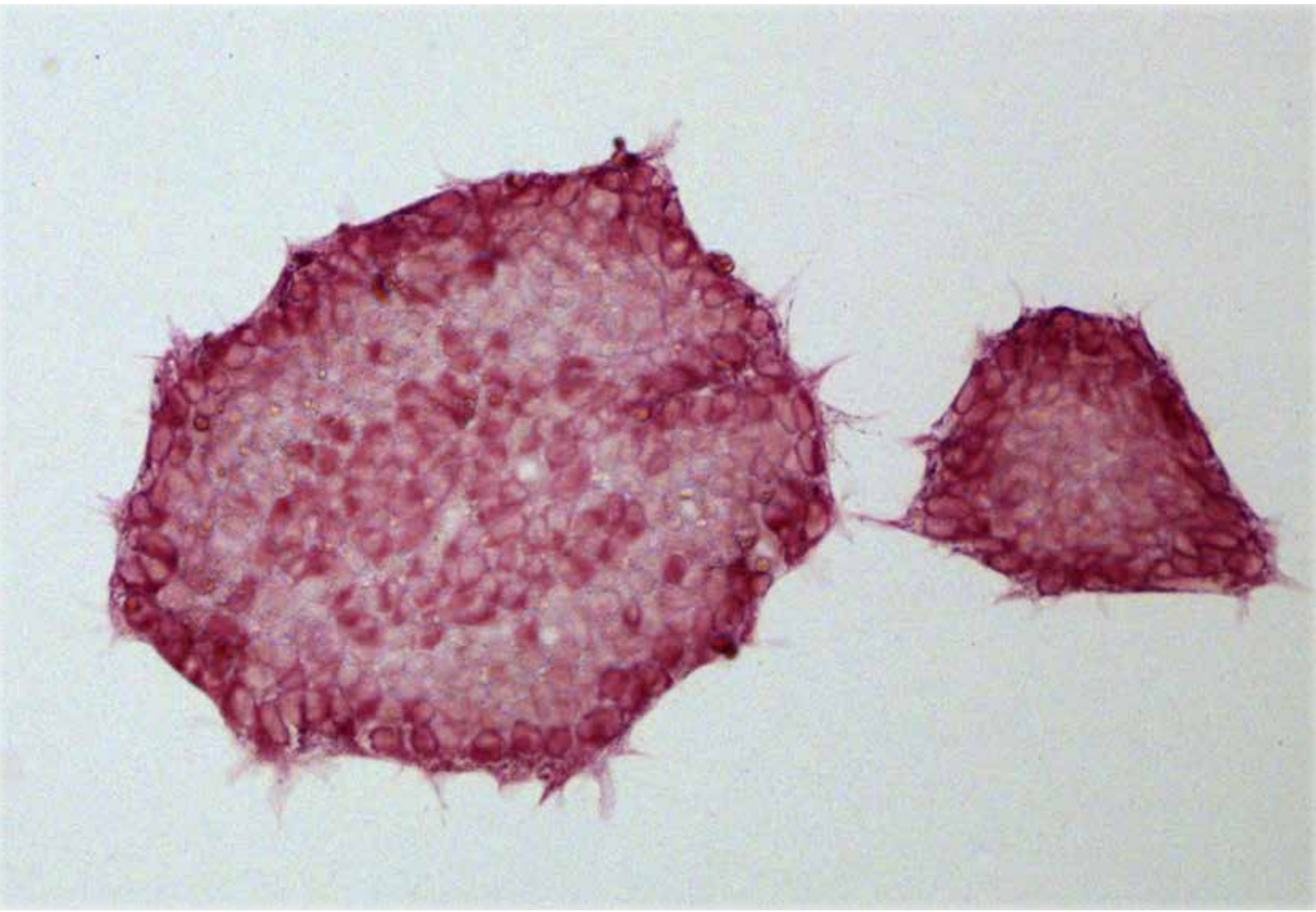
The amylin receptors consist of a sequence of amino acids which Debbie's Maurice Wilkins Centre-funded PhD student Joseph Gingell has been modifying one at a time, using a molecular technique called site-directed mutagenesis. Signalling is then measured to determine which amino acids are important for receptor function. "We can use that information to design modified forms of amylin that interact with the receptor and could then be used as drugs" says Joseph.

Unlocking the molecular secrets of the receptor has taken years of research which Debbie says has been made all the more challenging by the presence of 'accessory' proteins – small "clip-on" proteins that modify the GPCR's function, rather unimaginatively called Receptor Activity-Modifying Proteins or RAMPs.

Joseph's work has helped unravel what part of the receptor is important for amylin interactions and, despite previous assumptions, he has also shown that the RAMPs don't always directly affect how the hormone binds. According to Debbie, it changes how drugs could be developed because "we would have assumed that we had to develop a drug that also interacted with that accessory protein sub-unit, but actually that would probably be the wrong approach."

The MWC is one of the few groups in the world working on amylin receptors. "We're the absolute international leaders in this work," says Debbie. "People come to us for advice on how to take this forward from a global perspective."

Her lab is also collaborating with chemists and molecular computational modellers to develop new drugs based on the amylin template. This work has already produced more potent molecules than the existing amylin-like drug pramlintide. "We're feeding information on the fundamentals of how this natural hormone engages with this receptor directly into a drug development programme. So this is not just theory, it's actually producing practical results here within the Maurice Wilkins Centre," says Debbie.



Two colonies of induced Pluripotent Stem Cells, stained red for alkaline phosphatase enzyme activity.

Image courtesy of Aneta Przepiorski.

Cells get increasing coverage

Human cells have always been important in Maurice Wilkins Centre research, but new developments open up new ground for both research and therapy.

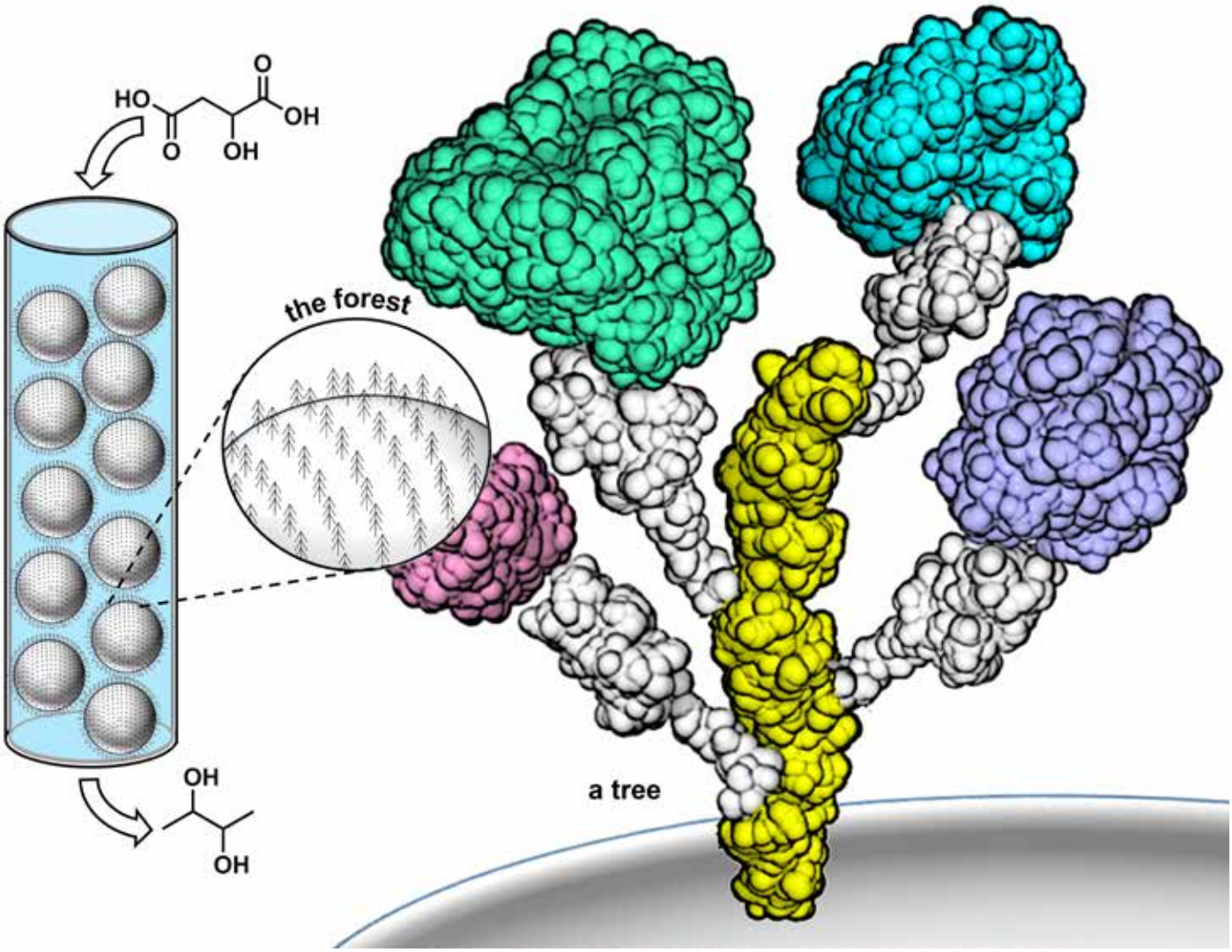
The human body has over 400 different types of cells, all with different forms and function. For example, while some human cells stay in one place and join up to make sheets of tissue like skin, others can move about independently, like the white blood cells that spend their lifetime roaming around the body looking for enemies. Small wonder then that scientists are fascinated by different cells – and that Maurice Wilkins Centre investigators devote much of their time in the lab to studying particular cell types.

An exciting recent development in the Maurice Wilkins Centre is the establishment of New Zealand's first "induced Pluripotent Stem Cells" (iPSCs). iPSCs are adult cells that have been reprogrammed to become embryonic-like stem cells that are capable of generating any cell type within the body. The reprogramming technology was discovered in Japan about 10 years ago and although it has since been refined, it remains technically challenging.

Professor Alan Davidson and Dr Teresa Holm at the University of Auckland had grown iPSCs in the USA before returning to New Zealand, and with support from the Maurice Wilkins Centre have now established the first iPSC lines from New Zealanders' cells. These cells will be used initially in diabetes research, in collaboration with Maurice Wilkins Centre Deputy Director Professor Peter Shepherd. Alan says "Peter wants to study how a particular mutation associated with diabetes affects the production of insulin. We can use the latest gene editing techniques to introduce the mutation into the iPSC lines, then coax the iPSCs to mature into pancreatic cells that make insulin. These mutated cells can then be compared with unmutated cells to see exactly how the mutation affects insulin secretion." Many other projects are already aiming to use the power of iPSCs and gene editing technology, so Alan and Teresa's platform will help launch many new ships.

Other human cell types are being used directly in therapy, especially immune cells to treat cancer. The Malaghan Institute of Medical Research recently announced an agreement to conduct clinical trials of a new immune cell therapy for leukaemia patients, called "CAR-T" therapy. This particular form of CAR-T treatment was developed by scientists who are part of the Maurice Wilkins Centre's collaborative network in China, and the clinical trial will represent a new milestone in the Centre's engagement with leading Chinese researchers. A new cell therapy facility is also being established at the University of Auckland to support clinical trials of both immune cell therapy and engineered human tissue, such as the full-thickness skin product spun out into new company Upside Biotechnologies (see p9). Cell therapy and tissue engineering are therefore now firmly established within the Maurice Wilkins Centre's research portfolio, with the capability to take research from the bench to the clinic mirroring that available to the Centre's drug and vaccine researchers.

As new lab-based cell technologies are brought into the clinical arena to prepare cells and tissues for human therapy, the Maurice Wilkins Centre will be well equipped to translate its knowledge of human cells into practical advances in medicine.



Using so-called ‘molecular superglue’, up to a dozen different proteins can be joined together to construct highly complex nanomaterials, which have been likened to ‘protein trees’.

Image courtesy of Chris Squire

Using ‘molecular superglue’ to build protein‘trees’

Biological batteries, new vaccines and more cost-effective pharmaceuticals are just some of the potential benefits of Maurice Wilkins Centre research into the use of so-called molecular superglues.

"It's big, it's important and we've only just started publishing this work so we think there'll be a lot of interest," says Associate Professor Chris Squire from the University of Auckland's School of Biological Sciences.

"We're taking something that nature uses to make very thin long proteins strong, and turning this into an equivalent of superglue to stick other proteins together," says Chris. The work was inspired by the long thin filaments used by bacteria to stick to surfaces such as teeth. The proteins in these filaments are strengthened by special bonds within the protein molecules that Chris and his collaborator Dr Paul Young helped characterise.

Using the technology developed by Chris and Paul, up to a dozen different proteins can be joined together in a specific spatial arrangement to build highly complex protein nano-materials. The researchers liken these to trees, where the proteins form a central trunk with numerous branches in a pre-determined design. As Chris says "we have this really exquisite control over which proteins we stick together in which order and in which location on our tree." And yet, as Paul puts it, the molecular design means "we just mix it all together and spontaneously the proteins form this structure. It's a self-forming scaffold that can’t come apart."

Over the past decade, overseas researchers have identified three or four molecular superglue variants. However the Maurice Wilkins Centre research has uncovered another ten variants in just 18 months thanks to some hard work by MSc and PhD students. "We're now doing molecular superglue exponentially better than previous methods," says Chris. "We're way ahead of where we thought we might be at this stage of the project."

The ability to hold different proteins together lends itself to enzymes that are part of the same metabolic pathway – building very futuristic sounding "synthetic metabolons". For example, where chemically-complex natural products have shown potential as medicines, the process of making sufficient quantities for medical use could be short-cut by combining a series of enzymes to carry out the trickiest parts of the chemistry.

"Maybe we can identify things that are in the 'too difficult' basket for traditional synthetic chemistry" says Chris. "It's that combination of synthetic chemistry and biosynthesis that could be really powerful and useful in medicine."

Other possibilities range from joining antigens together to produce new vaccines, to the creation of a biological battery that could be implanted inside the body and powered by glucose in the bloodstream. As Chris says, "we've got two or three different things that we're working on, but it's limited only by our imagination - and by funding of course!"

The new funding for immune therapy research underscores the potential impact of this line of work.

Maurice Wilkins Centre collaborators. L-r: Dr Geoff Williams (University of Auckland), Prof Gavin Painter (Victoria University of Wellington), Dr Sung Hyun Yang (University of Auckland), Prof Ian Hermans (Malaghan Institute), Prof Dave Larsen (University of Otago), Prof Margaret Brimble (University of Auckland), Dr Greg Walker (University of Otago), Prof Rod Dunbar (University of Auckland).

Image courtesy of Rod Dunbar

Newly funded research highlights MWC collaborations

Professor Gavin Painter from Victoria University's Ferrier Research Institute has been awarded nearly $10M in the Ministry of Business, Innovation and Employment's 2016 Endeavour Fund science investment round.

Professor Painter will lead a team of fellow investigators from the Maurice Wilkins Centre to develop vaccine technologies to complement existing immune therapy for cancer immunotherapies.

Current immune therapy drugs, such as anti-PD1 drugs, work by blocking molecules on immune cells that prevent them from destroying cancer cells. However these drugs don't work in all patients. The aim of the newly funded research programme is to develop non-toxic cancer vaccines that can trigger stronger immune attack on tumours, and enable more patients to get benefit from immune therapy.

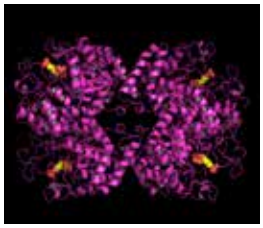
The five-year research programme will draw on the expertise of chemists and biologists from across New Zealand's Maurice Wilkins Centre network, with funding split between a number of existing research groups.

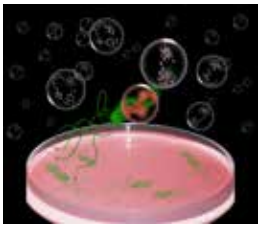
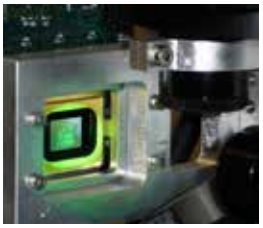
"The funding enables us to bring together mature research programmes from Maurice Wilkins Centre investigators based at the Ferrier and Malaghan Research Institutes and the University of Auckland," Professor Painter said."Researchers at the University of Otago will also provide support."

Professor Painter acknowledged the track records of Wellington and Auckland based groups to develop commercial entities around their research: "It's exciting to be able to combine our knowledge and expertise in translational drug development."

Director of the Maurice Wilkins Centre, Professor Rod Dunbar, said such a major investment in immune therapy from the Endeavour Fund underscores both the potential impact of the research and the strength of the team.

Maurice Wilkins Centre investigators involved include Professor Ian Hermans from the Malaghan Research Institute, and Professor Rod Dunbar and Distinguished Professor Margaret Brimble from the University of Auckland. The research will combine their complementary chemistry and immunology skills, and the University of Otago's drug formulation experience.



Research Programme

The MWC divides its research into four themes – three disease-based themes and a fourth that develops new technologies that can be applied in many disease contexts. Progress under each theme is tracked against milestones set by each of the research teams, and these milestones were all met in 2016. Some of the most important achievements under each theme are set out below, with more detail to be found in the Highlights stories, and the publications listed in section 7.

Cancer

The main focus of the MWC's cancer theme has been the development of new therapeutic agents, including developing new analytical tools to identify new therapeutic targets and monitor patients undergoing new therapy.

- The MWC's immune therapy programme achieved a major milestone in 2016, with the founding of the spin-out company SapVax LLC to take novel cancer vaccine molecules to clinical trial (see Highlights story). This is the second vaccine company spun out by MWC investigators, following the incorporation of Avalia Immunotherapies in 2015. The MWC team also developed several "fast-follower" molecules that will provide backups to the lead compounds being developed by these two companies. (Investigators: Margaret Brimble, Geoff Williams, Rod Dunbar, Dan Verdon, Ian Hermans, Gavin Painter)

- The MWC's cancer drug design programme also focused on targeting a molecule in the human immune system – a molecule on immune cells (called CSF1R) that acts to slow down the immune attack on cancer. A series of potent new drugs that can block this molecule are now being evaluated in cancer models, and a patent application on this series of molecules has been filed to enable one of them to be taken forward into clinical trials. (Investigators: Bill Denny, Peter Shepherd)

- Other MWC cancer drug development projects focused on a range of targets within cancer cells, from proteins involved in cancer cell division and movement (e.g. PI3K enzymes, tubulin) to proteins involved in regulating cell behaviour (e.g. the transcription factor YB-1). (Investigators: Bill Denny, Jack Flanagan, Cris Print, Antony Braithwaite, Annette Lasham)

- A new biological method to target cancer cells was optimised using a microorganism that migrates into tumours. This microorganism (spores from Clostridium sporogenes) was modified so it carries an enzyme capable of activating a novel toxic drug inside tumours. Development of a probe that is also activated by this enzyme will now allow the microorganism to be tracked using hospital PET scanners, so uptake of the

organisms into tumours can be confirmed in treated patients. All the components are now in place for progression into the clinic, and $3.6M of external funding was awarded to take the project into Phase 1 clinical trials. (Investigators: Adam Patterson, Jeff Smaill, Chris Guise, Alex Mowday, Amir Ashoorzadeh)

- New imaging techniques were developed to visualise the release of drugs targeted into areas of tumours that are low in oxygen. These studies use a technique called MALDI imaging mass spectrometry, and are the first to directly image drug release in this way. (Investigators: Gus Grey, Maria Abbattista, Adam Patterson, Jeff Smaill)
- The MWC developed several new methods to read out human immune responses from blood samples (using a technique called flow cytometry). These will be used to pre-screen and monitor patients in clinical trials of immune therapy, and some of these tests were used to support a clinical trial conducted in Auckland by an international pharmaceutical company. (Investigators: Anna Brooks, Dan Verdon, Rod Dunbar)
- New computational tools for analysing the genetic sequences of human cancers were developed, and made available to MWC investigators. These and other tools enabled several new publications on genetic variation in melanoma in New Zealand, the different types of immune responses in breast cancer, and the contrasting roles of different forms of a key cancer gene (isoforms of TP53). (Investigators: Cris Print, Antony Braithwaite, Mike Eccles, Nick Knowlton, Euan Rodger, Aniruddha Chatterjee)

Diabetes and metabolic disorders

Work under this theme has largely been focused on mechanisms of disease, including the role of genetic factors in the development of diabetes. New therapeutic agents also continue to be developed and tested.

- In a major MWC project, a genetic variation linked to increased body weight was studied in NZ people of Polynesian ancestry. This variant (in the gene called CREBRF) was found in many Maori, Tongan, and Cook Island people, as well as Samoan people where the variant was first identified. Individuals with this variant had higher Body Mass Index – an increase in body weight of around 4kg for an adult of 1.7m in height. However these individuals had a significantly lower occurrence of type 2 diabetes, despite their higher weight. Together with wider genetic studies that are underway, this work will not only reveal new information about the causes of type 2 diabetes, but will also help guide how to best prevent and treat obesity and diabetes in different groups of New Zealanders. (Investigators: Tony Merriman, Peter Shepherd)
- Two novel transgenic mouse lines were established, with variants in genes related to diabetes risk from human genetic studies. One will improve the understanding of the role of impaired insulin secretion in type 2 diabetes (a variant in the beta catenin gene) while the other will enable investigation of the role of the common gene variant found exclusively in Polynesian people discussed above (a variant in the CREBRF gene). (Investigators: Peter Shepherd, Dave Grattan)

- The first fully potent human stem cell lines were established from adult New Zealand donors (Induced Pluripotent Stem Cells – see Highlights story). This now enables growth of cells similar to the ones that fail during the development of diabetes (pancreatic beta cells), especially from New Zealanders with genetic variants that put them at higher risk of developing diabetes. These cells can be used to examine the causes of diabetes, and to test new protective or therapeutic agents in the lab. As the technology for making these cells evolves, they themselves may even be used to treat diabetes in the future. (Investigators: Teresa Holm, Alan Davidson, Peter Shepherd)

- New drugs that mimic or block natural hormones were synthesised (using peptide chemistry) and tested for their potential to treat obesity and (pre-)diabetes. Some of these are designed to be long-acting (based on the hormones amylin and CGRP), while others are hybrids that combine parts of existing drugs used to treat diabetes (e.g. combination pramlintide and exendin-4). (Investigators: Margaret Brimble, Debbie Hay, Paul Harris, Kerry Loomes, Christopher Walker, Alex Tups)

- Bariatric surgery is very successful for many obese patients in reversing their type 2 diabetes, and studies are continuing to understand why this can occur well before significant weight loss after surgery. New biomarkers were discovered that correlate with improvement in type 2 diabetes (including changes in certain circulating free fatty acids). It was also discovered that there are distinct differences in the gut microbiome before surgery between those who subsequently achieve diabetes remission and those that do not. These findings may ultimately suggest non-surgical means to gain remission of type 2 diabetes in obese people. (Investigators: Rinki Murphy, Peter Shepherd)

Infectious disease

Streptococcal disease and TB remained the major foci for the MWC's work in infectious disease. New antibiotics were also synthesised, and molecules in other bacteria investigated as potential drug targets.

- Streptococcal bacteria continue to place a very high burden on New Zealand's Maori and Pacific communities, especially through the Rheumatic Heart Disease that can follow infection with Group A Streptococcus ("GAS"). It is still unknown how the immune response against these bacteria causes heart disease, so an important MWC project has been to use the latest high-throughput techniques to look at how antibodies to GAS proteins can "cross-react" with normal human proteins. Related work generated a new test that is likely to improve the diagnosis of rheumatic fever, and this test will be patented in 2017 to allow its clinical development. Substantial progress was also made towards a new GAS vaccine, since the need for new vaccine approaches was confirmed in an international collaboration led by MWC investigators and Australian colleagues. MWC investigators have been using novel protein technology to develop vaccines targeting molecules on GAS called "T-antigens", and in 2016 generated vaccine molecules covering most of the different GAS variants found in New Zealand. These vaccines are being tested in a new system that measures how well the antibodies stimulated by the vaccine protect against GAS infection. (Investigators: Nikki Moreland, Thomas Proft, John Fraser, Jacelyn Loh)

- Tuberculosis (TB) remains a massive challenge in global health, and still infects over 300 New Zealanders per year. In 2016 MWC investigators developed new DNA-based tests to distinguish between different strains of TB in New Zealand, including one strain ("Rangipo") thought to cause recurring re-infection within the country. The MWC also co-ordinated New Zealand's effort in developing new drugs for TB. In a major breakthrough the molecular structure of one of the most important new TB drug targets was determined. The structure of the target molecule (called "NDH-2") was captured with an inhibitor trapped in its active site – crucial information for designing drugs that can inhibit the TB bacterium's ability to generate energy. A second important molecule within TB ("MenD") was also targeted by MWC investigators, and two different binding sites for inhibitors were identified within that molecule, opening up another path to new TB drugs. Collaborative work also continued with the TB Global Alliance, investigating new drugs designed by MWC investigators based on an effective though toxic new TB drug (second generation bedaquiline analogues). This continued collaboration with the world leaders in TB drug development ensures all the TB drug discovery work carried out by the MWC can readily be translated to effective therapy for this global scourge. (Investigators: Vic Arcus, Greg Cook, Shaun Lott)

- Potential drug targets were investigated in other bacteria harmful to humans, including Staphylococcus aureus and Pseudomonas aeruginosa, including confirmation of their importance in causing disease (using gene deletions) and discovery of inhibitors (using chemical screens and structure-based design). (Investigators: Emily Parker, John Fraser, Ries Langley)

- A major new chemistry programme focused on the synthesis of novel antibiotics. In 2016 MWC investigators produced molecules that mimic a unique and exciting naturally-occurring agent called Glycocin F, and these were subsequently compared for their anti-bacterial activity. The chemistry needed to synthesise these antibiotics is highly specialised and a particular strength of the MWC (specifically solid phase peptide synthesis using unique chemical building blocks, including amino acid analogues that only occur in nature in particular bacteria). Similar approaches were used to build "scaffolds" of several other antibiotic peptides (including callyaerin, teixobactin and tikitericin) providing templates for antibiotic discovery in future MWC research programmes. (Investigators: Margaret Brimble, Gillian Norris)

- Current influenza A virus (IAV) vaccines generally induce antibody responses that target proteins on the virus surface that alter their chemical structures seasonally. As a result these vaccines need to be remanufactured (and subsequently re-administered) annually to match the specific strain. Also, these current vaccines are unlikely to offer much protection against the increasing threat of new global pandemics. In contrast to antibody mediated vaccines, T cell vaccines can recognize conserved viral proteins more likely to be shared between different virus strains and subtypes and hence provide effective cross-reactive IAV immunity. MWC researchers have developed a powerful T cell mediated vaccine for IAV that was tested by Melbourne-based researchers. The synthetic MWC vaccine provided stronger immunity than vaccination with whole virus (i.e. the gold standard) leading to ongoing development of the international collaboration and ongoing translational activities. (Investigators, Gavin Painter, Stephen Turner, Ian Hermans, Margaret Brimble, Geoff Williams and Dale Godfrey)

Innovative & integrative technologies

The fourth section of the MWC's research programme is not overtly disease-centric, but instead aims to develop new ideas about technologies that are likely to have impact on a range of human diseases.

- MWC researchers continued to develop their state-of-the-art computer-based tools to accelerate the discovery of new drugs. These tools revolve around 3D modelling of the interactions between chemical compounds that can be developed into drugs, and the protein molecules in cells that MWC investigators have selected for targeting. In 2016, these computer-based tools were extended to enable the discovery and development of chemical compounds able to disrupt targets where more than one protein is bound together in a "complex". This type of analysis led to the design and synthesis of new inhibitors of an important drug target involved in cancer cell signalling (PI3Kγ). 2016 also saw increasing integration of "molecular dynamics" tools that take account of how biological molecules flex and warp over time rather than remaining in the static fixed shape captured by most molecular structure techniques. (Investigators: Emily Parker, Jack Flanagan, Margaret Brimble)
- MWC investigators continued to refine techniques for engineering proteins and peptides for therapeutic use. In 2016 these techniques were used to build new enzymes with the ability to disrupt the ability of bacteria to form structures called biofilms. Biofilms enable bacteria to thrive on surfaces and to resist attack by the immune system or antibiotics, and they are a major problem in medicine, especially when they coat medical devices.




Outreach

International engagement

The Maurice Wilkins Centre is actively building international links for New Zealand biomedical science. As a national Centre of Research Excellence it is in a unique position to represent New Zealand on the global stage, providing a crucial connection between local and international researchers. In addition to investigators' links with scientists, laboratories and companies overseas (see page 53), the Centre is building strategic relationships with institutions and government agencies at city, provincial and national level, in particular in the Asia-Pacific region.

China

The MWC continued its programme of engagement with China in 2016 by building on relationships initiated over 2012 to 2015:

- May: Maurice Wilkins Centre and Guangzhou Institute of Biomedicine and Health (GIBH) were invited by Auckland City Council to take part in the Tripartite Economic Summit. The delegation of GIBH was led by the Director General Professor Duanqing Pei, who also gave a presentation on vitamin C and stem cells. Maurice Wilkins Centre Director Professor Rod Dunbar, Deputy Director Professor Peter Shepherd, Associate Professor Alan Davidson and Mr Peter Lai held an executive meeting with the parties present during the summit to discuss progression of the MWC-GIBH Joint Research Centre.

- July: A delegation from the China Science and Technology Exchange Centre visited the Maurice Wilkins Centre on the 22nd July. Deputy Director General of the China Science and Technology Exchange Centre, Dr Xinli Zhao, met with Maurice Wilkins Centre Deputy Director Professor Peter Shepherd to discuss scientist exchanges through the China-New Zealand Scientist Exchange Programme. This programme provides funding for 20 scientist exchanges between New Zealand and China each year to collaborate on joint research programmes. The programme is co-sponsored by China's Ministry of Science and Technology (MOST) and New Zealand's Ministry of Business, Innovation and Employment (MBIE), and administered by the China Science and Technology Exchange Centre and the Royal Society of New Zealand.

- September: The University of Auckland hosted Maurice Wilkins Centre and the Shanghai Institute of Materia Medica (SIMM) signed a Memorandum of Cooperation (MOC) regarding staff exchange, drug development and clinical drug trials. The MOC

paves the way for the two organisations to facilitate the work of drug development companies within the newly established China-New Zealand (Suzhou) Innovation Centre or other parts of China to carry out clinical trials in New Zealand. The MOC was signed at a September 20 event at Suzhou Industrial Park following a signing on the establishment of the China-New Zealand (Suzhou) Innovation Centre.

- November: Maurice Wilkins Centre hosted a delegation from Jinan University, China, led by the Vice President, Professor Wencai Ye. The purpose of this visit was to sign the memorandum of understanding (MoU) between University of Auckland and Jinan University. This MoU is based on previous engagements between Dr Jeff Smaill, Associate Professor Adam Patterson and Professor Ke Ding. It aims to deepen collaboration between the institutions. An MWC delegation comprising Director Professor Rod Dunbar, Deputy Director Professor Peter Shepherd, Dr Jeff Smaill, Associate Professor Adam Patterson, and Mr Peter Lai attended the signing event. The event was also witnessed by representatives of the Guangdong Province Science and Technology Centre, who are responsible for project matching between the institutions.
- December: Delegations from China National Center for Biotechnology Development (CNCBD) and Shanghai Institute of Materia Medica (SIMM) visited the Maurice Wilkins Centre from the 30th November to the 4th December to discuss opportunities for engagement. The delegations met with leaders from the Maurice Wilkins Centre to discuss engagement with non-communicable disease and infectious disease research in New Zealand, opportunities for drug discovery, and general access to the New Zealand translational research community. The CNCBD delegation commented that they were impressed by the level of aggregated excellence of the Maurice Wilkins Centre's research network and the nation-wide access provided by the Centre. The visits were enabled by existing relationships between MWC investigators and Chinese scientists that aim to foster collaborative research and drug discovery projects.

Japan

- May: Maurice Wilkins Centre Director Professor Rod Dunbar, Professor Cris Print, and Professor Dave Grattan, accompanied by Ms Aya Inagaki of the NZ Embassy, travelled to Kanagawa to explore areas of potential future collaboration with IMS RIKEN Centre for Integrative Medical Sciences. During their visit they met Deputy Director Dr Michiaki Kobo, and had one-on-one discussion with key laboratory leaders across a wide range of research areas at IMS RIKEN.

Industry engagement

Maurice Wilkins Centre investigators support innovation in the biotechnology and drug development sector by providing companies with the expertise and facilities that their research and development programmes require. MWC investigators also provide consultancy to industry as described on page 74.

In 2016 MWC investigators provided expertise and/or facilities to:

- **Allergan Pharmaceuticals**

  Allergan, headquartered in Ireland, is a global pharmaceutical company with a focus on developing new medicines in critical therapeutic areas. Associate Investigator Associate Professor Kerry Loomes from the University of Auckland is working with Allergan to develop new therapeutic strategies to combat metabolic disease.

- **Auckland Clinical Studies Ltd.**

  This company provides Phase I and II clinical research to local and international pharmaceutical and biotechnology companies. In 2016 Maurice Wilkins Centre investigators Professor Rod Dunbar, Dr Anna Brooks, Dr Dan Verdon and Dr Vaughan Feisst continued to work with Auckland Clinical Studies, providing analytical services such as immune monitoring to support ongoing clinical trials sponsored by a major pharmaceutical company.

- **Avalia Immunotherapies Ltd.**

  Newly formed Avalia Immunotherapies is developing immunotherapies that support the treatment of cancers and other diseases. Investigators Professor Gavin Painter from the Ferrier Research Institute and Professor Ian Hermans from the Malaghan Institute of Medical Research have patented a new cancer immunotherapy technology and will be working with Avalia Immunotherapies to further advance the technology and progress it to clinical trials. (Gavin Painter is Chief Technical Officer and Richard Furneaux is the Board Director for Avalia)

- **Comvita**

  Comvita New Zealand is an international natural health products company with offices across Asia, the USA and UK. Comvita are working with investigators Distinguished Professor Margaret Brimble and Associate Professor Kerry Loomes to identify the active components and biomarkers present in Manuka honey.

- **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 Distinguished Professor Margaret Brimble is working with the company on designing and synthesizing new molecules as humane rodenticides to replace the widely used but controversial pesticide 1080.

- **L2 Diagnostics, Ltd.**

  L2 Diagnostics is a biotechnical research company based in Connecticut, USA. L2 Diagnostics is collaborating with Associate Investigator Professor Kurt Krause to identify and confirm inhibitors to alanine racemase in pathogenic organisms.

- **New Zealand Pharmaceuticals Ltd.**

  New Zealand Pharmaceuticals Ltd. manufactures pharmaceutical intermediates and diagnostic products for the pharmaceutical and biotechnology companies. Professors Gary Evans and Richard Furneaux are working with New Zealand Pharmaceuticals Ltd on bile acid chemistry.

- **Threshold Pharmaceuticals, Inc.**

  This NASDAQ listed biotechnology company, based in south San Francisco, USA, is focussed on discovery and development of drugs targeting tumour hypoxia. Investigators Associate Professor Patterson and Dr Smaill from the Auckland Cancer Society Research Centre are paid scientific consultants of Threshold Pharmaceuticals and have received a UniServices Commercial Research Contract from Threshold Pharmaceuticals to undertake particular pre-clinical studies relating to TH-4000.

In addition to these examples above, 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 fight human disease (see page 74).

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 2016 Maurice Wilkins Centre investigators were involved in a number science education initiatives including;

- **Maurice Wilkins Centre biology teacher development scholarships**

  In 2016 the MWC provided sponsorship for scholarships for high-school biology teachers to attend the Queenstown Research Week in August. 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 practising biologists from around the world. Recipients of the awards in 2016, the seventh year of the programme, were; Pru Casey from Otago Boys' High School, Dunedin, Tony Cairns from Wellington High School, Wellington, David Hithersay from Mount Roskill Grammar School, Auckland, and Andrea Roberts, Karamu High School, Hastings.

- **Biology teacher professional development days**

  In 2016 the Centre ran one teacher professional development day in conjunction with the Queenstown Research Week. The Centre offered free registrations for high-school biology teachers to attend the Friday 2nd September sessions with topics on that day including plant biology, diabetes/obesity and genomics. This offer was taken up by 13 teachers, in addition to the four teachers offered the Biology Teacher Development Scholarships. A full tour of eight professional development days will again be run in 2017.

  The Centre will be running further biology teacher professional development days in early 2017, led by Professor Peter Shepherd, Maurice Wilkins Centre Deputy Director, and Ms Rachel Heeney, Head of Biology at Epsom Girls Grammar School. These days are very popular with high-school biology teachers from across New Zealand and feature presentations from scientists on key topics relevant to the NCEA Level 3 curriculum, developed based on feedback from the biology teacher community through direct communications and a dedicated Facebook page.

- **Other science education initiatives**

  Over 2016 MWC investigators were involved in science education initiatives and programmes led by other organisations including the Royal Society CREST programme, LENScience 'Meet a scientist' sessions, the Rotary National Science and Technology Forum and the L'Oreal-UNESCO Girls into Science Forum Auckland, as well as many school visits and presentations to students and teachers.

Public engagement

The Maurice Wilkins Centre actively engages with the public by sharing news of its research successes and by providing commentary on topical scientific issues. Over 2016 MWC investigators have also communicated with community groups affected by cancer, rheumatic fever and diabetes.

MWC investigators communicate with New Zealanders through the news media, public lectures and presentations, and through school visits. In 2016 MWC investigators were involved in public events and national and regional media coverage on a variety of scientific topics. Examples of public engagement activities include:

- **SciGlow**

  Microbiologist and MWC investigator Dr Siouxsie Wiles organised this free exhibition over two days at Silo Park, Auckland, in December 2016. Siouxsie teamed up with artists and schoolchildren who used bioluminescent bugs to create unique artwork in petri dishes which were displayed in the Silos. The public were also given the opportunity to create their own artwork during the exhibition. This event was sponsored by the MWC, Te Punaha Matatini and the University of Auckland.

- **Patient group organisation workshop**

  In November Professor Peter Shepherd hosted a one day workshop to provide patient group organisations with up to date information on scientific and medical developments in two research topics; New strategies to deal with the challenges of major diseases and Stem cells – what are we up to? The workshop was attended by 30 representatives of patient group organisations and was a great success with requests for more workshops on other topics. In addition to Prof Shepherd, the workshop also featured presentations from Dr Teresa Holm and Professors Bill Denny, Rod Dunbar and Andrew Shelling.

- The publication of a major international study in Nature Genetics in July regarding the discovery of a genetic variant that contributes to obesity risk in Samoans provided an opportunity for MWC investigators to lead New Zealand commentary and link to the MWC obesity and diabetes genetics research. MWC investigators Professor Peter Shepherd, Professor Tony Merriman, Professor Dave Grattan, Associate Professor Rinki Murphy and Dr Ofa Dewes were involved in commentary which was featured on TV, radio, print and online; One News, Radio New Zealand, the New Zealand Herald, NewstalkZB, Newshub.co.nz, Stuff.co.nz, Paul Henry Show, Radio 531PI, Sciblogs, World TV and NZDoctor.co.nz.

  Professors Peter Shepherd and Dave Grattan along with Dr Ofa Dewes were featured in an article in the Pacific People's Health magazine (Issue 9, 2016) 'The sweetness that sours our lives,' talking about diabetes, obesity and the science of sugar, and Professor Shepherd also commented on the genetic predisposition to obesity and diabetes in an article 'Just the weigh you are?' in the May 2016 issue of North and South magazine.

- Professor Peter Shepherd fronted media coverage in August of a new study to begin in 2017 looking at how fructose absorption with high school students. This was featured in the New Zealand Herald, on Radio New Zealand and NewstalkZB, Yahoo NZ news and Waatea news websites. He also gave public lectures on the 'Science of sugar' in Tauranga and Nelson.

- In 2016 there was significant publicity about cancer drugs and immunotherapy. A number of MWC investigators provided commentary on these topics including; Professor Bill Wilson, Dr Francis Hunter and Professor Rod Dunbar (Radio New Zealand, 14th February), Professor Rod Dunbar and Dr Robert Weinkove (Radio New Zealand, 18th February), Dr Francis Hunter (Stuff.co.nz, 7th March) and Professor Bill Denny and Professor Mike Berridge (New Zealand Herald, 11th June).

- There was also significant publicity around the topic of antimicrobial resistance in 2016 with MWC investigators also featuring in news articles and commentary on the topic including; Dr Siouxsie Wiles (One News on the 1st June, and as a regular contributor to the Nine to Noon show on Radio New Zealand), Dr Jeremy Owen and Associate Professor David Ackerley (One News, 15th June) and Professor Kurt Krause (Radio New Zealand, 23rd August). Several MWC investigators featured in a one hour documentary 'Peak antibiotics' that screened on Prime TV in April 2016 that highlighted the rise of antibiotic resistance and the risks to the New Zealand population. MWC investigators featured were; Professor Greg Cook, Dr Debbie Williamson, Professor Bill Denny, Dr Siouxsie Wiles and Dr Sally Roberts.

- Professor Greg Cook gave public lectures in Wellington and Auckland on 'The race against antimicrobial resistance: can we win?' in August as part of the University of Otago 2016 Winter Series. In July he was featured in an article in the New Zealand in relation to a project to re-purpose an existing diuretic drug to treat drug-resistant TB, which received new funding from the Health Research Council in 2016.

- A New Zealand Herald Brand Insight on the 29th March featured Associate Professor Adam Patterson and Dr Jeff Smaill's research in the development of 'stealth technology' to target cancer treatments to tumour cells.

- The New Zealand Herald published a feature article on the 7th April highlighting four drug development projects at the Auckland Cancer Society Research Centre. This article involved a number of ACSRC scientists who are also members of the MWC; Professor Bill Wilson, Associate Professor Lai-Ming Ching, Associate Professor Adam Patterson, Dr Jeff Smaill, Dr Moana Tercel and Dr Frederik Pruijn.

- A study by researchers from the University of Otago, published in May 2016, found differences in the levels of NRAS mutations in melanomas when comparing South Island and North Island patients. Authors of the paper included MWC investigators Professor Mike Eccles, Dr Peter Ferguson, Dr Aniruddha Chatterjee, Mr Antonio Ahn and Professor Peter Shepherd. The study received significant coverage on TV (Prof Eccles, One News, 14th May and Dunedin TV), radio (Dr Chatterjee, Radio New Zealand, 14th May), in print and online; New Zealand Herald, Stuff.co.nz, Newshub.co.nz, Yahoo.com.

- Dr Goetz Laible and Professor Peter Shepherd were interviewed in coverage of research on producing anti-cancer drugs in the milk of transgenic goats; Newshub 10th March and the Listener magazine 15th June.
- Associate Professor Rinki Murphy was featured on Radio New Zealand on the 2nd of January talking about medical trials that she was involved in, including the MWC diabetes genetic study.
- Professor Rod Dunbar and Dr Vaughan Feisst were interviewed on their new technology to grow human skin in the lab by Radio New Zealand on the 16th June. The announcement of a new spinout company based on this technology was reported on Voxy.co.nz on the 15th November.
- Awards to MWC investigators received coverage in the media; Dr Siouxsie Wiles, Blake Leader Award, 1st July (Newshub, New Zealand Herald, National Business Review), Professor Antony Braithwaite, Shorland Medal, 8th September (Radio New Zealand and Otago Daily Times), Professor Margaret Brimble, Marsden Medal, 8th September (Radio New Zealand and the New Zealand Herald, Voxy.co.nz) and Professor Debbie Hay, James Cook Fellowship, 11th November (theweekendsun.co.nz and voxy.co.nz).
- Professor Debbie Hay's research into migraine also received coverage on radio (NewstalkZB), print (New Zealand Herald) and a number of online sites.
- Professor Margaret Brimble also featured in publicity focussed on recruiting women into STEM subjects and getting them to stay (Idealog magazine and Villainesse.com). She was also interviewed for a speaker spotlight for the 17th International Biotechnology Symposium and Exhibition.

Many more MWC investigators gave or hosted public lectures and presentations and were featured in media coverage of their research or commentary on their areas of expertise throughout 2016.

Supporting the New Zealand science community

Research symposium and workshops

During 2016 the Centre ran the following research symposium and workshops:

Maurice Wilkins Centre symposium

The 2016 Maurice Wilkins Centre Research Symposium was held on the 13th of December and highlighted research from across all the Centre themes; cancer, diabetes and obesity, infectious disease and innovative and integrative technologies. The symposium featured talks by Centre post-doctoral and research fellows and was a great opportunity to hear about the wide variety of research being undertaken by this talented group. Travel prizes were awarded to the presenters who did the best job of communicating to the MWC audience on the day;

First prize – Dr Chris Guise, University of Auckland

Highly commended – Dr Monica Gerth, University of Otago and Dr Jacelyn Loh, University of Auckland

Maurice Wilkins Centre thematic workshops and flagship meetings

During 2016 the Maurice Wilkins Centre held four 'thematic' workshops on specific research topics of relevance to the Centre. The aim of these workshops is to bring together New Zealand researchers in a particular research area to brainstorm future directions and decide how best to achieve outcomes to benefit New Zealand. Many of the ideas that come from these workshops inform the strategic direction of the Centre's research programme.

Workshops were held on the following topics;

- Diabetes and obesity – 22nd April in Dunedin and 3rd September in Nelson
- Viral proteins as vaccine components and drug targets – 27th and 28th June in Auckland
- Molecular approaches to cancer therapy – 7th July in Wellington

The Centre also held a number of more focussed 'flagship' meetings during 2016;

- Harnessing the immune system to treat cancer – 30th May in Auckland
- Genomic approaches to cancer diagnosis and treatment – 10th June in Wellington
- Protein and peptide engineering - 11th August in Wellington

The Maurice Wilkins Centre NZIC Prize for Excellence in Chemical Science

The New Zealand Institute of Chemistry awards The Maurice Wilkins Centre Prize for Excellence in Chemical Science annually and in 2016 the recipient was Professor Christian Hartinger of the University of Auckland for his work in the synthesis of bioorganic-metallic compounds and their potential use as targeted anticancer drugs.

Professor Hartinger's research focuses on compounds based on ruthenium, osmium, rhodium or iridium that have been designed to accumulate in tumours or to target relevant proteins in tumours and his group uses innovative bioanalytical methods to study the mode of action of metal-based drugs. He has established himself as one of the world leaders in the development of metal-based anticancer drugs, has published more than 160 papers and has over 7,500 citations.

Conferences, meetings and organisations

Scientific conferences, meetings and networks are important fora to share knowledge and form collaborative relationships. In addition to the Symposia and workshops that the Centre and its investigators convene, the Maurice Wilkins Centre supports national and international scientific meetings held in New Zealand and sponsors speaking slots at international conferences where these help to raise the profile of New Zealand science. In 2016 the Maurice Wilkins Centre provided support for:

Queenstown Research Week

This is the largest annual science event in New Zealand. In 2016 this event was held in Nelson and attracted over 1200 registrations for the twelve individual scientific meetings held over the course of the week. These included the Queenstown Molecular Biology Meeting and satellite meetings focussed on: cancer, drug discovery, stem cells and regenerative medicine, heart disease, genomics, diabetes, cell communications and plant biology. The Centre is a premier academic sponsor for this event that provides an important opportunity for Centre investigators to meet and hear about some of the latest national and international research. The Centre also provides sponsorship for New Zealand secondary school teachers to attend the Queenstown Molecular Biology meeting (See page 36)

New Zealand Society of Oncology

The annual conference of the New Zealand Society of Oncology was held in Palmerston North from the 26th to the 27th November and was attended by 120 researchers and clinicians from across New Zealand.

The MWC provided support for the following student prizes at the conference;

- Clinical prize – Weng Mak, University of Auckland
- Scientific prize – Pulari Thangavelu, University of Queensland
- People's choice – Kimberly Dainty, University of Otago

Victoria University of Wellington Biodiscovery Centre Conference 2016

The topic for this conference held on the 5th July was 'Brain – cancer, biology and drugs'. The Centre provided support for keynote speaker Associate Professor Kerrie McDonald from the University of New South Wales, Sydney.

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 2016 Maurice Wilkins Centre investigators served in advisory and governance roles in many New Zealand organisations including;

- AgResearch Ltd
- Auckland Medical Research Foundation
- Auckland Regional Tissue Bank
- Australia NZ Neuro-Endocrine Tumour Group
- Australian and New Zealand Council for the Care of Animals in Research and Teaching
- Biomolecular Interaction Centre (University of Canterbury)
- Callaghan Innovation
- Cancer Society of New Zealand
- Cancer Trials New Zealand
- Diabetes Auckland
- Freemasons Roskill Trust
- Gastro Intestinal Cancer Institute
- Genesis Oncology Trust
- Genetics Otago
- Greenlane Research and Educational Fund
- Health Research Council of New Zealand
- Institute of Environmental Science and Research
- Kea World Class NZ Awards Selection Panel
- Landcare Research Ltd
- Leukaemia and Blood Cancer NZ
- L'Oreal-UNESCO Women in Science Fellowships in Australia and NZ
- Marsden Fund Council
- Maurice and Phyllis Paykel Trust
- Melanoma Network of New Zealand
- Ministry of Business Innovation & Enterprise
- Ministry of Health
- National Institute of Water & Atmospheric Research

- New Zealand Association of Scientists
- New Zealand Bioinformatics Institute
- New Zealand Chemical Education Trust
- New Zealand eScience Infrastructure
- New Zealand Genomics Ltd
- New Zealand Health Quality & Safety Commission
- New Zealand Institute for Cancer Research Trust
- New Zealand Institute for Rare Disease Research Ltd
- New Zealand Microbiology Society
- New Zealand Neurological Foundation
- New Zealand Organization for Rare Disorders
- New Zealand Society for Biochemistry and Molecular Biology
- New Zealand Society for Medical Sciences
- New Zealand Society for Oncology
- OBodies Ltd
- Otago Medical Research Foundation
- Otago Postgraduate Medical Society
- Queenstown Molecular Biology Meetings Society
- Royal Society of New Zealand
- Tertiary Education Commission
- The Physiological Society of New Zealand
- Upstream Medical Technologies Limited
- Wellington Health and Biomedical Research Society

International roles

In 2016 members of the Maurice Wilkins Centre served in more than 120 advisory, editorial and governance roles in international organisations based in the United States of America, Australia, the United Kingdom, Canada, France, Germany, Singapore and Switzerland.

Organisation Development

Flexible research programme

One of the Maurice Wilkins Centre's main objectives is to encourage collaborations between investigators from different scientific disciplines, achieved through the contestable Flexible Research Programme. Two rounds of this programme were held in 2016; in March and August/September. Three categories of support were open for applications from MWC investigators in 2016; new initiatives involving postgraduate students, access to specialised facilities and equipment and access to specialised international facilities and training (see page 45 for details).

New initiatives involving post-graduate students

The Maurice Wilkins Centre supports new collaborative research involving MWC investigators by providing working expenses for new interdisciplinary postgraduate student projects that also promote progress in scientific areas of importance to the MWC.

Eight projects awarded funding in 2015 were ongoing in 2016 and ten new projects were awarded working expenses in 2016 **(project leader, host institution and student names are in bold):**

- Actions of the neuropeptide calcitonin gene related peptide (CGRP) on adipose stem cell-derived adipocytes; **Kerry Loomes,** Rod Dunbar, Vaughan Feisst, Chris Walker, **University of Auckland**. BSc (Hons) student **Soha Gomaa**.
- Synthesis of Tikitericin – A New Lantipeptide from the NZ Extremophilic Microorganism Thermogemmatispora strain T81 (PhD project); **Margaret Brimble, University of Auckland,** Rob Keyzers, Victoria University of Wellington, Greg Cook, University of Otago. PhD candidate **Buzhe Zu**
- Effect of small molecule probes on the PI3Kg membrane interaction; **Jack Flanagan**, Peter Shepherd, Bill Denny, Gordon Rewcastle, **University of Auckland**. BSc (Hons) student **Brady Cress.**
- Developing Therapeutics Targeting the Replication Machinery of the Human Parainfluenza Viruses; **Richard Kingston**, John Taylor, Esther Bulloch, **University of Auckland.** PhD candidate **Nicole Herr.**
- Engineering scaffolded enzymes to complement natural product synthesis; **Chris Squire**, Wayne Patrick, Paul Young, **University of Auckland**. MSc students **Robert Kerridge** and **William Bramley.**

- Assess the metabolism and pharmacokinetics of peloruside. **Stephen Jamieson**, Jagdish Jaiswal, **University of Auckland**, John Miller, Victoria University of Wellington. MSc student **Shanan Chand.**
- The importance of warhead placement in selective FGFR targeting; **Chris Squire**, Jeff Smaill, Chris Guise, Adam Patterson, **University of Auckland.** Postgraduate student **Xiaojing (Sean) Lin**
- Targeting Glutamate Racemase to Discover Antibiotics for Drug Resistant Human Bacterial Pathogens; **Kurt Krause,** Greg Cook, Jack Flanagan, **University of Otago**. MSc student **Daniel Palmer.**
- Of microbes, mice and men: targeting diabetes through prebiotics and the microbiome; **Mike Taylor,** Garth Cooper, **University of Auckland**. PhD student **Akarsh Mathrani.**
- 3D Breast Tumour Models for Drug Discovery; **Tim Woodfield,** Margaret Currie, **University of Otago.** PhD student **Jessika Wise.**

Access to specialised equipment & facilities

In September 2015 the MWC launched a new contestable scheme, as part of its Flexible Research Programme, to support access to specialised facilities and equipment across New Zealand for all MWC investigators. The scheme is intended to cover the costs of user charges attracted by these facilities or equipment, as well as travel and accommodation necessary to enable MWC investigators to work in facilities away from their host institution.

As part of the development of this scheme, a register of New Zealand facilities and equipment was set up within the members section of the MWC website. Over 60 facilities and items of equipment were registered initially in 2015 and over 2016 the number of facilities and items of equipment increased to 83. It is intended that MWC investigators will use this register as a resource to identify and compare facilities and equipment across New Zealand that they can use for their research.

Eleven projects awarded funding in 2015 were ongoing in 2016 and 29 new applications to this scheme were approved in 2016;

- Purification of recombination Cas9 protein for CRISPR-mediated gene editing; **Alan Davidson**, Peter Shepherd, **University of Auckland.**
- Identification of enzymes that catalyse the activation of Tarloxotinib bromide (TH-4000); **Chris Guise,** Adam Patterson, Cris Print, Shevan Silva, **University of Auckland.**
- Fragment screening to probe the active site and protein-protein interfaces of PI3K□; **Chris Squire**, Jack Flanagan, Dan Furkert, Woo-Kyong Paik, **University of Auckland.**
- Simultaneous quantitative mapping of peptide hormones in mouse brain and pituitary using MALDI Imaging Mass Spectrometry; **Angus Grey**, Kathy Mountjoy, Yufei Hu, **University of Auckland**.
- Sex-dependent and melanocortin peptide hormone-dependent differences in high-fat diet-induced obesity in mice – are these associated with altered gut microbiome? **Kathy Mountjoy**, Justin O'Sullivan, Rinki Murphy, Bo Sun, **University of Auckland.**

- RNase HI: A tractable novel TB drug target with species specificity; **Shaun Lott**, Stephanie Dawes, James Dalton, Siouxsie Wiles, Abeer Al-Zubai, **University of Auckland.**
- Structural insight into the assembly of immature poxvirus particles; **Alok Mitra,** Paul Harris, Margaret Brimble, Max Ashmore, **University of Auckland.**
- NMR Studies of MenD from the Human Pathogen M. tuberculosis; **Jodie Johnston**, Ghader Bashiri, Esther Bulloch, Shaun Lott, Hank Chaung, **University of Auckland.**
- Elucidating the mechanism of poly-γ-glutamation – from infectious diseases to cancer; **Ghader Bashiri,** Chris Squire, **University of Auckland**.
- Sequencing ACSRC panel on melanoma cell lines; **Peter Shepherd**, Bruce Baguley, Cris Print, **University of Auckland**, Mike Eccles, University of Otago.
- Development of potent antimicrobial peptides containing the unusual amino acid enduracididine (End) for treatment of multidrug resistant infection; **Margaret Brimble,** Daniel Furkert, Andrew Wadsworth, **University of Auckland,** Greg Cook, University of Otago.
- Biological Evaluation of Chemically Synthesised Trichoderin A and Analogues as Anti-Tuberculosis Agents; **Greg Cook, University of Otago**, Margaret Brimble, Paul Harris, University of Auckland.
- A fluorescent toolbox for studying amylin receptor regulation; **Debbie Hay,** Paul Harris, Margaret Brimble, **University of Auckland.**
- Chemical Synthesis and Evaluation of Callyaerin Cyclic Peptides as Potential Anti-TB Agents; **Greg Cook, University of Otago**, Margaret Brimble, Paul Harris, Luis Manuel De Leon Rodriguez, Allan Zhang, University of Auckland.
- Sequencing the T cell repertoire to identify the mechanism of synergy with vaccination and checkpoint blockade. **Lindsay Ancelet,** Ian Hermans, **Malaghan Institute of Medical Research.**
- Using modelling to inform inhibitor screening and design for MenD from the human pathogen M. tuberculosis. Jodie Johnston, **Ghader Bashiri**, Daniel Furkert, Shaun Lott, Ted Baker, **University of Auckland**, Greg Cook, Wanting Jiao, University of Otago, Hank Chaung, Shaun Ferris, University of Auckland.
- Understanding the functional implications of the coding variant in CREBRF that is associated with BMI in Samoans; **Peter Shepherd**, Dave Grattan, Alex Tups, Sharon Ladyman, Kathy Mountjoy, Troy Merry, Kerry Loomes, Mohinder Kaplish, **University of Auckland.**
- Modulating the tumour microenvironment with hypoxia-activated prodrugs to improve the outcome of immunotherapy. **Ian Hermans**, Adam Patterson, Jeff Smaill, Regan Fu, **Malaghan Institute of Medical Research.**
- MALDI imaging mass spectrometry to develop a spatial map of hypoxia activated FGFR inhibitor metabolisn in tumour xenograft models. **Angus Grey,** Maria Abbattista, Adam Patterson, Jeff Smaill, Chris Guise, **University of Auckland.**

- Oxygen-enhanced magnetic resonance imaging (OE-MRI) of tumour hypoxia as a biomarker for treatment with SN 37960, the lead nitroCBI hypoxia activated prodrug. **Moana Tercel**, Frederick Pruijn, Beau Pontre, **University of Auckland**.
- Production of Flaviviral and Paramyxoviral Polymerases, Enabling Structural Analysis and Development of Iminoribotol-C-nucleosides as Anti-Virals. **Richard Kingston, University of Auckland.**
- Peptides that mimic Collagen as Diagnostic Biomarkers for Rheumatic Fever. **Nikki Moreland**, Paul Harris, Margaret Brimble, **University of Auckland.**
- Analysis of TH-4000 metabolic activation in patient-derived head and neck cancer xenografts and correlation with pharmacodynamics endpoints. **Adam Patterson**, Maria Abbattista, Matthew Bull, Chris Guise, Jeff Smaill, **University of Auckland.**
- Combined analysis of an IL6 promoter variant and p53 mutation status, may provide clinically useful stratification of colorectal cancer patients. **Nicholas Fleming,** Antony Braithwaite, John McCall, **University of Otago.**
- The effects of encapsulation on the gut microbiome. **Justin O'Sullivan**, Thilini Jayasinghe, **University of Auckland**.
- Crystal structure of CSF1R with inhibitor bound. **Jack Flanagan**, Bill Denny, Peter Shepherd, Chris Squire, James Dickson, Gordon Rewcastle, **University of Auckland.***
- In vivo protein nano-crystals: innovative scaffolds for vaccines, biosensors and biomarkers. **Peter Metcalf,** Guangmei Huang, Michael Oliver, **University of Auckland**.
- Transcriptomic investigation of Δ133p53 as a potential prognostic biomarker for prostate cancer. **Antony Braithwaite,** Sunali Mehta, **University of Otago**.
- Zebrafish models of cohesin-mutant leukaemia. **Julia Horsfield**, Stefan Bohlander, Nabila Tahsin, Sarada Ketharnathan, Alice Chin, **University of Otago.**

*This project is currently provisionally approved

New investigators

In 2016 the Maurice Wilkins Centre continued to strengthen its national network of investigators with 12 new associate investigators invited to join the Centre. In addition, 36 postdoctoral researchers and postgraduate students were appointed as affiliate investigators.

New associate investigators appointed in 2016;

- Professor Chris Battershill, Faculty of Science and Engineering, University of Waikato
- Professor Stefan Bohlander, Department of Molecular Medicine and Pathology, University of Auckland
- Dr Margaret Currie, Department of Pathology, University of Otago, Christchurch
- Dr Austen Ganley, School of Biology Sciences, University of Auckland
- Professor Christian Hartinger, School of Chemical Sciences, University of Auckland
- Dr Kim Mellor, School of Medicine, University of Auckland

- Dr Troy Merry, Department of Molecular Medicine and Pathology, University of Auckland
- Dr Xochitl Morgan, Department of Microbiology and Immunology, University of Otago
- Associate Professor Mike Taylor, School of Biological Sciences, University of Auckland
- Dr Andrew Thompson, Auckland Cancer Society Research Centre, University of Auckland
- Dr James Ussher, Department of Microbiology and Immunology, University of Otago
- Professor Vernon Ward, Department of Microbiology and Immunology, University of Otago

Human capability

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

Support for postgraduate students

The MWC supports a large cohort of postgraduate students within its associated research groups by providing funds for stipends, working expenses and travel, as well as opportunities to access specialised research facilities and equipment. Over 2016 the MWC provided direct financial support for 69 postgraduate students and 12 postgraduate students who received MWC support prior to or during 2016 completed their degrees in 2016.

In 2016 11 new PhD students started their studies with support from the MWC for fully or partially funded PhD scholarships previously awarded through the Flexible Research Programme (Category 1). One further student was recruited to start in early 2017.

Support for emerging scientists

The success of the core MWC research programmes is dependent on the skills and expertise of a large cohort of research and post-doctoral fellows, many of whom are in the early to mid-stage of their careers.

In 2016 the MWC provided full or partial salary support for 29 research and post-doctoral fellows (16.28 FTE) at the University of Otago, the University of Canterbury, the Malaghan Institute of Medical Research, the University of Waikato and the University of Auckland.

The research of a number of members of this cohort was featured in the 2016 Maurice Wilkins Centre Symposium held on the 13th December 2016 (see page 40).

The MWC also provided support for four research technicians (0.63 FTE) to carry out specific roles in the core MWC research programme over 2016.

Early Career Steering Group

In August 2016 the Centre enabled the formation of an MWC Early Career Steering Group, a committee of young scientists formed specifically to empower, develop and support the Centre's early career researchers.

As one of their first tasks the group planned the programme for the 2016 Early Career Researcher Forum (see following). They also began planning for 2017; a country-wide event schedule, technical presentations and webinars, web resources and networking opportunities.

Inaugural members of this group were; Dr Dan Furkert (University of Auckland), Dr Chris Guise (University of Auckland), Dr Joanna McKenzie (University of Waikato), Dr Jodie Johnston (University of Auckland), Dr Sunali Mehta (University of Otago) and Dr Gert-Jan Moggre (University of Canterbury).

Early Career Research Forum

On December the 12th the MWC Early Career Steering Group convened their first symposium 'Making the most of the MWC: Empowering our early career researchers'.

The symposium was well attended and featured a science communication workshop facilitated by Dacia Herbulock from the Science Media Centre as well as a workshop on writing grants and funding applications facilitated by Ms Anne French.

The symposium also gave early career MWC researchers the opportunity to present either a short research talk or research poster, selected from submitted abstracts, with travel prizes offered for both categories. Eight early career researchers were selected to present short research talks, which were of a very high standard that impressed the audience. There were also some great posters displayed on the day.

Travel prizes were awarded to;

Research talks: 1st equal - Grace Gong (University of Auckland) & Claire Mulholland (University of Waikato), 3rd - Hannah Read (University of Auckland)

Research posters: 1st - Tom Wiggins (University of Otago), 2nd - Jennifer Eom (University of Auckland), Highly commended - Melissa Webby (University of Auckland) & Luke Stevenson (Victoria University of Wellington)

Entrepreneurship workshop

On the 11th and 12th October the Centre ran a two-day 'Entrepreneurship workshop'.

Under the guidance of former Queensland Chief Scientist Professor Peter Andrews, and science and innovation policy analyst Dr Fiona Wood, 17 early career MWC researchers learnt some of the key characteristics of highly-successful entrepreneurs, and the skills required to develop and run a business.

The participants were inspired by Steve Henry from Kode Biotech Ltd and Ben O'Brien, co-founder of StretchSense, who shared their own pathways as change-makers. The two successful Kiwi entrepreneurs also provided invaluable insight and advice for those keen to understand the link between innovation and entrepreneurship.

The workshop culminated with participants pitching their ideas to a panel of high-level players in the investment, science, public or NGO spaces. Scott Ferguson from the University of Otago delivered the winning pitch of the day and described the workshop as a valuable opportunity to interact with a varied group of researchers. "We all gained a clear understanding in the importance of being able to present our research projects in a concise and clear manner for potential investors."

Technical training opportunities

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 MWC provides support for early career investigators to access specialised international facilities and training, and share what they learn with their New Zealand colleagues. This contestable programme supports investigators' 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.

During 2016, ten investigators travelled under this scheme

Dr Htin Lin Aung, a postdoctoral fellow at the University of Otago, visited the University of Melbourne to carry out whole genome sequencing of a local strain of Mycobacterium tuberculosis. One third of all TB notifications in NZ can be assigned to clusters of infection; the largest TB cluster is known as the Rangipo cluster, which has been the cause of ongoing outbreaks for at least the last 25 years. Recent analysis has shown that Rangipo strains causes active disease at a rate 4 times that normally expected from contact tracing suggesting this cluster is hypervirulent, but the reason for this remains unknown. To start to understand at a genome level the transmission and virulence of large TB clusters, a reference genome of the Mycobacterium tuberculosis Rangipo strain was required and with the MWC support, this sequencing was done on the Pacific Biosciences RS-II platform at the University of Melbourne.

The resulting reference genome sequence by PacBio will be used for subsequent whole genome sequencing using HiSeq on a large number of Rangipo strains for development of fast, Rangipo-specific molecular diagnostic tests to control the spread of this strain, the cause of a prolonged and sustained outbreak in parts of the New Zealand population.

Ms Waruni Dissanayake, a PhD student in the Department of Molecular Medicine and Pathology at the University of Auckland, visited the Garvan Institute of Medical Research in Sydney to perform Total Internal Reflection (TIRF) microscopy experiments in the laboratory of Dr William Hughes. One aspect of Waruni's research project is based upon her recent

finding that beta-catenin is involved in the glucose uptake into adipocytes. The glucose uptake process is mediated by glucose transporter GLUT4 and in response to insulin stimulation GLUT4 containing vesicles move to the plasma membrane.

The best way to dynamically image these vesicles as they fuse with the membrane is TIRF microscopy and the team at the Garvan have both the instruments and the cell models to study these processes. During Waruni's visit she successfully performed TIRF experiments which provided information regarding how beta-catenin regulates GLUT4 translocation to the plasma membrane. With the TIRF-microscopy data they were able to identify a novel role for beta catenin in glucose uptake process.

Waruni acknowledged that this visit was a great opportunity for her as she gained valuable experience working on this TIRF instrument in one of Australia's leading research institutes. The findings have been included in a paper submitted to the Journal of Biological Chemistry.

Dr Joseph Gingell is a research fellow in the School of Biological Sciences at the University of Auckland. Joseph visited the laboratories of Professor Mark Wheatley at the University of Birmingham and Professor David Poyner at Aston University, in Birmingham, UK, with the purpose to learn a novel method of solubilising membrane proteins using styrene-maleic acid co-polymer (SMA).

This method allows the extraction of membrane proteins and their surrounding lipids intact into SMA lipid particles or SMALPs, while avoiding the use of detergents that remove lipids and can denature proteins. Joseph learned how to prepare the SMA and successfully performed the solubilisation procedure on a G protein-coupled receptor (GPCR), the calcitonin receptor.

The preliminary results generated on this trip formed part of a successful Marsden Grant application by his supervisor Professor Debbie Hay, in which they will use SMA to solubilise GPCRs for native mass spectrometry analysis. The skills Joseph learned and the contacts he made during my trip will help greatly with this new project.

Mr Liam Harold, a University of Otago PhD student in the Department of Microbiology and Immunology, visited the laboratory of Professor William Jacobs Jr at Albert Einstein College of Medicine in New York to learn and transfer technology for constructing marker-less gene deletion mutants in *Mycobacterium tuberculosis* (MTB) using a specialised transduction phage-based (high throughput) methodology.

Liam successfully used this technology in the Jacobs lab and is now in the process of implementing the methodology in NZ. This will be an important scientific milestone for the MWC as it will give us the capacity to create marker-less gene deletion mutants in MTB allowing us to gain insight into potential future drug target candidates placing us at the cutting edge of MTB drug discovery and development.

Ms Alice Chin and Dr Julia Horsfield visited the laboratory of Professor Ross Hannan at the John Curtin School of Medical Research (JCSMR) at the Australian National University. Julia is an MWC Associate Investigator and Alice is a PhD candidate in the Department of Pathology at the University of Otago.

Alice's PhD project involves identifying novel drug targets for acute myeloid leukemia with cohesin mutations. During the visit they worked on optimising drug screening assays in their cohesion-mutant cell lines using live-cell imaging. They also generated preliminary data on an Opera Phenix High Content Screening system to determine if this technology would be suitable for performing future high content screening experiments for Alice's project.

Ms Fengyun (Fiona) Hu, a PhD student from the University of Auckland, travelled to the University of New South Wales in Australia to work with Dr Greg Smith to conduct a series of transgenic animal experiments using specific mouse strains and equipment not accessible in New Zealand; an EchoMRI and the Columbus Oxymax Comprehensive Laboratory Animal Monitoring System (CLAMS) metabolic cage system.

Fiona carried out a series of general phenotype and metabolic tests on the matched wild type mice and a S552A □-catenin knock-in mice and is now using this data to complete her PhD project and inform the direction of future research in the MWC research programme.

Ms Elsie Jacobson, a PhD student at the Liggins Institute, University of Auckland, attended the Summer Institute in Statistical Kenetics at the University of Washington in Seattle in 2016. Elsie participated in three statistical genetics modules over two weeks, which both reinforced the foundations of statistics and introduced her to new statistical approaches such as Bayesian data analysis.

Elsie says these courses have really helped her understanding of the statistical methods used in her field, and will be invaluable when she receives her large genomics datasets later this year. She has also been able to discuss analysis methods with other students in her department and share the knowledge she has gained. Elsie comments that "this course has prepared me to analyse the Hi-C and RNA-seq data I am currently generating."

Ms Claire Mulholland, a PhD student at Waikato University, attended a five-day workshop titled "Working with Pathogen Genomes" at the Wellcome Genome Campus in Cambridge. This workshop taught Claire the latest in computational skills for genomic analysis which she is now applying to her PhD project 'Local and International Origins of Tuberculosis in New Zealand'.

The mapping of next-generation Illumina sequence data, the ability to detect variations in a single nucleotide or DNA building block in the genome (known as single nucleotide polymorphisms or SNPs) were some of the skills Claire has learnt which she is already using to advance her research in Tuberculosis. Claire described this workshop as "an invaluable experience providing her with the skills to undertake a thorough analysis of sequencing data."

Dr Michael Petridis, a research fellow in the Department of Microbiology and Immunology at the University of Otago, visited the laboratories of Professor William R. Jacobs Jr. at the Albert Einstein College of Medicine and Professor Kyu Y. Rhee at the Weill Cornell Medical College in New York in May 2016. During Michael's two-week stay he got first-hand experience in metabolome analysis from two world-leading experts in the investigation of mycobacterial physiology.

Metabolome analysis is a powerful technique and the missing key to undoubtedly reveal how changes in the transcriptome and proteome are reflected on a metabolite level. The collaborations with Prof Jacobs and Prof Rhee allowed Michael to develop the skills to generate, analyse and understand metabolome data. Michael is currently using these newly acquired skills in several projects comparing the metabolome of different knockout strains of mycobacteria. The results of this collaboration will be published in two manuscripts that are currently in preparation.

International visits

The Maurice Wilkins Centre runs an international engagement programme to build partnerships with priority international institutions that benefit the Centre's investigator network. In 2015 this involved MWC investigators travelling to China and hosting visiting delegations in New Zealand. The Centre also hosts visits from international and national scientists and officials.

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.

Maurice Wilkins Centre investigators hosted the following visitors to the centre in 2016:

- Prof Yuxing An, Guangzhou Sugarcane Industry Research Institute, Guangdong Provincial Bioengineering Institute, China
- Prof Bingxu Chen, Researcher, Plant Protection Research Institute, Guangdong Academy of Agricultural Sciences, China
- Prof Lihua Cheng, Guangdong University of Petrochemical Technology, China
- Professor Don Craig, Imperial College London, UK
- Assistant Professor Mike Curran, MD Anderson Cancer Center, USA
- Dr Jilly Evans, San Diego, USA
- Dr Richard Henderson, University of Cambridge, UK
- Prof Yiwen Lin, South China University of Technology, China
- Associate Professor Kerrie McDonald, University of Sydney, Australia
- Associate Professor Lance Miller, Wake Forest School of Medicine, USA
- Dr Mike Murphy, University of Cambridge, UK
- Dr Tom Parks, Oxford University, UK
- Professor Marc Pellegrini, Walter and Eliza Hall Institute of Medical Research, Australia

- Roger Williams, University of Cambridge, UK
- Dr Xiao Christopher Zhang, Territorial Life Science Core Facility, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Science, China
- Prof Yaping Zhang, Chinese Academy of Sciences, China

International and national officials and delegations

In 2016 Maurice Wilkins Centre investigators hosted or participated in visits by the following officials and delegations:

- *Guangzhou Institute of Biomedicine and Health (GIBH) Delegation, May 2016*
  - Prof Duanqing Pei, Director General
  - Prof Yinxiong Li, Director, Institute of Public Health
  - Dr Donghai Wu, South China Institute for Stem Cell Biology and Regenerative Medicine
- *China Science and Technology Exchange Centre Delegation, July 2016*
  - Dr Xinli Zhao, Deputy Director General
  - Dehua, Jiang, Director, Division of Americas and Oceania, Department of International Cooperation
  - Guojing, Liu, Program Officer, Division of Americas and Oceania, Department of International Cooperation
- *Guangzhou Institute of Biomedicine and Health (GIBH) Delegation, August 2016*
  - Prof Yinxiong Li, Director, Institute of Public Health
  - Prof Peng Li, South China Institute for Stem Cell Biology and Regenerative Medicine
  - Dr Donghai Wu, South China Institute for Stem Cell Biology and Regenerative Medicine
- *Jinan University Delegation, November 2016*
  - Prof Wencai Ye, Vice President
  - Prof Ke Ding, Dean, School of Pharmacy
  - Prof Weimin Chen, Vice Dean, School of Pharmacy
  - Prof Anding Xu, Vice Dean, Affiliated Hospital of Jinan University
  - Prof Yangqiu Li, Director, Blood Research Institute, Medical School
  - Ms Ruihong He, Section Chief, International Affairs Office
- *Guangdong Science and Technology Cooperation Center Delegation, November 2016*
  - Hanrong Wu, Director
  - Yan Yuan, Division Chief

- *China National Center for Biotechnology Development Delegation, December 2016*
  - Dr Zhifeng Dong, Deputy Director General
  - Dr Penghui Xu, Acting Chief, Division of International Cooperation
  - Ms Rui He, Biological Resources and Biosafety Division
- *Shanghai Institute of Materia Medica, Chinese Academy of Sciences (SIMM) Delegation, December 2016*
  - Prof Yang Ye, Deputy Director General
  - Prof Shuhong Guan, Director, Technology Transfer Department
  - Ms Dongying Lu, Technology Transfer Department
- *Taizhou Medical Hi-Tech Industrial Development Zone Delegation, December 2016*
  - Mr Qiufeng Gu, Director, Science and Technology Bureau
  - Mr Xiaohua Xu, Office of Taizhou Medical Hi-Tech Industrial Development Zone
- *The Chinese Embassy in New Zealand, December 2016*
  - Mr Wei WU, Chief of Science and Technology

External funding

Many of the projects within the Maurice Wilkins Centre research programme are supported by co-funding from other sources. The Centre also targets a proportion of its research budget to initiate and develop new projects to the point where they will become successful in securing competitive funding.

New Zealand funding

In 2016 Maurice Wilkins Centre investigators were awarded new grants worth more than $40 million from New Zealand funding sources (other than the TEC) for research projects to be carried out over the next one to five years, including over $16 million from the Health Research Council of New Zealand, $11 million from the Marsden Fund and $9.68 million from the Ministry of Business, Innovation and Employment Endeavour Fund.

International funding

In 2016 Maurice Wilkins Centre investigators secured new funding of $300,000 from international sources to support future research.

Governance and management

Maurice Wilkins Centre Board

In 2016 the MWC Board Members were; Mr Bill Falconer (Chair), Professor Conan Fee (University of Canterbury), Professor John Hosking (University of Auckland), Professor Jim Metson (University of Auckland), Ms Maxine Simmons (Biocatalyst Ltd), Professor Warren Tate (University of Otago) and Professor Mike Wilson (Victoria University of Wellington).

The MWC Board met three times in 2016; April, August and November. The Board reviewed and advised on strategy for international activities, a process for appointment of new non-management principal investigators and engagement with Māori led research organisations. They also approved recommendations from the March and September MWC Project Review Committees for allocation of resources to projects submitted for inclusion in this programme and monitored progress of the MWC research programme through the year for compliance with the funding mandate and budget.

Management Committee

The Maurice Wilkins Centre Management Committee consists of the following principal investigators; Professors Rod Dunbar (Director), Peter Shepherd (Deputy Director), Margaret Brimble, Bill Denny and John Fraser (University of Auckland), Professors Anthony Braithwaite, Greg Cook and Dave Grattan (University of Otago), Professor Emily Parker (Victoria University of Wellington) and Professor Ian Hermans (Malaghan Institute of Medical Research).

The Management Committee controls the operation of the Centre, under the guidance of the MWC Board and the Scientific and Clinical Advisory Boards. The Committee met eight times during 2016 and its focus was on the implementation of the 2015-2017 MWC Plan. This included implementing strategy and making recommendations of refinements in strategy to the MWC Board and managing the MWC research, training and outreach programmes.

Non-management Principal Investigators

This role includes leading specific areas of the research programme and potentially other initiatives of strategic importance. Six Non-management Principal Investigators appointed in 2015 continued in this position in 2016; Professor Vic Arcus (University of Waikato), Professor Mike Eccles (University of Otago), Associate Professor Shaun Lott, Associate Professor Rinki Murphy, Associate Professor Adam Patterson and Professor Cris Print (University of Auckland).

In 2016 Professor Gary Evans from Victoria University of Wellington was also appointed as a Non-management Principal Investigator.

Investigator Strategy Forum

This forum, convened by the MWC Director, is a representative body for all MWC principal and associate investigators and meets twice a year with one forum involving all principal investigators (management, non-management and emeritus) and a second forum which all principal and associate investigators are invited to attend.

The first forum, attended by principal investigators and associate investigators who were involved in leading flagship projects, was held in Wellington on the 17th August. The main item of business at this forum in 2016 was to monitor progress of the large-scale collaborative 'flagship' research projects.

The second forum, attended by principal and associate investigators, was held in Auckland on the 13th of December. The purpose of this forum was to update investigators on progress in 2016, identify areas of future strategic opportunity and address general items raised by investigators.

Scientific Advisory Board and Clinical Advisory Board

The members of the Scientific Advisory Board (SAB) for 2015 to 2017 are; Professor Peter Andrews (Australia), Dr Christopher Cooper (USA), Professor Suzanne Cory (Australia), Dr Jilly Evans (USA), Professor David James (Australia), Dr Warwick Tong (Australia) and Dr Jeanette Wood (Switzerland).

A meeting of the SAB was held on the 28th and 29th November at which they reviewed the progress of the MWC research programme.

Members of the Clinical Advisory Board (CAB) for 2015 to 2017 are; Professor Ian Reid (Chair, Auckland DHB and University of Auckland), Professor Mark McKeage (Auckland DHB and University of Auckland), Associate Professor Rinki Murphy (Auckland DHB, Counties Manukau DHB and University of Auckland), Dr George Laking (Auckland DHB and University of Auckland), Dr Helen Lunt (Canterbury DHB and University of Otago), Dr Sally Roberts (Auckland DHB and University of Auckland), Professor John McCall (Southern DHB and University of Otago), Dr Deborah Williamson (The Royal Melbourne Hospital and University of Melbourne), Associate Professor Jeremy Krebs (Capital and Coast DHB and University of Otago) and Dr James Ussher (Southern Community Laboratories and University of Otago).

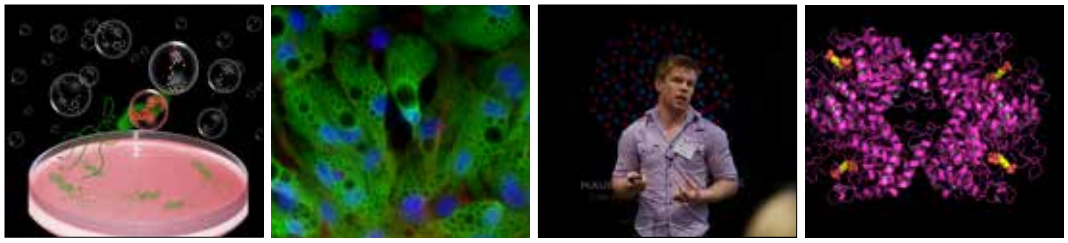
The CAB met on the 8th December to discuss strategies for future engagement of clinicians with the MWC research programme.

Project Review Committee

The Project Review Committee was convened twice, in March and September 2016, to review applications submitted in 2016 for inclusion in the Flexible Research Programme and make recommendations to the Management Committee and MWC Board on which applications should be approved.

In March the Project Review Committee consisted of 4 principal and 8 associate investigators from the University of Otago, University of Canterbury, Victoria University of Wellington, Massey University and the University of Auckland. They reviewed applications for Categories 2, 3 and 4 of the Flexible Research Programme.

In October the Project Review Committee consisted of 5 principal and 7 associate investigators from the University of Otago, Massey University, Victoria University of Wellington and the University of Auckland. The committee reviewed applications for Categories 2, 3 and 4 of the Flexible Research Programme.



Research Outputs

Publications

In 2016 research outputs from Maurice Wilkins Centre investigators included more than 450 peer-reviewed scientific papers published in international journals, and numerous patents granted, published or filed. Maurice Wilkins Centre contributed support to the following 93 scientific papers and reviews and 10 patents published or filed.

Six of the publications below were also featured on the front cover of their journal issue (marked with an asterisk). In particular, Distinguished Professor Margaret Brimble and her group had five of their papers featured as front covers, and in addition their paper 'Radiation Damage and Racemic Protein Crystallography Reveal the Unique Structure of the GASA/Snakin Protein Superfamily' in Angewandte Chemie International Edition was selected as a 'Very Important Paper' (an accolade that less than 5% of papers Angewandte Chemie International Edition papers receive). Dr Jodie Johnston and her colleagues' work, which is described in the highlight story on page 11, was also featured on the front cover of the journal Structure.

Papers and reviews

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Patents

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Presentations

The international significance of the research being done by Maurice Wilkins Centre investigators and their teams is demonstrated by more than 200 invitations to give international and national presentations in 2016. The presentations included invited lectures at conferences and seminars at academic institutions in Australia, Brazil, Canada, China, Cyprus, the Czech Republic, Denmark, Finland, France, Germany, Greece, India, Japan, the Philippines, Russia, Scotland, Singapore, Switzerland, Taiwan, the Netherlands, the United Kingdom, the United Arab Emirates and the United States of America, as shown in the diagram below.

Presentation highlights

Significant presentations given by Maurice Wilkins Centre investigators in 2016 include:

- Distinguished Professor Ted Baker, an emeritus principal investigator from the University of Auckland was awarded the Lawrence Bragg Medal from the Society of Crystallographers in Australia and New Zealand for "Distinguished contributions to science involving X-ray, neutron or electron diffraction and/or imaging, for work done primarily in Australia or New Zealand". As part of the acceptance of the award, Professor Baker gave a lecture entitled "Discovering the natural world through crystallography" at the 30th Conference of the Society of Crystallographers in Australia and New Zealand held at Hobart in late March. Professor Baker also gave the keynote presentation "Seeing molecules" at the Queenstown Molecular Biology meeting, held in Nelson, New Zealand.

- Distinguished Professor Margaret Brimble was invited to give five plenary presentations on her work in peptide chemistry at meetings held in 2016: the 17th International Biotechnology Symposium and Exhibition (Melbourne, Australia); the NYUAD International Chemistry Conference on Organic and Bioorganic Chemistry (Abu Dhabi, United Arab Emirates); The Royal Society Theo Murphy International Scientific Meeting (Buckinghamshire, UK); 31st Lady Masson Memorial Lecture (Melbourne, Australia). Prof Brimble also gave the RSC Australasian Lectureship plenary presentation at locations throughout Australia and New Zealand (at Victoria University of Wellington and Massey University, New Zealand, and in Australia at University of Tasmania, Monash University, University of Western Australia and Curtin University).
- Professor Greg Cook was invited to give the keynote presentation "Persisting on thin air: the role of atmospheric hydrogen in starvation, adaptation to hypoxia, and survival of mycobacteria and streptomycetes" at the 13th International Symposium on the Genetics of Industrial Microorganisms, held in Wuhan, People's Republic of China in October. He also gave a plenary presentation, titled "Regulation of cytochrome bd in mycobacteria in response to carbon and oxygen availability" at the 19th International Conference on Oxygen Binding and Sensing Proteins (O2BIP) held in Hamburg, Germany.
- Professor Dave Grattan was invited to give a plenary presentation at the Perinatal Society of New Zealand Annual Meeting in Wellington, titled "Prolactin and the neuroendocrine adaptation of the maternal brain". Professor Grattan also gave two plenary presentations of his research in Dunedin, NZ at events for the Brain Health Research Centre and the Edgar Centre on Diabetes and Obesity Research.
- Professor Emily Parker was invited to give the plenary presentation titled "Twisting tails and curious channels deliver both reaction chemistry and allostery for the phosphoribosyltransferases" at the 23rd IUPAC Conference on Physical Organic Chemistry in Sydney, Australia in July 2016.
- Professor Rod Dunbar gave a plenary presentation titled "Immune therapy for cancer" at the Shanghai Queenstown Molecular Biology meeting, Shanghai, Peoples Republic of China.
- Professor Geoff Jameson was invited to give the keynote presentation titled "Origin of Life Scenarios: Chemical and physical properties of oligonucleotides and their constituents at extremes of pressure and temperature" at the New Zealand Institute of Chemistry meeting in Queenstown, New Zealand.

Collaborations

The Maurice Wilkins Centre contributes to and benefits from an extensive network of national and international collaborations that have 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 and national reach of these collaborations is shown in the diagram below.

New academic collaborations

- Allergan (USA)
- Australian Institute of Marine Science (Australia)
- British Columbia Cancer Agency (Canada)
- Cedars-Sinai Medical Centre (USA)
- Consejo Superior de Investigaciones Cientificas (Spain)
- Defence Science and Technology Laboratory (UK)
- Edith Cowan University (Australia)
- Estacion Experimental del Zaidin (Spain)
- Goethe University Frankfurt (Germany)
- Helmholtz Centre for Ocean Research (Germany)
- Institute of Basic Science (Korea)
- Jinan University (China)
- London School of Tropical Hygiene and Medicine (UK)

- Ludwig Maximilian University of Munich (Germany)
- Moffitt Cancer Center (USA)
- Northern Arizona University (USA)
- Peking University (China)
- Royal Veterinary College (UK)
- Sanford Burnham Prebys Medical Discovery Institute (USA)
- Stowers Institute for Medical Research (USA)
- Swiss Federal Institute of Technology (Switzerland)
- The Peter Doherty Institute for Infection and Immunity (Australia)
- University of Bern (Switzerland)
- University of Calcutta (India)
- University of Central Florida (USA)
- University of Georgia (USA)
- University of Glasgow (UK)
- University of Leiden (Netherlands)
- University of Liverpool (UK)
- University of Lodz (Poland)
- University of London (UK)
- University of North Carolina (USA)
- University of Oslo (Norway)
- University of Pavia (Italy)
- University of Sao Paulo (Brazil)
- University of Sargodha (Pakistan)
- University of Texas South Western (USA)
- University of the Sunshine Coast (Australia)
- University of Utah (USA)
- University of Vienna (Austria)
- University of Western Australia (Australia)
- University of Zurich (Switzerland)

Continuing academic collaborations

North America

- McGill University (Canada)
- University of British Columbia (Canada)
- York University (Canada)
- Albert Einstein College of Medicine (USA)
- Arkansas State University (USA)
- Boston College (USA)
- Boston University (USA)
- Brandeis University (USA)
- Brown University (USA)
- Colorado State University (USA)
- Cornell University (USA)
- Fox Chase Cancer Center (USA)
- Global Alliance for TB Drug Development (USA)
- Harvard University (USA)
- Hendrix College (USA)
- Houston Methodist Research Institute (USA)
- Johns Hopkins University (USA)

- MD Anderson Cancer Center, University of Texas (USA)
- Methodist Medical Center (USA)
- National Institutes of Health (USA)
- Rochester Institute of Technology (USA)
- Sanford Burnham Medical Research Institute (USA)
- Stanford University (USA)
- Stony Brook University (USA)
- University of California (USA)
- University of Colorado (USA)
- University of Houston (USA)
- University of Illinois at Chicago (USA)
- University of Michigan (USA)
- University of Minnesota (USA)
- University of Missouri (USA)
- University of North Carolina (USA)
- University of Oklahoma (USA)
- University of Pennsylvania (USA)
- University of Pittsburgh (USA)
- University of Tennessee (USA)
- University of Toledo (USA)
- University of Virginia (USA)
- University of Washington (USA)
- Vanderbilt University (USA)
- Wake Forest University (USA)
- Weill Cornell Medical College (USA)

UK and Europe

- University of Eastern Finland (Finland)
- Pasteur Institute (France)
- Université Pierre et Marie Curie (France)
- Jacobs University (Germany)
- Johannes Gutenberg University (Germany)
- Max Planck Institute for Infection Biology (Germany)
- Max Planck Institute for Molecular Genetics (Germany)
- University of Kassel (Germany)
- Vilnuis University (Lithuania)
- Leiden University (Netherlands)
- MAASTRO Clinic (Netherlands
- University of Maastricht (Netherlands)
- University of Bergen (Norway)
- Karolinska Institute (Sweden)
- University of Gothenburg (Sweden)
- Uppsala University (Sweden)
- Aston University (UK)
- Birmingham University (UK)
- Essex University (UK)
- Francis Crick Research Institute (UK)
- Imperial College London (UK)
- MRC Mitochondrial Biology Unit (UK)
- Queen Mary University of London (UK)
- University of Cambridge (UK)

- University of Cardiff (UK)
- University of Huddersfield (UK)
- University of Lincoln (UK)
- University of Liverpool (UK)
- University of Manchester (UK)
- University of Nottingham (UK)
- University of Oxford (UK)
- University of St. Andrews (UK)
- University of Southampton (UK)

Asia Pacific

- Australian National University (Australia)
- Centenary Institute (Australia)
- Children's Medical Research Institute (Australia)
- Commonwealth Scientific and Industrial Research Organisation (Australia)
- Garvan Institute of Medical Research (Australia)
- La Trobe University (Australia)
- Macquarie University (Australia)
- Monash University (Australia)
- Murdoch Children's Research Institute (Australia)
- Peter MacCallum Cancer Centre (Australia)
- QIMR Berghofer Medical Research Institute (Australia)
- Royal Melbourne Institute of Technology (Australia)
- Telethon Kids Institute (Australia)
- University of Melbourne (Australia)
- University of New South Wales (Australia)
- University of Queensland (Australia)
- University of Sydney (Australia)
- University of Technology Sydney (Australia)
- University of Wollongong (Australia)
- Walter and Eliza Hall Institute (Australia)
- Guangzhou Institute of Biomedicine and Health (China)
- University of Hong Kong (Hong Kong)
- Indian Institute of Science (India)
- Okinawa Institute for Science and Technology (Japan)
- Tokyo Institute of Technology (Japan)
- University of Hokkaido (Japan)
- National University of Singapore (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 this 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 Maurice Wilkins Centre also partners with established companies, and the knowledge and expertise developed by its investigators 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 34 of this report. The Centre's investigators also act as consultants for a number of national and international companies.

In 2016 the expertise of Maurice Wilkins Centre investigators was sought by:

- Abcam (UK)
- Adrenomed
- Alder Biopharmaceuticals (USA)
- Allergan Pharmaceuticals (USA)
- ArborVita Associates LLC (USA)
- Ardea Biosciences Inc (USA)
- Astra Zeneca
- Auckland Clinical Studies Limited
- Auckland UniServices Ltd
- Avalia Immunotherapies Ltd
- Bayer Animal Health Germany
- Biomatters Ltd
- BioMotiv (USA)
- Biotelliga Ltd
- BLIS Technologies Ltd
- Caldera
- Callaghan Innovation
- Cancer Research (UK)
- Canterbury Scientific Ltd
- Claridges Organic Ltd
- CoDa Therapeutics (NZ) Ltd
- CoDa Therapeutics, Inc. (USA)
- Comvita Ltd
- Connovation Ltd
- Dairy Goat Cooperative Ltd
- Deosan NZ
- Fonterra Co-operative Group
- Gilead Sciences Ltd
- GlycoSyn
- Glythera
- Hi-Aspect Ltd
- Innate Therapeutics Ltd

- L2 Diagnostics, Ltd LLC (USA)
- Landcare Research NZ Ltd
- LFB USA
- Medtronic NZ Ltd
- Merck Sharp & Dohme
- Metavention (USA)
- National Institutes of Health USA
- New Zealand Genomics Limited
- New Zealand Leather and Shoe Research Association
- New Zealand Pharmaceuticals Ltd
- Ossis Ltd
- Plant and Food Research
- Recombinetics Inc (USA)
- Roche Products Ltd
- Seattle BioMed (USA)
- Seattle Genetics (USA)
- Syngenta
- Threshold Pharmaceuticals (USA)
- Upside Biotechnologies
- Upstream Medical Technologies 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, Maurice Wilkins Centre investigators are involved with international organisations such as the Alliance for TB Drug Development

Awards and honours

International and national honours awards to Maurice Wilkins Centre investigators, affilates, and students in 2016:

Medicinal Chemistry Hall of Fame
Distinguished Professor Bill Denny was inducted into the American Chemical Society Division of Medicinal Chemistry Hall of Fame at an August 23 ceremony in Philadelphia (see highlight story on page 7 for more details).

Lawrence Bragg Medal
Distinguished Professor Ted Baker, an emeritus principal investigator from the University of Auckland was awarded the Lawrence Bragg Medal from the Society of Crystallographers in Australia and New Zealand for "Distinguished contributions to science involving X-ray, neutron or electron diffraction and/or imaging, for work done primarily in Australia or New Zealand".

New Zealand Association of Scientists award
Cancer biologist Professor Antony Braithwaite, a principal investigator from the University of Otago, has received the New Zealand Association of Scientists (NZAS) Shorland Medal in recognition of his work on the tumour suppressor protein p53 and other cancer associated genes. The award acknowledges major and continued research that has significantly contributed to an understanding of cancer biology.

Marsden medal
Distinguished Professor Margaret Brimble, a principal investigator from the University of Auckland, received the 2016 Marsden Medal from the New Zealand Association of Scientists (NZAS) to honour her lifetime of outstanding service to science.

Blake Leader Award
Dr Siouxsie Wiles, an associate investigator from the University of Auckland, received national recognition when she was named a Blake Leader 2016 from the Sir Peter Blake Trust. This award recognises inspirational leaders who have determination, a will to succeed and a belief in achieving extraordinary things. Dr Wiles is a renowned science communicator and microbiologist who uses bioluminescence to study infectious disease.

James Cook Research Fellowship
Professor Debbie Hay, an associate investigator from the University of Auckland was awarded the James Cook Research Fellowship from the Royal Society of New Zealand for her research "Medicines and mechanisms of migraine". Debbie will receive two years' funding as a part of the fellowship for her research. Debbie was also awarded the British Journal of Pharmacology Editor Performance Award for 2016.

Hercus Fellowships
Affiliate investigators Dr Ghader Bashiri and Dr Christopher Walker have received Sir Charles Hercus Health Research Fellowships in the latest round of funding from the Health Research Council. Both investigators will each receive four years' funding as part of the fellowships to pursue their respective areas of research.

Oxford Nuffield Medical Fellowship
MWC affiliate investigator and PhD graduate Dr Imogen Roth was successful in obtaining a Nuffield Medical Fellowship to work at Oxford University in the United Kingdom on inflammatory disease Barrett's Oesophagus. She took up the fellowship in early 2017.

Royal Society of New Zealand Fellows
Three Maurice Wilkins Centre principal investigators have been announced as Fellows of the Royal Society of New Zealand this week, an honour recognising their international distinction in research and scholarship. Professor Tony Merriman, Deputy Director Peter Shepherd and Director Rod Dunbar join 16 other Maurice Wilkins Centre investigators already elected as Fellows of the Royal Society. The Fellowships are annually conferred to the nation's top researchers for demonstrating distinction in research or in the advancement of science, technology or the humanities.

Fellow of the Royal Society of Chemistry (UK)
Professor Vic Arcus, a principal investigator from the University of Waikato, was announced a fellow of the Royal Society of Chemistry, United Kingdom, in 2016.

Roche Translational Research Fellowship
Dr Roslyn Kemp, an associate investigator from the University of Otago, was awarded the inaugural Roche Translational Research Fellowship for her work investigating the immune response within cancer cells to improve treatment outcomes for bowel cancer patients. This award was announced at the NZ Society of Oncology Annual Conference and will provide Dr Kemp with $30,000 of funding to put towards her cancer research.

Hatherton Award
Dr Jason Busby from the University of Auckland was awarded the Hatherton Award from the Royal Society of New Zealand for his paper titled 'The BC component of ABC toxins is an RHS-repeat-containing protein encapsulation device' which was published in Nature in 2013.

Thermofisher Award for Excellence in Molecular Biology
Associate Professor Jane Allison won the Thermofisher award for 'Excellence in Molecular Biology' at the Queenstown Research Week where she gave an award talk titled "From physical chemistry to viral evolution"

The Maurice Wilkins Centre also congratulates the numerous investigators and students who received local and institutional honours and student prizes throughout 2016.

Summary

Broad category	Detailed Category	2015	2016
FTEs by category	Principal investigators	1.70	1.72*
	Associate investigators	2.09	2.50*
	Postdoctoral fellows	7.29	13.98*
	Research technicians	0.57	0.63*
	Administrative/support	2.81	3.27
	Research students	14.58	18.44**
	Total	**29.04**	**40.54**
Headcounts by category	Principal investigators	19	20
	Associate investigators	145	155
	Postdoctoral fellows	20	24
	Research technicians	2	4
	Administrative/support	7	5
	Research students	23	69
	Total	**216**	**277**
Peer reviewed research outputs by type	Journal articles	84	93
	Book Chapter	1	1
	Conference proceedings	9	-
	Total	**94**	**94**
Value of external research contracts awarded by source	Vote Science and Innovation contestable funds	2,831,00	2,350,770
	Domestic – other non-Govt	372,977	431,677
	Overseas	2,067,798	1,153,198
	Other	117,500	153,769
	Total	**5,389,275**	**4,089,414**
Commercial activities	Patent applications	4	10
	Patents granted	5	0
Students studying at CoRE by level	Doctoral degree	21	58
	Other	2	11
	Total	**23**	**69****
Number of students completing qualifications by level	Doctoral degree	-	5
	Other	1	7
	Total	**1**	**12**
Immediate post-study graduate destinations	Employed in NZ	1	4
	Employed overseas	-	5
	Unknown	-	3
	Total	**1**	**12**

*In addition to the directly funded FTE in the above table in 2016, Principal Investigators contributed an additional 1.62 FTE in time only and 0.9FTE was co-funded; Associate Investigators contributed an additional 0.71 in time only and 4.29 FTE was co-funded; Postdoctoral fellows and Research technicians had additional 3.97 FTE and 3.65 FTE co-funded respectively.

**Research students had an additional 38.22 EFT co-funded from other sources.

Summary Financial Statement 2016

Funding summary for the year ended 31 December 2016

	Actuals
	$000
Funding received	
Tertiary Education Commission grant	7,082
Total Funding received	**7,082**
Expenditure	
Salaries and salary related costs	2,324
Overheads	2,452
Project Costs	1,903
Travel	340
Postgraduate students	526
Total Expenditure	**7,545**
Net Surplus/(Deficit)	**- 463**

This report covers the period from 1 January 2016 - 31 December 2016 and details funding received and funds distributed to collaborative partners of the CoRE.

All amounts are shown exclusive of Goods and Service tax (GST)

In 2015 the CoRE carried forward a net surplus of 2,290. This surplus has been added to the 2016 income to fund the CoRE's research programme in 2016. The CoRE therefore has a net surplus of 1,827 that will be carried forward into 2017 to fund future expenditure of the CoRE.

Directory

Governing Board

Mr Bill Falconer (Chair)
Prof Conan Fee
Prof John Hosking
Prof Jim Metson
Ms Maxine Simmons
Prof Warren Tate
Prof Mike Wilson

Scientific Advisory Board

Prof Peter Andrews (Chair)
Dr Chris Cooper
Prof Suzanne Cory
Dr Jilly Evans
Prof David James
Dr Warwick Tong
Dr Jeanette Wood

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Prof Peter Shepherd (Deputy Director)	Department of Molecular Medicine and Pathology	University of Auckland
Prof Antony Braithwaite	Department of Pathology	University of Otago
Prof Margaret Brimble	School of Chemical Sciences	University of Auckland
Prof Greg Cook	Microbiology and Immunology	University of Otago
Prof Bill Denny	Auckland Cancer Society Research Centre	University of Auckland
Prof John Fraser	Faculty of Medical and Health Sciences	University of Auckland
Prof Dave Grattan	Department of Anatomy	University of Otago
Prof Ian Hermans	Malaghan Institute of Medical Research	
Prof Emily Parker	Department of Chemistry	University of Canterbury

Principal investigators (non-management)

Prof Vic Arcus	Department of Biological Sciences	Waikato University
Prof Michael Eccles	Department of Pathology	University of Otago
Prof Gary Evans	Ferrier Institute	Victoria University
Assoc Prof Shaun Lott	School Of Biological Science	University of Auckland
Assoc Prof Rinki Murphy	Department of Medicine	University of Auckland
Assoc Prof Adam Patterson	Auckland Cancer Society Research Centre	University of Auckland
Assoc Prof Cris Print	Department of Molecular Medicine and Pathology	University of Auckland

Principal investigators (emeritus)

Prof Ted Baker	School of Biological Sciences	University of Auckland
Prof Garth Cooper	School of Biological Sciences	University of Auckland
Prof Peter Hunter	Auckland Bioengineering Institute	University of Auckland

Associate investigators

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Assoc Prof Bob Anderson	Auckland Cancer Society Research Centre	University of Auckland
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Dr Adam Bartlett	Department of Surgery	University of Auckland
Prof Chris Battershill	Faulty of Science and Engineering	University of Waikato
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Assoc Prof Mik Black	Department of Biochemistry	University of Otago
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Prof Stefan Bohlander	Department of Molecular Medicine and Pathology	University of Auckland
Mr Michael Booth	Waitemata Specialist Centre	Waitemata District Health Board
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Prof Vicky Cameron	Department of Medicine	University of Otago, Christchurch
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*Full support provided by MWC. All other students received partial support.

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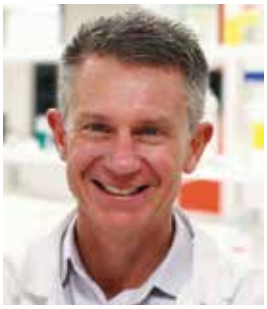

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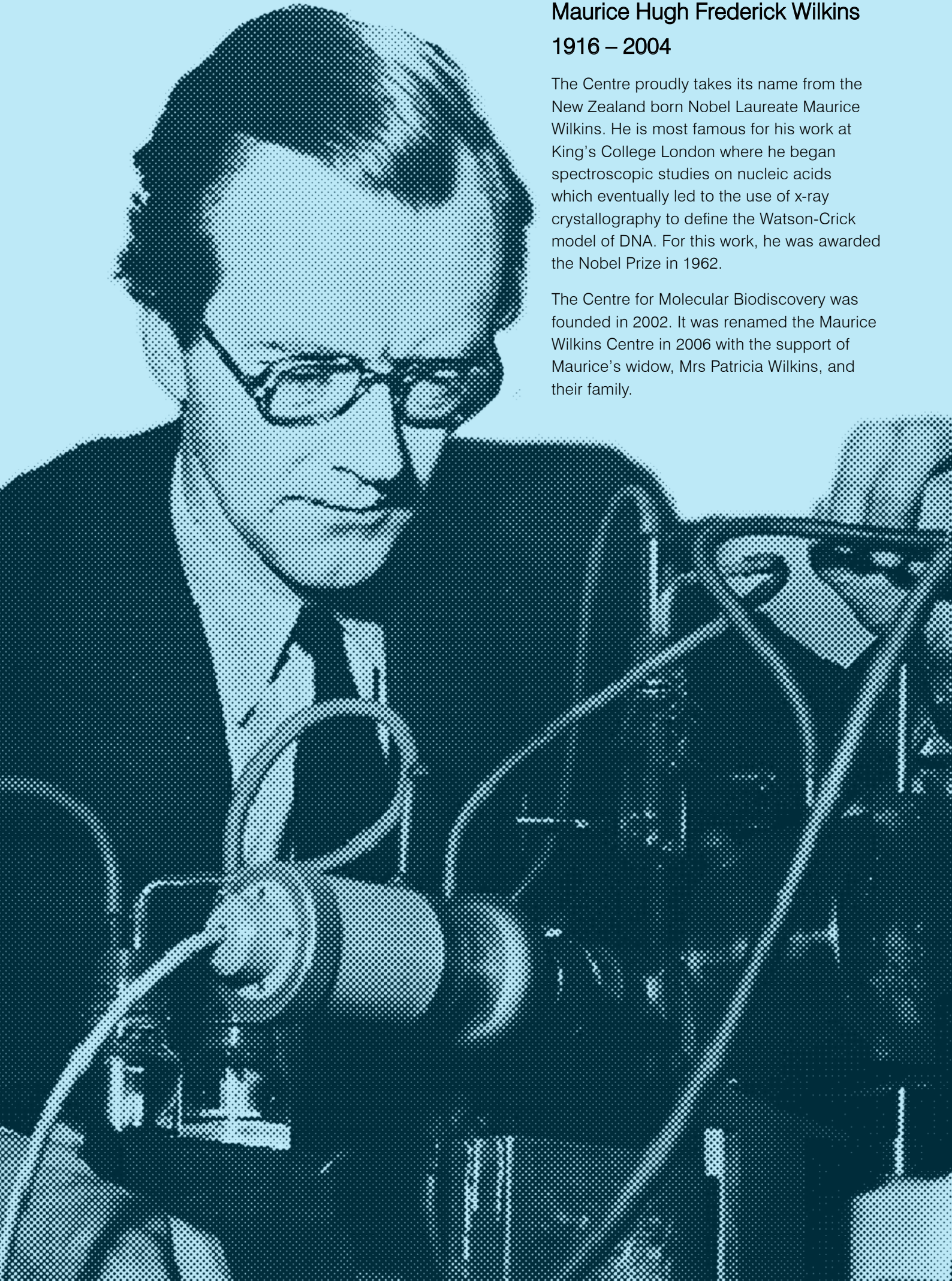

Maurice Hugh Frederick Wilkins
1916 – 2004

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.