

MAURICE WILKINS CENTRE

New Zealand's Centre of Research Excellence targeting human disease

Annual Report 2018

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 2018 it comprised of 203 investigators throughout the country, over 240 early-career affiliates, and 13 clinical associates, linking researchers and clinicians from six Universities, three Crown Research Institutes, one private research institute and nine district health boards. These investigators represent most of New Zealand's expertise in discovering new drugs, vaccines and diagnostic tools that proceed to clinical trials. The Centre has also partnered with two Māori organisations to improve the health outcomes of Māori and Pacific peoples.

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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Director's Report



Looking back over 2018 there is again plenty for the MWC to celebrate – from spectacular individual milestones, such as those achieved by Distinguished Professor Margaret Brimble (p.9) to outstanding science from our inter-disciplinary multi-institutional research teams. It's clear that the MWC continues to fulfil its role bringing together New Zealand's top research talent to develop new therapies and diagnostics for human disease.

One highlight marks a new benchmark in bringing MWC research programmes to fruition, and deserves some extra background and explanation. In 2018 inventions by MWC investigators drew \$58M from private investors. This follows over

\$12M of private investment in other inventions from MWC investigators over 2016 and 2017 – but the scale of the investment in 2018 sets a new annual record.

Why is private investment in MWC discoveries so important – or even necessary? Simply put, this is part of the process of research commercialisation, where discoveries in research laboratories are licensed into companies that can translate them into products. While the MWC can drive discoveries that will lead to new medicines and cell therapies, the costs of bringing those treatments through clinical trials to market can reach over a billion dollars – and unfortunately the MWC's budget doesn't stretch quite that far ...

When our projects mobilise private investment, it's a sign that sophisticated investors value our research very highly, and believe our inventions have a good chance of becoming therapeutic breakthroughs. In practice these inventions need to be literally world-leading, since the patents that underpin commercial investment are only awarded to our discoveries if they are proven to be unique world-firsts. MWC researchers also celebrate the fact that private investment means our research is more likely to have direct impact on patients' lives. Many of our scientists begin their path into biomedical research out of a wish to use their skills to alleviate suffering. So it's particularly satisfying to see their work culminate in new therapies being offered to patients in clinical trials.

How do MWC investigators set up their projects so they can lead to clinical trials? It certainly takes patience. First they need to be expert in their fields – typically a PhD followed by several years of post-doctoral research. As well as assimilating new knowledge wherever it pops up, our investigators need to generate ideas of their own – creative flashes of insight enabled by their deep understanding of the problems they are tackling. They also need to anticipate how the medicine might be used, effectively steering their science towards unmet need. Achieving this combination – world-first patentable discoveries, targeted clearly at unmet clinical need – is no mean feat. Successful private investment into so many MWC projects indicates we are now carrying off this feat with reassuring regularity. And crucially the MWC is also helping ensure the torch is being passed from the early kiwi pioneers in this field to a new generation of innovators, who are clearly building on their mentors' knowledge and success.

Of course propelling new therapies into clinical trials is by no means the only positive impact of MWC research. The MWC focuses much of its investment on fundamental research that will benefit society in other ways. For example, as highlighted on p.15, MWC investigators are leading new approaches to one of the scourges of New Zealand society, rheumatic fever. This work spans new basic science to understand how Group A Streptococcus bacteria cause the disease, right through to translational work developing a new vaccine to prevent rheumatic fever. The work is underpinned by deep concern about the devastation to the wellbeing of Māori and Pacific communities that this disease causes.

Similar concerns about health inequities have driven the MWC to partner with Māori health organisations in Northland and the East Cape. The establishment of our joint research centres with Moko Foundation in Kaitaia and Ngāti Porou Hauora in Te Puia Springs mark a new level of partnership with Māori. These partnerships encompass not only locally-led approaches to health research questions but also vastly improved sharing of knowledge and insights between Māori communities and our national network of scientists and clinicians. Over time these partnerships are also expected to improve appreciation of the value of science to these communities, and accelerate the flow of talented Māori into science leadership. As the government asks the research community to take holistic approaches to improving the wellbeing of our disadvantaged communities, the MWC's widening network seems very well placed to respond.

As always it's our people who drive every element of our success. It's been a great pleasure working with my colleagues on the MWC's management team, with our wide



network of talented investigators, and with our operations team led by our indefatigable Research Operations Manager, Rochelle Ramsay. We've been very well supported by our Board and our partner institutions, and we are delighted to see inter-institutional co-ordination continuing to grow year on year. This year I'd like to pay particular tribute to our Deputy Director Peter Shepherd, who has led so many of our outreach and strategic activities, from the establishment of our joint research centres with Māori, to our professional development programme for secondary school biology teachers. I'd also like to publicly thank our Early Career Steering Group who are driving innovative events and programmes to develop the next generation of leaders in New Zealand bio-medicine. We hope you enjoy reading about all our people and their outstanding contributions to society in the following pages.

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.





Professor Margaret Brimble, recently made a dame by the Royal Society of London in 2018 Image courtesy of Margaret Brimble

Highlights

Margaret Brimble elected a Fellow of the Royal Society of London

Professor Dame Margaret Brimble, MWC Principal Investigator at the University of Auckland, added a wonderful achievement to her exceptional scientific career in 2018 – becoming the first New Zealand woman elected a Fellow of the Royal Society of London.

"This Fellowship really is an honour and a milestone not just for women scientists in New Zealand but for our science sector in general and for New Zealand. To have one of our leading scientists recognised in this way is a wonderful achievement," says University of Auckland Vice-Chancellor Stuart McCutcheon.

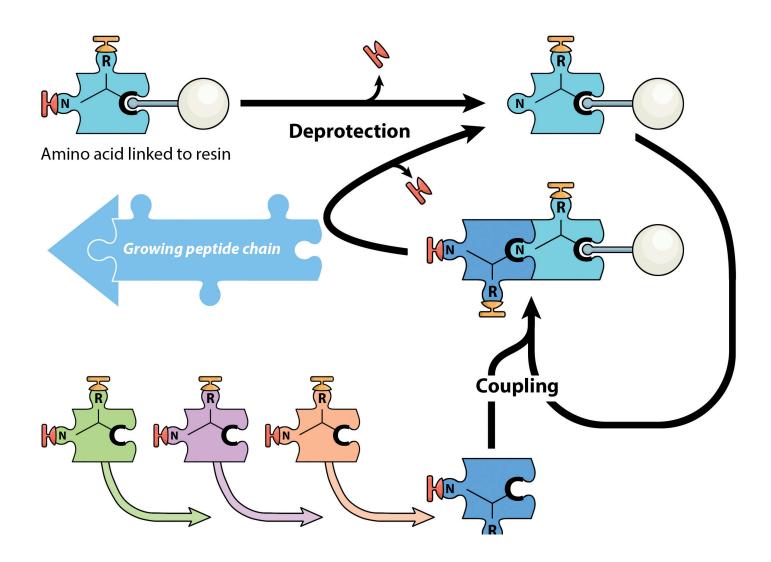
Professor Brimble, born and raised in Auckland, attended the University of Auckland and has carried out almost all her research in New Zealand. As a young woman she was encouraged to consider a career in medicine but the horror of being asked to dissect a rat in biology class steered her towards chemistry, a field she had always loved as an undergraduate.

Her work sits at the interface of chemistry and medicine and focuses on developing bioactive compounds from natural products such as marine algae or fungi. These compounds are synthesised in larger amounts for further research and development as potential drugs to treat a range of diseases including cancer and infectious disease. Developing these compounds can take several years.

Professor Brimble's research in drug discovery in New Zealand is pioneering, developing a new drug called trofinetide for Rett Syndrome, Fragile X Syndrome and autism disorders. Trofinetide is now undergoing phase III human clinical trials, the last stage of development before a drug is released for use in patients. The drug is the fourth drug discovered in New Zealand to make it to this final stage of development. A second of her drug candidates NNZ-2591 also demonstrated positive effects in Phelan-McDermid syndrome pre-clinical model and is being progressed to the clinic. Importantly, the world's leading drug regulatory body, the US Food and Drug Administration, recognising it as a novel breakthrough in the field of neurology, has granted trofinetide 'orphan drug status', meaning that it is being fast-tracked through the usual approval application channels.

Professor Brimble's research group is also developing innovative chemical technology to generate cancer vaccines. This work is being translated for clinical use by the spin-out company SapVax LLC which is developing a pipeline of products for the treatment of different cancers.

Among her many awards over the years, Professor Brimble was a recipient of the 2012 RSNZ Rutherford Medal (New Zealand's top science prize) and was named the 2007 L'Oreal-UNESCO Women in Science laureate in materials science for Asia Pacific. Professor Brimble is a passionate advocate for women in science and regularly speaks to groups of young women to encourage them to consider science as a career. To cap another brilliant year, Professor Brimble was honoured as a Dame Companion of the New Zealand Order of Merit for services to science on New Year's Day 2019.



Peptide chemistry allows scientists to build peptides by joining together amino acids in a specific, pre-determined sequence. This technique is being used to design peptides to be used as drugs or vaccines for different diseases.

Image designed by Dr Mia Jullig

Building blocks for new medicines

The MWC uses New Zealand's outstanding medicinal chemistry expertise to discover new medicines. A particular kind of chemistry that uses natural building blocks is now being used to make new medicines for cancer, infectious disease and metabolic illness.

Inside all the cells of your body, tiny biological factories work tirelessly to produce the molecules your body needs. Proteins – and their smaller cousins called peptides – are made in your cells by joining together amino acids, like a string of beads. There are 20 different amino acids, and the final shape and function of each protein or peptide is determined by the order in which those 20 different amino acids appear. It's as if you have 20 different types of bead, each a different colour and shape, and you're stringing them onto a thread of stretched elastic. Let the elastic go and the beads collapse into a blob – with the order of the coloured beads determining the final shape of the blob.

Peptide chemistry allows peptides and proteins to be built in the same way – by joining amino acids together – but this time in a machine supplied with amino acids as chemical building blocks. For some years, the MWC has invested in developing its peptide chemistry capability, centred around the laboratory of Professor Dame Margaret Brimble.

Dame Margaret has taken peptide chemistry to new levels, and her team is now supplying novel molecules to teams right across the MWC, from new vaccines to treat cancer, to new antibiotics, to new hormones for treating obesity and diabetes. Some of this work has involved making new building blocks – adding new molecular tags such as sugars and fats to the amino acids, and in many cases making building blocks that don't occur in the human body at all, such as those that appear in bacterial proteins. These novel building blocks are opening up opportunities for all kinds of new molecules with potential as therapies and several have featured in high profile international chemistry journals.

By way of example Dame Margaret says her team originally developed and patented new methods to add fat molecules ("lipids") to peptides in order to make cancer vaccines. "These molecules resemble cell wall components from bacteria so they are really powerful stimulants of the human immune system," she says. At the same time she was working with MWC investigators Professor Debbie Hay and Associate Professor Kerry Loomes to synthesise metabolic hormones for the treatment of diabetes and obesity. "Debbie and Kerry wanted to make new versions of these hormones that would persist in the body for much longer than their natural versions so they wouldn't need to be injected as often. We quickly realised our cancer vaccine "lipidation" technology could help," says Dame Margaret.

"We soon found that the lipidated versions of these hormones – called amylin and CGRP – worked very well in animal models," says Kerry. "These new molecules have now been licensed to a New Zealand pharmaceutical company and are being developed towards clinical trials," says Debbie.

"This shows the power of the leading edge technology within the Maurice Wilkins Centre to impact many different fields," said the centre's director Professor Rod Dunbar. "Chemistry developed for cancer therapy has spawned unexpected progeny across our whole research programme."





Top: MWC Principal Investigators Professor Tony Merriman and Professor Peter Shepherd, with Conor O'Sullivan from the Moko Foundation, at the opening of Te Rangawairua o Paratene Ngata.

Bottom: (I-r) Dr Lance O'Sullivan (Moko foundation), Mr Matiu Kingi, Sir Hekenukumai Puhipi (Sir Hector Busby), Mr Eru Harawira and Mr Conor O'Sullivan.

Photos courtesy of Prof Peter Shepherd.

Celebrations as regional research centres open

The MWC continued to strengthen its relationships with Māori communities in 2018. MWC Deputy Director Professor Peter Shepherd and Principal Investigator Professor Tony Merriman, in particular, have led the way in forging these relationships, culminating in the opening of two research centres, on the East Coast and in Northland.

Setting the scene, the MWC and Ngāti Porou Hauora co-organised 'Tātai Oranga: Joining forces to tackle metabolic conditions', a landmark conference held on the North Island's East Coast in April. Attended by a large number of local community and iwi members, it featured presentations by leading scientists and clinicians in the metabolic disease field from around New Zealand and overseas.

A few months later, the first of two Maurice Wilkins Centre-partnered regional research centres became a reality. The Te Rangawairua o Paratene Ngata Research Centre, led by Ngāti Porou Hauora, was officially opened on Thursday 2 August at Te Puia Springs Hospital. Named after the late Dr Paratene (Pat) Ngata, a renowned East Coast GP widely recognised for his contributions to improving Māori health, the centre was opened with representatives from the MWC, national and international health experts, policy makers and funders joining with members of the local community to celebrate a further realisation of Dr Pat's aspirations.

Professor Shepherd said the MWC whole-heartedly shares Dr Pat's vision. "We want to change the world by working together. To solve these problems, it needs all of our efforts together. We are proud and honoured to be part of this."

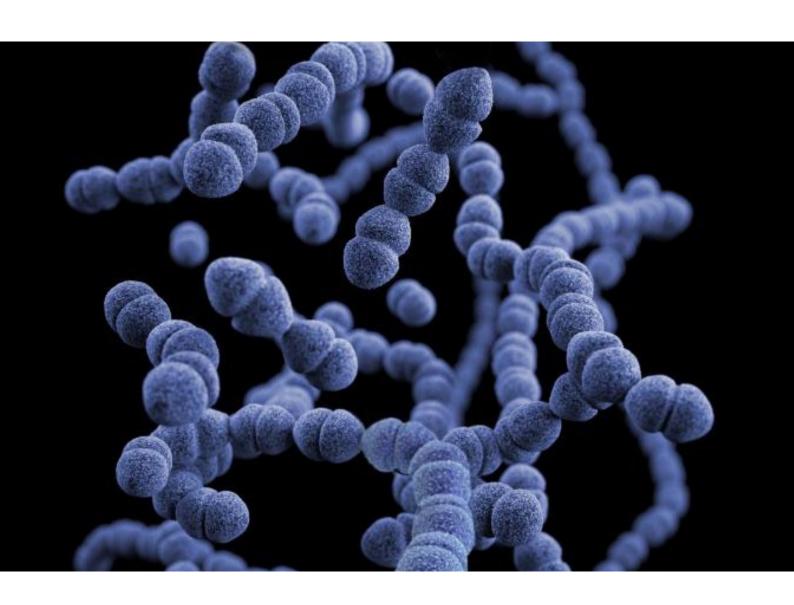
The Centre will initially be involved in studies to assess the links between genetic factors and metabolic disease risk in Māori, and in the MWC's 'Sugar in Schools Study' to measure the ability of New Zealand school children to absorb fructose. It will also develop its own research questions based on health issues of most importance to Ngāti Porou people.

Soon after, the Waharoa ki te Toi Health Research Centre, a partnership between The Moko Foundation and the MWC, officially opened in Kaitaia. Waharoa ki te Toi had already commenced testing of patients as part of the nationwide 'CREBRF Study', which is looking at potential links between peoples' genetics and their risk of developing metabolic diseases such as diabetes and heart disease.

"Delivering precise treatments based on our individual genetic characteristics is going to be a big part of our future," said Dr Lance O'Sullivan, Founder and Chairman of The Moko Foundation. "This research is an exciting opportunity to further that knowledge and reduce the inequities in healthcare outcomes that are so prevalent in many communities throughout New Zealand."

Kaumatua Sir Hekenukumai Puhipi (Sir Hector Busby) is the centre's patron. Dr Joel Pirini, Clinical Director of the Waharoa kit e Toi, said: "Just like [Papa Hector] used the stars and tides on his journey of cultural discovery, Waharoa ki te Toi will be searching for genetic variants or genetic stars that will allow us to chart a pathway to better health."





MWC scientists are developing novel early diagnostic tools and vaccines to identify and target Group A Streptoccocus infection .

3D computer generated image above depicts a gram positive streptococcus.

Image courtesy of Dan Higgins (Centres for Disease Control and Prevention)

Developing a vaccine to prevent rheumatic fever

Group A Streptococcus (GAS) infection is widespread around the world, but causes particularly serious complications in New Zealand – especially rheumatic fever that damages the heart. Maurice Wilkins Centre scientists have developed exciting new technology that offers hope for a vaccine to prevent GAS infection and its damaging consequences.

Although GAS infection is common in New Zealand, it is Māori and Pacific children that bear most of its burden. Rheumatic fever that follows some GAS infections is far more common in New Zealand than in most high income countries, and 95% of the children affected are Māori or Pacific islanders. Prevention programmes focused on treating sore throats with antibiotics in communities at high risk initially appeared to reduce the incidence of rheumatic fever, but rates have been steadily increasing since 2016.

It is now clear that eliminating rheumatic fever will require multiple strategies, including improving early diagnosis and ultimately developing vaccines to prevent GAS infection. The MWC GAS Flagship Programme, led by Associate Professor Thomas Proft and Dr Nikki Moreland from the University of Auckland, is focused on developing vaccines and new diagnostics, as well as improving understanding how GAS causes rheumatic fever.

The development of a multivalent vaccine called TeeVax is being spearheaded by team member Dr Jacelyn Loh, a Senior Research Fellow funded by the MWC and the National Heart Foundation. Data suggests that TeeVax has the potential to be an effective vaccine against most strains of GAS. Mice immunised with the vaccine are significantly better protected against GAS infection compared to non-vaccinated animals and serum from vaccinated animals had bactericidal (killing) activity towards GAS. "Our recent results are very exciting and show that TeeVax works in animals and has a very broad GAS strain coverage," says Jacelyn. "The positive results from these mouse studies allow us to take TeeVax to the next stage of development, such as a non-human primate model."

The team has now developed a roadmap that demonstrates the feasibility to move TeeVax into phase II clinical trials within the next 5 years.

TeeVax is well placed to benefit from ongoing Trans-Tasman initiatives to accelerate GAS vaccine development such as "CANVAS [Coalition to advance new vaccines against group a streptococcus]". This programme was initiated following a MWC funded meeting of global GAS vaccine developers in Auckland in 2013 and was co-led by Professor John Fraser, Emeritus Principal Investigator at the Maurice Wilkins Centre. "A vaccine that is effective against all strains of Group A Strep is a terribly difficult nut to crack but they may just have done it," says John. "The investment in fundamental and very clever science through Thomas Proft, Jacelyn Loh and Nikki Moreland plus the MWC bringing together international experts to make a road map for how to move on this has put this group centre stage of the global rheumatic fever and streptococcal field."





In 2018, the Centre appointed Professor Debbie Hay, Dr Nikki Moreland and Associate Professor Rinki Murphy (left to right) as members of the leadership team.

Photo courtesy of Dr Charlotte Johnson

MWC senior leadership team welcomes new appointees

We highlight the recent appointments of three exceptional scientists – Associate Professor Rinki Murphy, Professor Debbie Hay and Dr Nikki Moreland – to the Maurice Wilkins Centre leadership team.

Diabetologist Rinki Murphy, Associate Professor in Medicine at the University of Auckland and physician at Auckland DHB and Counties Manukau Health, was promoted to a Management-Principal Investigator (PI) position. Rinki is a co-leader of our 'Genetic Predisposition to Obesity and Diabetes in NZ Populations' flagship research programme.

"I am delighted to join the management PI team within the MWC," said Rinki. "Through this role, I am excited to contribute to discussions about the future vision and structure of the MWC.

"I see that the MWC network of investigators can provide such research opportunities on a collaborative basis with clinicians for synergistic outcomes that will ultimately improve health of New Zealanders more rapidly than efforts from each group in isolation."

Pharmacologist Debbie Hay, Professor of Biochemistry and Pharmacology in the School of Biological Sciences, University of Auckland, was also made a MWC PI. Debbie and her research lab have a particular interest in class B (peptide) G protein-coupled receptors and their potential as drug targets for metabolic disease, as well as other conditions such as migraine, pain and cancer. "I'm thrilled and very much looking forward to leading the Maurice Wilkins Centre's 'Therapeutics for metabolic disease' flagship research programme," said Debbie.

In addition to her many awards, Debbie has been appointed a James Cook Research Fellow (Royal Society of New Zealand) and a Fellow of the British Pharmacological Society. She is also an Editor of the British Journal of Pharmacology, an International Union of Basic and Clinical Pharmacology (NC-IUPHAR) corresponding member, and is Chair of the NC-IUPHAR subcommittee on calcitonin family receptors.

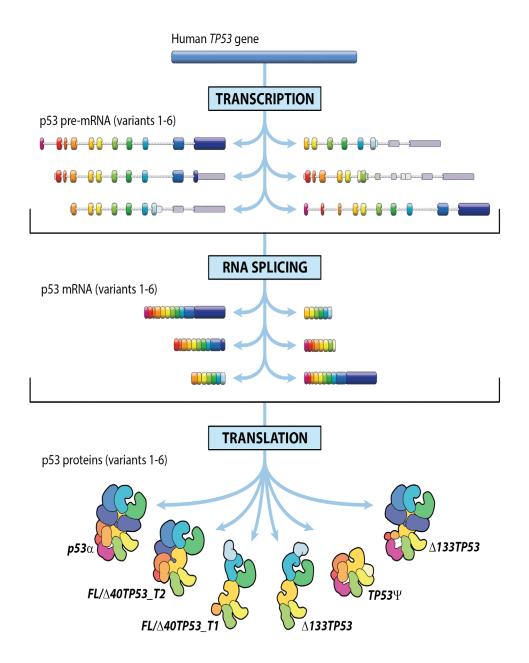
Rheumatic fever specialist Nikki Moreland, a senior lecturer in immunology based in the School of Medical Sciences, University of Auckland, and co-leader of the MWC's 'Group A Streptococcus' flagship research programme, was also appointed as a PI with the MWC.

Nikki has research expertise in humoral immunology and infectious diseases, and her group uses a wide range of techniques to study antibody-antigen interactions at the molecular level.

She completed her PhD at the University of Auckland and had postdoctoral training in Scotland, Auckland and at Duke-NUS Graduate Medical School in Singapore. Nikki returned to New Zealand in 2012 to commence her rheumatic fever research.

"I really do value the ongoing support of the Maurice Wilkins Centre for our work on rheumatic fever," said Nikki. "The PI appointment is something I'm very excited about. I'm sure that it will help us to continue building on the important research we have been doing in this area."





The human p53 gene has several different protein isoforms, produced by processes like RNA splicing or the use of alternative promoters. Due to the presence, absence or variations in the different functional domains, these isoforms often have different phenotypes in the cell.

Image designed by Dr Mia Jullig

One cancer gene - but several different proteins

Cancer arises due to changes in DNA in a single cell. Many changes are needed over time to a cell's DNA to make it cancerous – which is why cancer is usually a disease of later life. Yet as scientists have learned more and more about the DNA changes that combine to cause cancer, some patterns have emerged.

No matter which tumour type is being studied, a molecule called p53 looms large. p53 is the most commonly mutated gene across all cancers, and most of the mutations to p53 are assumed to simply reduce its function. p53 is often referred to as the classic "tumour suppressor" gene – it performs such important functions in normal cells that when these functions are lost due to mutations, tumours are much more likely to result. However work by MWC Principal Investigator Professor Antony Braithwaite at the University of Otago is showing this well-known story in cancer biology has some subtle twists and turns.

As with all genes, the p53 gene in our DNA encodes proteins. But importantly – like many other genes – the same sequence of DNA can encode several different versions of the p53 protein. These proteins are called isoforms of p53, and many of them behave very differently. In fact Antony's team developed the first mouse model of one of these isoforms (called "delta-133") and proved that it acted very differently from the main form of p53 that is so well known – and caused cancer through a completely different mechanism¹.

The team noticed that the mice with high levels of delta-133 had extensive inflammation that preceded the development of cancer. They hypothesized that the cancer was caused by the inflammation – backed by the knowledge that high levels of inflammation in a normal tissue increase the chances of that tissue developing a cancer. An important driver of inflammation is a hormone-like molecule called IL-6 which was at very high levels in the delta-133 mice. So to test their hypothesis these mice were mated with mice lacking an IL-6 gene.

The results were dramatic!

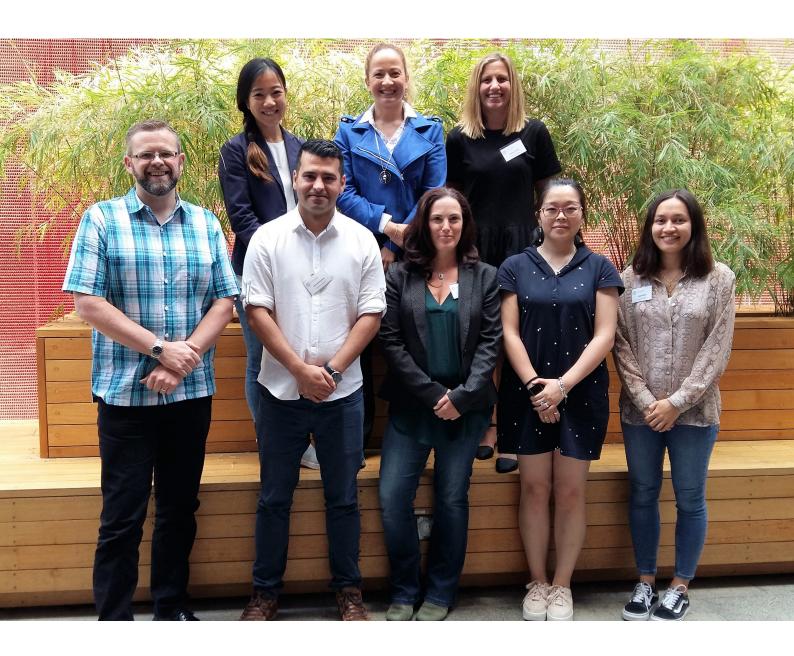
With no IL-6, the levels of many markers of inflammation were reduced to normal levels, and the mice developed fewer cancers². The cancers that did arise did not spread as much to other tissues – an important finding given that such "metastasis" is a major reason why cancer causes so much damage to the human body.

These findings suggested that too much of the delta-133 isoform in human cancers might be particularly dangerous. To test this idea the team examined human bowel cancers. They found that about 1/3 had high levels of the isoform and this group of patients had the shortest survival². In other cancers, including the aggressive brain cancer glioblastoma³, the team found groups of cancer samples with high levels of the delta-133 isoform. These cancers also had high levels of a molecule called PD-L1 that stops immune cells from killing the cancer

These discoveries show that the delta-133 isoform of p53 is an important molecular link between inflammation and cancer. They also remind us that even when you think you understand a cancer molecule really well, there are often surprises lurking in the alternative isoforms of proteins that the same gene can encode.

- 1. Slatter TL et al. (2011) Blood 117:5166-7.
- 2. Campbell H et al. (2018) Nature Communications 9:254
- 3. Kazantseva M et al. (2018) Journal of Pathology 246:77-88





The MWC Early Career Steering Committee at the end of 2018. Back row l-r: Dr Catherine Tsai, Ms Marina Rajic, Dr Joanna Hicks (Chair). Front row, l-r: Dr Euan Rodger, Dr Iman Kavianinia, Dr Kate Lee, Dr Wanting Jiao, Ms Indigo Matisi. Absent: Dr Sunali Mehta. Photo courtesy of MWC

Young MWC scientists drive upskilling of peers nationwide

The Maurice Wilkins Centre is committed to developing a new generation of scientific leaders. In 2018, our Early Career Steering Committee, a talented and vibrant group of young leaders, organised two educational workshops and a 'Future Science Day'. These provided excellent learning outcomes for their peers from all over New Zealand, as well as opportunities to meet and network.

The first workshop in April introduced young scientists to current microscopic and imaging techniques and consisted of a series of short talks by experts from Otago, Victoria, Massey, and Auckland universities. Topics included the latest microscopy technology and techniques, future directions in the field of microscopy, and pragmatic advice on how to gain access to advanced equipment and facilities both within New Zealand and overseas.

The Committee hosted a second workshop on flow cytometry in August, facilitated by Dr Anna Brooks, an MWC Senior Research Fellow and leading flow cytometry expert at the University of Auckland. Attendees, many of whom were new to the technology, were treated to an informative introduction and the types of instrumentation available to MWC investigators.

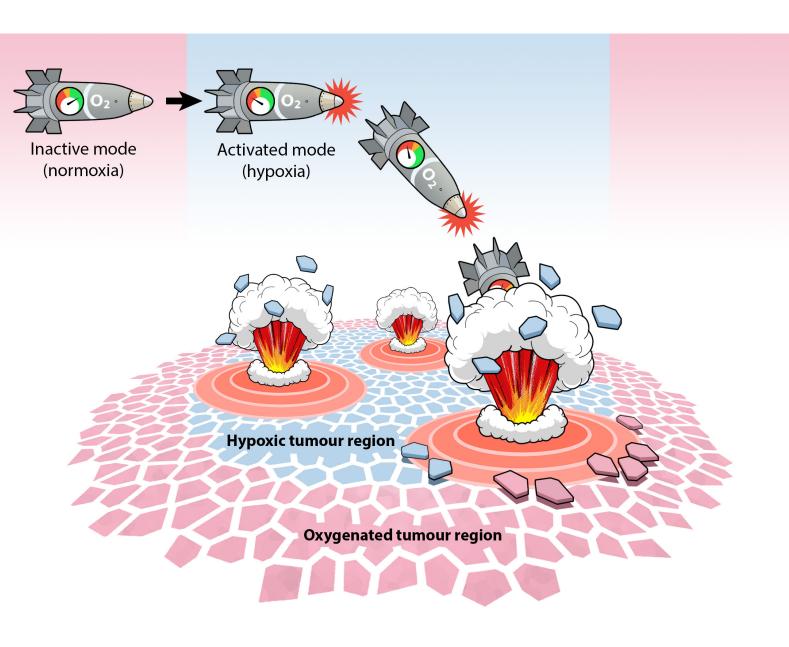
At the end of the year, the Committee also organised the third annual 'Future Science Day' in conjunction with the MWC's Annual Research Symposium. Held at the University of Auckland in early December, this year's theme was 'networking'.

"The aim was to encourage MWC affiliates to meet other affiliates and experts in particular fields to facilitate collaboration and research," said Dr Joanna Hicks (University of Otago). "Alongside the networking and 'meet the expert' events, we had an exciting series of talks from our peers, selected from submitted abstracts. This was followed by a very well attended, vibrant poster session featuring over 50 posters."

A special awards ceremony saw best oral presentation prizes going to Effie Fan from Victoria University of Wellington (1st place) and Jennifer Eom from the University of Auckland (2nd place). Best poster presentations went to Elyse Williams (1st place), Aqfan Jamaluddin (2nd place) and Regan Fu (highly commended), all from the University of Auckland.

"Organising the future science day can be very challenging," said Joanna. "However, committee members gain many important skills from organising these events, for example critiquing of abstracts from a wide range of topics and more importantly how to work together as a team. Being part of the ECR committee increases our network of colleagues outside our fields of expertise, equips us with the skills to identify and approach key people for organising workshops, critically evaluate others work, and increases our personal profiles within the MWC and the wider scientific community."





Hypoxia activated prodrugs (HAPs) convert from an inactive to an active-state when in the hypoxic centre of a solid-tumour. Once active, the HAPs are toxic and these effects penetrate into the surrounding tumour cells.

Image designed by Dr Mia Jullig

Turning the tables on cancer

Tumours often contain areas with less oxygen than is found in normal tissues. These areas are less vulnerable to many forms of cancer therapy and often drive development of a more aggressive disease state. However, Maurice Wilkins Centre scientists have learned to use the lack of oxygen in tumours to their advantage.

Two drugs invented by a team of Maurice Wilkins Centre investigators at the Auckland Cancer Society Research Centre are heading to clinical trials to test their effectiveness in cancer patients. The clinical trials will be run by two new drug companies, Convert Pharmaceuticals and Rain Therapeutics, that in 2018 raised more than NZ\$50M to support development of the drugs.

The team that invented these drugs is led by cancer biologist Associate Professor Adam Patterson, and medicinal chemist Associate Professor Jeff Smaill, and has been supported by a Maurice Wilkins Centre Flagship Programme, as well as funding from the Health Research Council of New Zealand, the Ministry of Business, Innovation and Employment, Cancer Society Auckland Northland, and Auckland UniServices.

Adam and Jeff's team have refined and optimised technology originally developed over decades by Maurice Wilkins Centre investigators Professors Bill Denny and Bill Wilson. This technology allows production of drugs that only become toxic to cells in low oxygen environments such as tumours, minimising their effects on healthy cells. The new drugs, one actively in a Phase 2 trial, the other expected to soon begin a Phase 1 trial, firmly establish New Zealand as the world centre for developing this type of drug – termed "hypoxia-activated prodrugs" or HAPs.

Although previous HAPs have failed in clinical trials, Jeff and Adam's team have made significant headway in the design and pre-clinical validation of a new generation of HAPs to circumvent the limitations of previous designs. "This area of drug design is very complex. The devil is in the details of how each compound is fine-tuned for precise activation under low oxygen conditions. It is also critical that the clinical development is informed by the use of appropriate biomarkers of response," said Jeff. "Selecting patients that have the potential to respond is very important."

"This Flagship programme demonstrates that to develop new cancer drugs we need to invest in people who understand both the biology and chemistry of their field at a very deep level", said Professor Rod Dunbar, Director of the Maurice Wilkins Centre. "Even when earlier generation drugs fail in clinical trials, this depth of understanding ensures that we can learn from the clinical data, and design next generation drugs that are more likely to help patients." Associate Professor Adam Patterson added that: "It demonstrates the importance of having an organisation like the MWC backing teams like the one we've formed, especially through times when the world has neglected certain approaches to drugs because of prior clinical failures. Without MWC support for our programme, it would have been very difficult to sustain."











MWC researchers are working with several companies to progress their novel drugs through clinical trials.

A record year for commercialisation

In 2018, NZ\$58M was raised by companies in New Zealand and overseas to take MWC discoveries through to the clinic – a new record in terms of annual investment in new medicines invented in New Zealand.

MWC research programmes aim to improve human health, often by discovering new therapies. Getting new treatments through to patients requires clinical trials – initially to test safety in humans ("phase I") and then to test their effectiveness against their target disease ("phase II)", compared to any existing treatments ("phase III").

Clinical trials are very expensive – and they get more expensive as they progress through their phases. Thus very large investments are needed to allow medicines invented by MWC investigators to progress all the way through to helping patients – and the major sources of these large investments are companies. Seeing our work through to fruition therefore involves working with biotechnology or pharmaceutical companies, or investment companies that specialise in taking new medicines through clinical trials. The MWC funds workshops and other training about research commercialisation to ensure our investigators know how to engage with these companies.

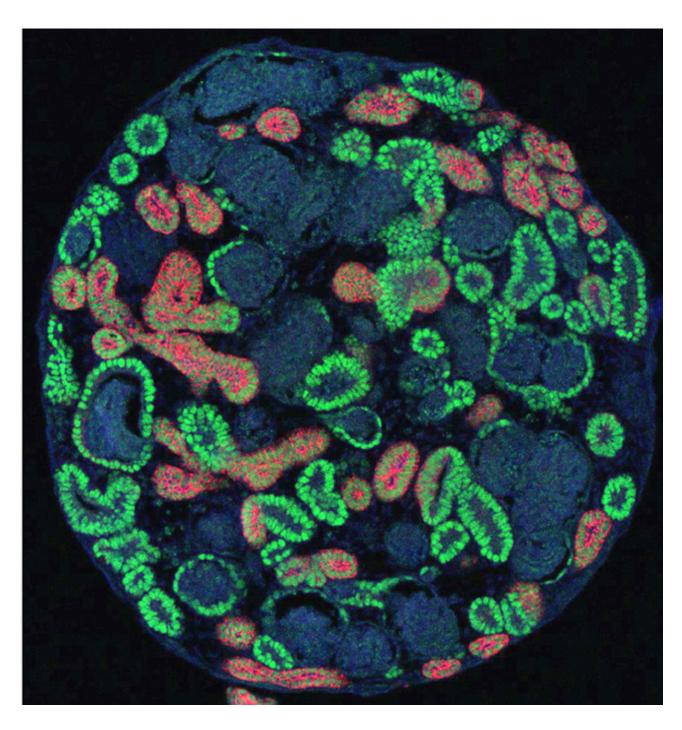
In 2018 several major investments underscored the very high value of new treatments discovered by MWC investigators – even before they're finished their clinical trials. Biotech company Convert Pharmaceuticals, raised NZ\$27M to support the first clinical trials of the cancer drug CP-506, invented by a team led by MWC investigators Professors Adam Patterson and Jeff Smaill, at the University of Auckland's Cancer Society Research Centre.

Rain Therapeutics raised NZ\$23M to support a Phase II clinical trial of the drug tarloxotinib in lung cancer patients. Remarkably this drug was also invented by Adam and Jeff and their team – under-scoring the productivity and acumen of the team in designing new drugs at the cutting edge of cancer therapy.

And to complete a trifecta of large investments, new start-up company Kea Therapeutics raised NZ\$8M from the Medical Research Commercialisation Fund to take a new pain medication to trial. This drug was invented by a team led by MWC Founding Principal Investigator Professor Bill Denny, who is Director of the Auckland Cancer Society Research Centre, and a 2016 inductee into the Hall of Fame of the American Chemical Society's Division of Medicinal Chemistry (www.acsmedchem.org/?nd=inductees).

These investments follow others over the last 3 years in several start-up companies founded by MWC investigators, such as SapVax LLC, Avalia Immunotherapeutics, and Upside Biotechnologies. Together they not only represent a huge vote of commercial confidence in therapeutics invented by MWC investigators – they also ensure pathways from our discoveries to patient benefit are open and active – and that MWC's research retains direct relevance to improving patient health.





Cross section through an organoid model, grown by members in the Davidson lab, showing fluorescently labeled profiles of renal tubules

Photo courtsey of Veronika Sander

Growing miniature human organs from stem cells

Stem cells are cells that can grow into different types of cells in the body. They sit in special zones throughout the body waiting to be called on to generate new cells. Different tissues in the body rely on their stem cells to keep them healthy – but stem cells from one tissue (e.g. skin) can't generally make another (e.g. heart).

Yet in 2006 Shimya Yamanaka discovered that some human cells could be re-programmed from their limited fates so they could turn into over 200 different types of cells – they became "pluripotent". This Nobel Prize-winning discovery was soon followed by many different discoveries about how to make similar pluripotent stem cells from many different kinds of adult cells, and a stem cell revolution began.

"Induced Pluripotent Stem Cells" or iPS cells can now be made in many different ways, and have raised hopes that we may soon be able to use them to rebuild or repair damaged tissues. Even before we are able to use them in the clinic, iPS cells are already revolutionising the study of disease processes.

The MWC supported the production of New Zealand's first iPS cell lines, by Associate Professor Alan Davidson and his team at the University of Auckland's Department of Molecular Medicine and Pathology. These iPS cell lines – dubbed MANZ1 and MANZ2 (with the "M" designating the MWC) – are already enabling research breakthroughs in understanding disease processes and testing new therapies on human cells and tissues that would normally be impossible to isolate in a laboratory dish.

Most recently Davidson and his team have used them to grow small models of human kidneys called kidney organoids. These model kidneys are no bigger than 1mm wide, so not yet useful in therapy for kidney disease. Yet because they contain many of the different cell types of a normal kidney, and they are organised in a similar way to a real human kidney, they can be used to model kidney diseases. In a recent paper¹ the team describes a new method to efficiently grow kidney organoids in large numbers, and then use gene editing to explore the function of a gene implicated in kidney disease. This sophisticated combination of generating human iPS cell lines, editing their genes with the "CRISPR/Cas" technique, then growing human tissue organoids to make discoveries about those genes, shows the power of the new techniques. They also illustrate how far stem cell science has come since Yamanaka's discoveries just over a decade ago.

"Now that we can make human kidney tissue in unlimited quantities," says Alan, "we can focus on using kidney organoids to discover and test new treatments for disorders such as acute kidney injury, kidney fibrosis and inherited conditions such as Cystinosis." As for the hope of growing a full kidney in a dish for renal transplantation: "Unfortunately not any time soon," says Alan, "but it's already possible to envisage helping restore some kidney functions with kidney cells generated in organoids from patients' own cells."

1. Pzrepiorski A et al. (2018) Stem Cell Reports 11:470-484











Outreach

International engagement

The Maurice Wilkins Centre (MWC) 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 pages 74 and 78), the Centre is building strategic relationships with institutions and government agencies at city, provincial and national level, in particular in the Asia-Pacific region. In 2018, the MWC continued to focus on deepening these relationships in China.

Visit of Party Secretary of Guangdong Province, China



In early September, the MWC and the University of Auckland had the privilege of hosting a delegation, led by Mr Xi Li, Party Secretary of Guangdong Province and including the Chinese Ambassador to New Zealand Ms Xi Wu and dignitaries from the Guangdong Provincial Government, accompanied by the New Zealand Ambassador to China Clare Fearnley and officials from the New Zealand Government.

The guests were welcomed to the University of Auckland by Professor Stuart McCutcheon (Vice-Chancellor), Professor Jenny Dixon (Deputy Vice-Chancellor, Strategic Engagement), and Professor Rod Dunbar (Director of the Maurice Wilkins Centre).



Following introductions, MWC Director Professor Rod Dunbar gave a 10-minute presentation outlining key research being conducted by our investigators. He also highlighted the strong relationships the MWC has developed with Chinese colleagues at the Guangzhou Institutes of Biomedicine and Health (GIBH) and Jinan University (JNU), which are both in Guangdong Province. Secretary Li, accompanied by China's Ambassador Wu and Guangzhou Mayor Wen, was taken on a tour of MWC laboratories at the end of the visit.

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Engagement with China

The MWC continued its programme of engagement with China in 2018 by building on relationships initiated over 2012 to 2017:

- August: A delegation from the Consulate-General of China in Auckland led by Consul-General Madam Erwen Xu and Vice Consul-General, Mr Yewen Xiao, visited MWC on 13th August. This was a preparatory tour before the official visit by Party Secretary Mr Xi Li of Guangdong Province later in September. During Consulate-General's visit, MWC Director Professor Rod Dunbar provided a presentation introducing the nature of the Centre and the highlights of its long-standing relationship with China over the past 6 years. Associate Professors Adam Patterson and Jeff Smaill also joined the host and gave an introduction on their joint research project with Guangzhou Institutes of Biomedicine and Health(GIBH) as a model of the successful collaboration between the Centre and China.
- August: Professor Peng Li from GIBH attended the Queenstown Molecular Biology
 Conference in late August. He was invited to this conference as a guest speaker by
 MWC to introduce his (CAR)-T cells therapy for cancer to the wider New Zealand
 audience. Afterwards, Prof Li travelled to Auckland in early September to visit the
 MWC headquarter and held an excellent seminar on his research in the School of
 Biological Sciences at University of Auckland.

- September: Three MWC investigators travelled to Guangzhou in late September to attend a 4-day workshop on induced pluripotent stem cell (iPSC) run by GIBH, China's top iPSC centre, with which MWC has a long-standing relationship. The attendees were Affiliate Investigators Ms Evie Templeton from Christchurch Heart Institute, University of Otago, Mr Denis Nyaga from Liggins Institute, University of Auckland, and Mr Jingwei Wei from Ruakura Research Centre, AgResearch. All of them had positive feedback on this workshop and said it was a worthwhile experience, as well as giving feedback on some of the challenges which will be very useful when considering similar future opportunities.
- October: GIBH Party Secretary Dr Hongming Hou and Principal Investigator Professor Donghai Wu visited MWC to meet with Director Professor Rod Dunbar and other MWC investigators including Associate Professors Alan Davison, Kerry Loomes, Adam Patterson and Jeff Smaill. In-depth discussions were held on the Centre's proposed visit to GIBH headquarter in November, and potential new collaboration opportunities in exchange programs, which would be fully supported by the recentlyfunded Guangdong Provincial Laboratory. During this visit, Secretary Hou and Professor Wu also visited UniServices and were updated on the commercialisation progress of the joint IP between University of Auckland and GIBH.
- November: On the 16th -18th, Professors Rod Dunbar, Garth Cooper and Greg Cook were invited to Guangzhou to attend the first Academic Advisory Board Meeting of the International Joint Laboratory on Traditional Chinese Medicine Modernization and Innovative Drug Design and Delivery talks at the Summit Forum. MWC is a key international partner of this joint laboratory and Professor Dunbar serves as Co-Director with Professor Ding. The aim of the Summit Forum was to exchange cutting-edge knowledge and research methods in this field, discuss ideas for future development and promote scientific collaborations among the partners.
- November: Six MWC investigators, Professors Rod Dunbar and Ian Hermans, and Associate Professors Alan Davidson, Kerry Loomes, Adam Patterson and Jeff Smaill, travelled to Guangzhou and paid an official visit to the GIBH on the 20th-21st with the purpose to expand on the existing strong collaborations with GIBH investigators. GIBH General Director Professor Duanqing Pei, Deputy Director Professor Ziyuan Duan, Party Secretary Dr Hongmin Hou warmly welcomed the MWC delegation and hosted the 2-day visit.

The visit began with a full-day scientific workshop where investigators from each side presented recent research and updated the group on the progress of their bi-lateral collaborations. The investigators also highlighted new opportunities for collaboration between the two institutions. Science and Innovation Counsellor from the New Zealand Embassy in Beijing, Mr Clinton Watson, and Consul-General from New Zealand Consulate-General in Guangzhou, Ms Rachel Maidment, attended the event and demonstrated strong support for the collaboration from the New Zealand Government in their opening speeches. A large number of students and staff from GIBH attended the workshop as well to listen to the presentations.



On the second day, matching investigators in each field of study held more in-depth discussions and took tours of laboratories and facilities, allowing exploration of ideas for future collaborative scientific programmes, as well as pragmatic discussions about increasing personnel exchanges and further developing the GIBH-MWC Joint Laboratory, as well as the Guangdong Provincial Laboratory.

- November: On 22nd, the MWC delegation visited the School of Pharmacy at Jinan University (JNU) in Guangzhou and met Professor Ke Ding, with whom MWC has had a long-standing scientific collaboration. A full-day scientific workshop with a similar format was held with leading principal investigators from the school. Collaborative opportunities were highlighted and discussed during the workshop. Strong support was expressed by Professor Pei Yu, the Vice Dean of JNU's International School for students and lecture exchange for educational programmes as well as research activities between the two institutions.
- November: Associate Professors Adam Patterson and Jeff Smaill and International
 Liaison Advisor, Mr Peter Lai, extended their trip from Guangzhou to Nanjing
 and went to the China Pharmaceutical University on the 24th. Professor Sophie
 Huang, Director of the National Drug Screening Library and Director of State
 Pharmacokinetics, hosted them. The main purpose of the visit was to scope out
 further collaboration opportunities in drug discovery.
- December: Professor Ke Ding from Jinan University was invited as a guest speaker to the 2018 MWC Symposium in Auckland on 6th December. Professor Ding delivered a talk introducing his recent work on drug resistance and the scientific collaboration he has with MWC to the audience. After the symposium, Professor Ding travelled to Wellington and Dunedin where he visited the Malaghan Institute and the Ferrier Research Institute at Victoria University of Wellington, and the University of Otago respectively. During the visits, he met with many MWC investigators including Professors Ian Hermans and Greg Cook, Associate Professor Paul Teesdale-Spittle, Dr Joanne Harvey, Dr Jeremy Owen, Dr Robert Keyzers, and Mr Jordan McCone to explore potential opportunities for future collaborations on topics such as immunotherapy and natural product effectiveness.

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 78.

In 2018 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. MWC 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 2018 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.

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 immunotherapy technology and are working with Avalia Immunotherapies to further advance the technology and progress it to clinical trials.

Comvita

Comvita New Zealand is an international natural health products company with offices across Asia, the USA and UK. Comvita are working with investigators Professor Dame 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 Professor Dame Margaret Brimble is working with the company on developing new molecules as humane rodenticides to replace the widely used but controversial pesticide 1080.

· SapVax LLC.

Sapvax LLC was founded in 2016 and is developing a pipeline of products for the treatment of different cancers, with an initial focus on tumours expressing NY-ESO-1. Professors Dame Margaret Brimble and Rod Dunbar are the academic founders of this company, which is headquartered in the USA, and in 2018 they continued to consult and carry out contract research for the company.

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 78.

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 2018 Maurice Wilkins Centre investigators were involved in a number science education initiatives including;

Biology Teacher Professional Development Days

In 2018 the Centre ran seven of the highly successful MWC Biology Teacher Professional Development (PD) days. Professor Peter Shepherd, Maurice Wilkins Centre Deputy Director, and Ms Rachel Heeney, Head of Biology at Epsom Girls Grammar School, led events in Hastings, Palmerston North, Nelson, Christchurch, Rotorua, Auckland and Kawakawa, Bay of Islands.

The days featured presentations from scientists on key topics relevant to the NCEA Level 3 curriculum. Presentations from scientists were on some of the following topics; assisted reproductive technologies, unpicking how marine animals respond to environmental stress, human evolution and migration of Polynesian people and the science of antimicrobial resistance.

Teachers were also given an update on the MWC 'Sugar in Schools' study at each of the development days (see below). Over 300 biology teachers attended these workshops. The content of the workshops is developed after feedback from the biology teacher community before, during and after the workshops through a dedicated Facebook page.

Each year the aim is to hold at least one of these workshops in a more isolated area of New Zealand where teachers often find it difficult to access professional development. The format of the workshops can be easily customised to fit the needs at each location. The final workshop for 2018 was held on Te Toka Whakakotahi Marae at Bay of Islands College in Kawakawa, which was attended by teachers from Whangarei Girls High School, Kerkeri High School and Kaitaia College. Feedback from this PD day was very positive, with the following comments made by teachers who attended;

"Thank you for the opportunity. This was most valuable personal PD I have undertaken."

"Thanks so much for coming up North here and not charging for this PD. I feel really refreshed from a biology perspective. It was amazing. It means a lot as we are so isolated up here and dont have the access to universities as the main centres do."

'Sugar in Schools' study

The MWC 'sugar in schools' study was launched in July 2017, with the aim to investigate the variation in fructose absorption in a healthy population. This study, led by Professor Peter Shepherd and coordinated by school biology teacher, Ms Helen Webber, continued throughout 2018, testing 1223 students in 31 schools around New Zealand.

One of the aims of this study was to collaborate in other parts of the country, especially with schools located furthest away from the main population centres. The study coordinators travelled to Kaitaia and assisted Kapowairua Stephenson, Conor O'Sullivan and Rhiaan Smith from the Moko Foundation with their first school visit and provided them with resources for their teachers and ongoing support during the year. The Moko Foundation researchers visited schools in the far north area, including Māori immersion schools. Some of their testing at these schools was delivered in a wananga setting.

The study also travelled to a number of schools at the other end of the country, including Mount Aspiring College in Wanaka, Waitaki Girls' High School in Oamaru and Ashburton High School.

This study has been well received by the participating schools and there is a long waiting list of schools wanting to participate in the study for the first time and also schools that have previously participated and want to run the study again with new students.

· Maurice Wilkins Centre biology teacher development scholarships

In 2018 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 2018 were Carrie van der Zwaag from Reporoa College, Philip Andrew from Trident High School in Whakatane, Calidah Wati from Whangarei Girls' High School & Michelle Goeth from Rotorua Girls' High School.



Teachers and MWC investigators at the Biology Teacher Professional Development Day in Christchurch

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. Throughout 2018, 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 2018, 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:

· Tātai Oranga: Joining forces to tackle metabolic conditions

Tātai Oranga, organised in partnership with Ngāti Porou Hauora, was held at Te Iritekura Marae at Waipiro Bay from the 4th to the 6th of April.

The meeting kaupapa was to bring together scientists, researchers and clinicians from New Zealand and overseas to meet with communities to discuss and develop strategies for how to use cutting edge medical and genetic research to improve health outcomes for Māori and Pacific peoples.

The meeting featured presentations by leading scientists and clinicians in the field of metabolic disease, including international speakers; Dr Giles Yeo from the University of Cambridge (UK), Dr Jose Florez from the Broad Institute (USA) and Dr Joseph Yracheta from the University of Washington (USA).

This meeting was highly successful and resulted in the 'Tātai Oranga Declaration' which is a new strategy to work in a more integrated way to optimise the impact of our metabolic disease research in New Zealand. Tātai Oranga will now become an annual national conference to continue discussing these important issues and empowering communities

· Honouring Professor Dame Margaret Brimble

Newstalk ZB and Nine to Noon (Radio NZ) independently interviewed MWC Principal Investigator Professor Margaret Brimble, to discuss her 2018 election as a Fellow of the Royal Society of London (both 10th May). The New Zealand Herald also featured a piece (10th March), titled "Science star: Margaret Brimble first New Zealand woman to be elected a Fellow of Royal Society of London". Margaret was also featured in the New Zealand Herald article "Best of NZ: New Year Honours pay tribute to 196 exceptional Kiwis" (31st Dec) in relation to her being made a Dame Companion of the New Zealand Order of Merit. See highlight story for further information (page 9).

· "Meet the Trailblazers: 125 Kiwi women who changed the world"

Professor Dame Margaret Brimble (MWC Principal Investigator) and Dr Siouxsie Wiles (Associate Investigator) were two of the 125 Kiwi women acknowledged in the New Zealand Herald article "Meet the Trailblazers: 125 Kiwi women who changed the world" (17th Sept). This article was in honour of 125 years of womens suffrage, and featured Kiwi women who have excelled in their respective fields over the last 125 years.

· NZ-developed chemotherapy drug heading for clinical trials

MWC Principal Investigator Professor Adam Patterson was interviewed by Newstalk ZB (12th March) about the future of the drug CP-505, a hypoxia targeting chemotherapy agent he co-invented. The story was also published in the New Zealand Herald (11th March) and European Biotechnology Magazine (1st March).

· Obesity and national income

The New Zealand Herald published a piece highlighting research conducted by MWC Principal Investigator Associate Professor Rinki Murphy (9th April), which found rates of obesity in adolescent women are higher in wealthier countries. Rinki was also interviewed by Stuff (9th April) relating to this same study.

· Discovery helps pave way for new anti-TB drugs

MWC Principal Investigator Professor Greg Cook and Affiliate Investigator Dr Kiel Hards were interviewed by both Newstalk ZB (4th July) and the New Zealand Herald (8th July) regarding their discovery of a novel property in the TB drug Bedaquiline. This discovery, which showed how the TB drug has a second activity of disrupting the bacteria's ability to generate energy, has the potential to be exploited to increase the success of future anti-TB drug developments.

Other engagement through the media and events

Many MWC investigators engaged the public through the media and some examples of this include;

MWC Associate investigators Associate Professors Bridget Stocker and Mattie Timmer were both interviewed by Radio New Zealand (2nd May) regarding their project targeting immune cells to combat cancer.

Professor Emily Parker (MWC PI) and Dr Effie Fan (MWC Affiliate) were featured in a New Zealand Herald article (8th April) which highlights their work in protein engineering for new vaccine and antibiotic development. Emily Parker was also independently interviewed for an episode within a series called "Five Minutes with", which focuses on young to mid-career researchers within New Zealand, where Emily describes work searching for new antibiotics (12th June).

MWC Director Professor Rod Dunbar, along with another scientist within the Auckland start-up Upside Biotechnologies were interviewed by RadioNZ, to discuss their revolutionary skin engineering technique (21st April). This work has been backed by the United States Military, as a method to quickly grow skin for people with traumatic skin damage (such as burns victims).

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 2018.



Supporting the New Zealand science community

Research symposium and workshops

Maurice Wilkins Centre Research Symposium

The theme for the 2018 Maurice Wilkins Centre Research Symposium held on 6th December at the University of Auckland was 'What to do when drugs don't work.' Resistance or non-responsiveness to drugs is a problem that spans many areas of biomedicine and the symposium outlined some of the challenges we face and progress towards solutions to this problem across the MWC themes; cancer, metabolic disease and infectious disease.

The symposium was very popular with over 200 registered attendees and featured presentations from two international speakers; Professor Ke Ding from Jinan University in China and Dr Debbie Williamson from The Peter Doherty Institute for Infection and Immunity in Australia, and over 15 MWC investigators.

The day ended with a strategy forum for senior MWC investigators and then a poster session in the evening organised by the Early Career Steering Committee.

Maurice Wilkins Centre flagship meetings

During 2018 the Maurice Wilkins Centre held five flagship meetings on specific research topics of relevance to the Centre. The aim of these meetings is to bring together MWC investigators in a particular research area to brainstorm future directions and decide how best to achieve outcomes to benefit New Zealand through the Flagship programmes. Many of the ideas that come from these meetings inform the strategic direction of the Centre's research programme.

Meetings were held on the following topics;

- · Metabolic diseases flagship meeting 8th February in Wellington
- · Cancer flagship meeting 9th February in Wellington
- · Therapeutics for metabolic disease flagship meeting 15th June in Auckland
- · Antimicrobial resistance flagship meeting 19th June in Auckland
- · Immuno-oncology flagship meeting 5th December in Auckland

Maurice Wilkins Centre Technology Workshops

The centre aims to hold at least two technology workshops each year which are designed to inform investigators about the technologies and facilities that are available across New Zealand, the most recent applications of the technology and give investigators information on how they could use the technology in their own research space.

In 2018, the following technical workshops were facilitated by the Early Career Steering Committee based on responses from early career researchers within MWC; · Microscopy and Imaging Workshop – 30th April

The MWC Early Career Steering Committee organised a workshop on 30th April in Auckland, designed to introduce young scientists from around the country to current microscopy and imaging techniques. The workshop was well attended and covered a range of topics from the latest microscopy technology and techniques and how New Zealand researchers can gain access to advanced equipment and facilities, to future directions in the field of microscopy.

· Flow Cytometry Workshop – 10th August

Dr Anna Brooks, MWC investigator and director of the University of Auckland Flow Cytometry centre coordinated with the Early Career Steering Committee to convene a workshop on Flow Cytometry. The workshop covered both the basics of flow cytometry and its application as well as an introduction to data analysis, experimental design and advanced instrumentation.

The Maurice Wilkins Centre NZIC Prize for Excellence in Chemical Science

The New Zealand Institute of Chemistry awarded the 2018 Maurice Wilkins Centre Prize for Excellence in Chemical Science to Professor Antony Fairbanks, an MWC Associate Investigator based at the University of Canterbury.

Antony was awarded this prize in in recognition of his excellent and impactful science undertaken in New Zealand at the University of Canterbury. His research is focussed on organic chemistry and chemical biology, particularly applied to carbohydrates and glycoconjugates. This is a highly complex and competitive field of research and when accepting the award Antony acknowledged the exceptional work by key members of his research group who contributed to research publications that led to the award.

Conferences, meetings and organisations

Scientific conferences, meetings and networks are important for 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 2018 the Maurice Wilkins Centre provided support for:

Queenstown Research Week

This is the largest annual science event in New Zealand. In 2018 this event was held in August and attracted over 1700 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 MWC 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 MWC provided scholarships for three alumni from the Summer Internship for Indigenous Genomics (SING) workshop to attend the conference; David Frost (Auckland), Nauvoo Begman (Waikato) and Katrina Bevan (Waikato).

The Centre also provides travel scholarships for New Zealand secondary school teachers to attend the Queenstown Molecular Biology meeting (See page 35).

AsCA 2018/CRYSTAL 32

A combined conference of the Asian Crystallographic Association (AsCA) and the Society of Crystallographers in Australia and New Zealand (SCANZ) was held in Auckland from the 2nd to the 5th of December and was attended by over 470 registrants from 25 countries. The conference was organised by MWC investigators Professor Ted Baker, Professor Kurt Krause and Associate Professor Chris Squire and provided MWC investigators an opportunity to present their research to an international audience. The MWC provided sponsorship for the keynote session 'Building chains: regulation of ubiquitin transfer by E3 ligases' featuring MWC Investigator Professor Catherine Day.

NZ Society for Oncology Conference 2018

The New Zealand Society for Oncology (NZSO) celebrated its 50th anniversary in 2018 by holding its annual conference in Queenstown on the 24th and 25th of August. The conference featured fundamental and clinical cancer research presented by leading national and international speakers. The MWC provided sponsorship for a session on 'molecular oncology'.

Joint NZMS and NZSMBM Conference

The New Zealand Microbiological Society (NZMS) held a joint conference with the New Zealand Society for Biochemistry and Molecular Biology (NZSBMB) at the University of Otago in Dunedin from the 26th to the 29th of November. The theme of the meeting was 'Microbes and Molecules' and the centre provided sponsorship for the infectious diseases session, featuring MWC investigator Dr Jodie Johnston.

Australasian Society for Immunology (ASI)

The New Zealand branch of the Australasian Society for Immunology held a satellite meeting during Queenstown Research Week on the 26th and 27th of August. MWC contributed to travel funding for international speakers Professor Cath Bollard, Professor Peng Li and Dr Yury Goltsev. In order to maximise the benefits of bringing these speakers to the country the centre also provided support for these speakers to spend some extra time in other locations in New Zealand.



Professor's Rod Dunbar, Cath Bollard, Sarah Young and Ian Hermans at the ASI satellite meeting in August 2018

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 2018 Maurice Wilkins Centre investigators served in advisory and governance roles in many New Zealand organisations including;

- · Auckland Medical Research Foundation
- · Auckland Regional Tissue Bank
- · Australasian Proteomics Society
- · Australasian Society for Biophysics
- · Australia and New Zealand Bone and Mineral Society
- · Cancer Society of New Zealand
- · Canterbury Society Tissue Bank
- · Diabetes Auckland
- · Freemason Roskill Trust
- · Greenlane Research and Education Fund
- · Health Research Council of New Zealand
- · Kea New Zealand
- · Landcare Research Ltd.
- · L'Oreal-UNESCO Women in Science Fellowships in Australia and New Zealand
- · Melenoma Network of New Zealand
- · Ministry of Business, Innovation and Employment
- Ministry of Health
- · Ministry of Primary Industries
- · Neurological Foundation of New Zealand
- · New Zealand Association of Scientists
- · New Zealand eScience Infrastructure
- · New Zealand Genetics Ltd
- · New Zealand Institute of Chemistry
- · New Zealand International Science Festival
- · New Zealand Microbiological Society
- · New Zealand Microbiology Network



- · New Zealand Organisation for Rare Diseases
- New Zealand Physiological Society
- · New Zealand Society for Biochemistry and Molecular Biology
- · New Zealand Society for Oncology
- · New Zealand Society for the study of diabetes
- · Queenstown Molecular Biology Society
- · Royal Society of New Zealand
- · SciFund
- · Society for Free Radical Research Australasia
- · Synthetic Biology Australasia
- · Te Manawa Museum of Art, Science and History
- · Tertiary Education Committee
- The Australasian and New Zealand Council for the Care of Animals in Research and Teaching
- The Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists
- · The Dunedin Basic Medical Sciences Course Trust
- · The Physiological Society of New Zealand

International roles

In 2018 members of the Maurice Wilkins Centre served in more than 150 advisory, editorial and governance roles in international organisations based in the United States of America, Australia, the United Kingdom, Belgium, Canada, France, Germany, Japan, Singapore and Switzerland.









Organisational development

Flagship research programme

The MWC Flagship programme enables MWC investigators to assemble nationally-integrated collaborative teams to accelerate research in areas that align with the MWC research programme and where MWC teams are internationally competitive.

Two new MWC Flagship programmes were selected in 2018 in addition to the four existing Flagship programmes; Therapeutics for metabolic disease and Antiviral drugs and vaccines.

Therapeutics for metabolic disease

This new Flagship programme focuses on understanding and exploiting hormonal systems for the treatment of metabolic disease. The global impact of obesity, prediabetes and diabetes (type 1 and 2) is immense and new pharmacological interventions are required. Flagship leadership comprises of Professor Debbie Hay, Associate Professor Kerry Loomes, Professor Dame Margaret Brimble (University of Auckland) and Associate Professor Alex Tups (University of Otago)

Antiviral drugs and vaccines

This Flagship focuses on four viral themes that address major local and global viral threats with wide ranging sites of infection and variable challenges for antiviral development; influenza A, arbovirus, norovirus and hepatitis B. The leadership group comprises Professor Kurt Krause and Professor Vernon Ward (University of Otago), Professor Gavin Painter (Victoria University of Wellington) and DrJohn Taylor (University of Auckland)

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 2018; in February and August. Four categories of support were open for applications from MWC investigators in 2018; new initiatives involving postgraduate students, access to specialised facilities and equipment, access to specialised international and national training (see page 44 for details) and support for publication in high quality journals.



A new process to review applications under \$10,000 in value on a continuous basis, initially launched in 2017 for two categories of the flexible research programme, was extended in 2018 to all four categories. This has proven to be an effective way of enabling MWC investigators to take advantage of new opportunities more quickly with 25 applications across all four categories being awarded support through this process in 2018.

Inter-disciplinary PhD training

The Maurice Wilkins Centre fosters new interdisciplinary collaborative research involving Centre investigators by supporting fully funded PhD student projects that will also promote progress in scientific areas of importance to the MWC.

All scholarships available through this training programme were allocated prior to 2018 and 23 PhD students were supported in 2018. Four of these students completed their PhD study in 2018.

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.

19 projects awarded funding in previous years were ongoing in 2018 and five new projects were awarded working expenses in 2018 (**project leader, host institution and student names are in bold**):

- Leveraging Natural Product Synthesis for the Development of Novel Antimicrobial Agents; Margaret Brimble, Daniel Furkert, Greg Cook, Jared Freeman, University of Auckland
- Molecular epidemiology of antibiotic resistance of invasive Enterobacteriaceae
 of New Zealand and Pacific based Samoans; Philip Hill, James Ussher, Lupe Isaia,
 University of Otago, Scott Beatson, University of Queensland, Susan Morpeth and
 Susan Taylor, Counties Manukau District Health Board
- Inhibiting and Engineering Bacterial Menaquinone Biosynthesis Enzymes; Jodie Johnston, Thu Ho, Tim Allison, Conor O'Rourke, University of Canterbury
- A new xenograft model for studying the role of growth hormone signalling in cancer; Jo Perry, Peter Shepherd, Stephen Jamieson, Karla Sousa, University of Auckland
- Development of novel antibodies for detecting advanced glycation end-products in diabetes; Margaret Brimble, University of Auckland

Access to specialised facilities and equipment

The Centre provides support for investigators to access specialised facilities and equipment across New Zealand. 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 80 facilities and items of equipment were registered in 2018. It is intended that MWC investigators use this register as a resource to identify and compare facilities and equipment across New Zealand that they can use for their research.

25 projects awarded funding in previous years were ongoing in 2018 and 24 new applications to this scheme were approved in 2018 (**project leader, host institution and student names are in bold**):

- Understanding the role of the IL-6 -174 G/C (rs1800795) promoter variant in metabolism and cancer; Nicholas Fleming, Troy Merry, University of Otago
- Defining the signals required to license mucosal associated invariant T (MAIT) cell activation; James Ussher, Rajesh Lamichhane, University of Otago
- Development of a whole-proteome database for a head and neck squamous cell carcinoma cell line using data-independent acquisition (DIA) mass spectrometry; **Yongchuan Gu,** Bill Wilson, Frederik Pruijn, Leo Payne, **University of Auckland.**
- Synthesis of CLipPA Analogues of the Antimicrobial Peptide Paenipeptin C; Greg
 Cook, Iman Kavianinia, University of Otago, Paul Harris, Margaret Brimble, University
 of Auckland
- Glycans as Diagnostic Biomarkers for Rheumatic Fever; Nikki Moreland, Reuben McGregor, University of Auckland
- Transcriptome profiling of cancer cells expressing $\Delta 133p53\alpha$, $\Delta 133p53\beta$ and $\Delta 133p53\gamma$ isoforms; **Marina Kazantseva**, Antony Braithwaite, Sunali Mehta, **University of Otago**, Cris Print, University of Auckland
- Simultaneous surface protein and transcriptome analyses to define single cell populations in human adipose tissue; Anna Brooks, Klaus Lehnert, Rod Dunbar, University of Auckland
- Comparison of Digital Spatial Profiling with gold standard fluorescent immunostaining to profile immune checkpoints in Merkel Cell Carcinoma; Cherie Blenkiron, Kate Parker, University of Auckland
- RNA-Sequence analysis of the remaining 34 New Zealand melanoma cell lines of the NZM cell line panel; Mike Eccles, Mik Black, Euan Rodger, Aniruddha Chatterjee, University of Otago, Cris Print, Peter Shephed, Bruce Baguley, University of Auckland
- The Jejunal Microbiome in Type-two Diabetes; Donia Macartney-Coxson, Institute
 of Environmental Science and Research, Xochitl Morgan, Jeremy Krebs,
 University of Otago, Richard Stubbs, Capital and Coast District Health Board
- Calming the cytokine storm in cancer immunotherapy with LCK inhibitors; Jack
 Flanagan, University of Auckland



- Genotyping of Pacific-specific variants for metabolic disease risk; Tony Merriman,
 University of Otago
- Crystallographic Studies of Bacterial MenD Enzymes; Jodie Johnston, Thu Ho,
 University of Canterbury
- · Cross-linking Glycocin F; **Gill Norris, Massey University,** Margaret Brimble, Paul Harris, University of Auckland
- Lexapeptide, a novel peptide antibiotic targeting antimicrobial resistance; Ghader Bashiri, Chris Squire, Paul Harris, Margaret Brimble, University of Auckland, Greg Cook, University of Otago
- Click-chemistry-enabled cancer vaccine displaying antigen and α -Gal-Cer at ~100:1 ratio; **Jasna Rakonjac, Massey University,** Ian Hermans, Malaghan Institute of Medical Research, Gavin Painter, Victoria University of Wellington
- Synthesis of new antibiotic malacidin A and its analogues; Greg Cook, University of Otago, Paul Harris, Margaret Brimble, University of Auckland
- Mapping amylin receptor expression in the rat brain: where are the molecular targets of amylin mimetics? Erica Hendrikse, Debbie Hay, Christopher Walker, University of Auckland
- Defining the transcriptional response to MOTSc and mutant MOTSc in skeletal Muscle; Troy Merry, Alex Chan, Jonathan Woodhead, University of Auckland
- Characterisation of the distribution and prevalence of T cell subsets in tumours from exercising mice receiving immune checkpoint therapy; Gabi Dachs, Margaret Currie, University of Otago, Christchurch, Rod Dunbar, University of Auckland
- Generation of peptide growth hormone receptor antagonists; **Jo Perry,** James Dickson, Ries Langely, Peter Shepherd, **University of Auckland**
- Tagging Glycocin F; Gill Norris, Massey University, Margaret Brimble, Paul Harris, University of Auckland
- Baculoviral expression of lipidated G-proteins for use in lipid kinase assays; **Jack Flanagan, Danielle Paterson, University of Auckland**
- Selective DNA-PK inhibitors; **Michael Hay,** Lydia Liew, Ben Dickson, Jack Flanagan, Kevin Hicks, Stephen Jamieson, Bill Wilson, **University of Auckland**

Support for publication in high quality journals

MWC aims to enable publication in high quality journals by supporting the preparation of new data requested by reviewers or editors as well as other costs associated with publications. In 2018 support was provided for three publications;

1. Campbell, H., N. Fleming, I. Roth, S. Mehta, A. Wiles, G. Williams, C. Vennin, N. Arsic, A. Parkin, M. Pajic, F. Munro, L. McNoe, M. Black, J. McCall, T. L. Slatter, P. Timpson, R. Reddel, P. Roux, C. Print, M. A. Baird, and A. W. Braithwaite, Δ133p53 isoform promotes tumour invasion and metastasis via interleukin-6 activation of JAK-STAT and RhoA-ROCK signaling. *Nature Communications* (2018) 9(1).

- 2. Williams, E. T., P. W. R. Harris, M. A. Jamaluddin, K. M. Loomes, D. L. Hay, and M. A. Brimble, Solid-Phase Thiol-Ene Lipidation of Peptides for the Synthesis of a Potent CGRP Receptor Antagonist. *Angewandte Chemie* International Edition (2018) 57(36): 11640-11643.
- 3. Zhang, S., L. M. De Leon Rodriguez, I. K. H. Leung, G. M. Cook, P. W. R. Harris, and M. A. Brimble, Total Synthesis and Conformational Study of Callyaerin A: Anti-Tubercular Cyclic Peptide Bearing a Rare Rigidifying (Z)-2,3-Diaminoacrylamide Moiety. *Angewandte Chemie International Edition* (2018) 57(14): 3631-3635.

New investigators

In 2018, the Maurice Wilkins Centre continued to strengthen its national network of investigators with the appointment of new associate and affiliate investigators and the announcement of a new clinical associate initiative.

Associate and affiliate investigators

During 2018 23 new associate investigators were invited to join the Centre, bringing the total number of principal and associate investigators to 203 at the end of the year. In line with the MWC strategy of supporting future leaders, 3 of these new associate investigators were previously MWC affiliate investigators and on review in 2018 had developed their careers to the stage that they were approved for promotion to associate investigators. In addition, 43 postdoctoral and postgraduate students were appointed as affiliate investigators in 2018, with the total number of over 240.

New associate investigators appointed in 2018:

- Dr Timothy Allison, School of Physical and Chemical Sciences, University of Canterbury
- Dr Cherie Blenkiron, Department of Molecular Medicine and Pathology, University of Auckland
- · Dr Mihnea Bostina, Department of Microbiology and Immunology, University of Otago
- · Professor Colin Brown, Department of Physiology, University of Otago
- Associate Professor Rebecca Campbell, Department of Physiology, University of Otago
- Professor Richard Cannon, Faculty of Denistry, University of Otago
- · Professor Murray Cox, Institute of Fundamental Sciences, Massey University
- Dr Kirsty Danielson, Department of Surgery and Anesthesia, University of Otago, Wellington
- · Dr Sarah Diermeier, Department of Biochemistry, University of Otago
- · Dr Allan Gamble, School of Pharmacy, University of Otago
- Dr Joanne Hewitt, Environmental and Food Virology/Norovirus Reference Laboratory, Institute of Environmental Science & Research (ESR) Ltd
- Professor Philip Hill, Department of Preventive and Social Medicine, University of Otago
- · Professor Iain Lamont, Department of Biochemistry, University of Otago
- Professor Rudi Marquez, School of Physical and Chemical Sciences, University of Canterbury
- Associate Professor Alexander McLellan, Department Microbiology & Immunology, University of Otago
- · Associate Professor Brian Monk, Department of Oral Sciences, University of Otago
- · Professor Ian Morison, Department of Pathology, University of Otago

- · Dr Raewyn Poulsen, Department of Medicine, University of Auckland
- · Associate Professor Glen Reid, Department of Pathology, University of Otago
- · Professor Stephen Robertson, Dunedin School of Medicine, University of Otago
- Dr Sebastian Schmeier, Institute of Natural and Mathematical Sciences, Massey University
- · Dr Christopher Walker, School of Biological Sciences, University of Auckland
- · Professor Lisa Stamp, Department of Medicine, University of Otago, Christchurch

Clinical associates

The MWC investigator cohort includes practising clinicians with clinical challenges and ideas being actively promulgated through the MWC's research programmes. The Clinical Advisory Board, made up of ten of NZ's leading clinician-scientists, also provides clinically-focused review of our research programmes and enables new collaborations between MWC and other clinicians within their clinical networks.

In 2018 the MWC launched a new 'Clinical Associate' membership category as part of a committment to expand its clinical networks to include a wider group of practising clinicians who wish to be involved with the MWC and 13 new clinical associates were appointed. Specific funding has been allocated to support collaborative research between clinical associates or clinically-active associate investigators and other MWC investigators which will be activated in 2019.

New clinical associates appointed in 2018:

- · Dr Lance O'Sullivan, Navilluso Medical Limited, I Moko, Northland DHB
- · Dr Helen Lunt, Canterbury District Health Board
- · Associate Professor Greg O'Grady, Auckland District Health Board
- · Dr Maggie Kalev, Auckland District Health Board
- · Dr Rosalie Stevens, Auckland District Health Board
- · Dr Joel Pirini, Northland District Health Board
- · Dr Michelle Wilson, Auckland District Health Board
- · Dr Andrew Wood, Auckland District Health Board
- · Dr Ole Schmiedel, Auckland District Health Board
- · Associate Professor Polly Atatoa Carr, Waikato District Health Board
- · Dr Rachel Webb, Waikato District Health Board
- · Dr Manish Khanolkar, Auckland District Health Board
- · Dr Ayesha Verrall, Capital and Coast District Health Board

Human capability development

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 2018 the MWC provided direct full or partial financial support for 74 postgraduate students at the University of Otago, University of Canterbury, Victoria University of Wellington, Massey University, University of Waikato and the University of Auckland. Fifteen postgraduate students who received MWC support prior to or during 2018 completed their degrees in 2018.

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 2018 the MWC provided full or partial salary support for 30 research and post-doctoral fellows (10.4 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 MWC also provided partial support for 19 research technicians (5.0 FTE) to carry out specific roles in the core MWC research programme over 2018.

Many of the members of this cohort have been involved in Flagship research communities and this has given them the opportunity to widen their networks and develop their careers. The MWC has provided for for emerging scientists to present their work in such as Flagship meetings and the Early Career Researchers Symposium.

Emerging scientists are also encouraged to apply to the MWC for funding through the flexible research programme to access specialised facilities, equipment and training both in New Zealand and internationally (see page 44). This programme is a good way for emerging scientists to start learning how to write research grants. Applicants are given feedback on unsuccessful applications which allows them to work on revising these and re-submitting to future rounds. In 2018, 11 emerging scientists were successful in being awarded support to enable access to specialised national and international training, facilities and equipment.

Early Career Steering Committee

In 2018, the MWC Early Career Steering Committee convened two technical workshops aimed to upskill early career researchers on techniques relevant to their work. The first workshop was on Microscopy and Imaging Techniques and a second workshop on Flow Cytometry was held later in the year. The committee also planned the annual Future Science Day in December (see story on page 21) and continued to publish newsletters throughout the year, keeping MWC members informed of news and events within the early career researcher space. The committee also began formulating plans for a

mentoring programme within MWC, which they plan to implement in early 2019. Members of this group were: Dr Joanna Hicks (University of Waikato), Dr Wanting Jiao (Victoria University of Wellington), Dr Kate Lee (University of Auckland), Dr Iman Kavianinia (University of Auckland), Ms Marina Rajic (Massey University), Dr Euan Rodger (University of Otago), Dr Catherine Tsai (University of Auckland) and Dr Sunali Mehta (University of Otago).

Maurice Wilkins Centre Future Science Day

The Maurice Wilkins Centre Future Science Day was held on 7th December in Auckland, and was organised by the MWC Early Career Steering Committee. A poster session took place on the evening of the 6th consisting of 50 great posters presented by early career researchers which sparked plenty of lively discussion among attendees during the course of the evening.

The following day started off with a discussion between the MWC Director and early career investigators on the current and future strategy of MWC where the investigators gave feedback on what parts of the MWC programme were working well for them and what additional support would be of value in future years.

The Future Science Day gave nine early career MWC researchers the opportunity to present a short research talk, all of which were of a very high standard and impressed the audience. The day also offered a chance for investigators to network and get expert technical advice on issues related to their work during the "meet the expert" session held during the lunchbreak.

Travel prizes were offered to both poster presentations and research talks and these were awarded to;

Research talks: 1st – Effie Fan (Victoria University of Wellington), 2nd – Jennifer Eom (University of Auckland)

Research posters: 1st – Elyse Williams (University of Auckland), 2nd – Aqfan Jamaluddin (University of Auckland), Highly commended – Regan Fu (Malaghan Institute of Medical Research)

Technical training opportunities

In order to maintain a world class research programme it is important that MWC 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 colleagues. This contestable programme supports investigators' travel to national and international workshops and laboratories to learn new technical skills.

During 2018, nine investigators travelled under this scheme:



Dr Emma Andrews attended a workshop on the analysis of RNA sequencing data in Leipzig, Germany. This course, run by ECSeq Bioinformtics, focused on equipping participants with essential knowledge for the analysis of raw next generation sequencing data with a focus on the analysis of RNAseq data, enabling the elucidation of expression profiles. Emma became familiar with essential commands useful to data analysis and with these, worked through the analysis workflow from; quality control, trimming, mapping and understanding the associated statistics, how to visualise results and carry out differential gene expression and basic enrichment analyses. The skills gained by attending this workshop have enabled Emma to work up a pipeline to implement in-house. This will enable others in Emma's lab to better understand their data and circumvent the requirement of outsourcing the analysis process by being able to analyse raw transcriptomic data themselves.

Mr Chris Horne visited the University of Lethbrige in Canada to work alongside Distinguished Professor Borries Demeler, a world leading researcher in biophysics. Here, Chris was introduced to multiwavelength sedimentation velocity experiments using an analytical ultracentrifuge. This is a powerful new method for analysing complex interactions within solution that are comprised of different types of molecules. Chris' research is focused on defining the DNA binding mechanism for a bacterial transcriptional regulator from Escherichia coli. This regulator negatively controls the expression of the genes necessary for the uptake and breakdown of sialic acid, an alternative nutrient source for bacteria. During his time at the University of Lethbridge, Chris successfully employed multiwavelength sedimentation velocity experiments to define the stoichiometry of the protein DNA complex. Initially spectral profiles were measured for the protein and DNA components. While Chris's project was focused on defining protein DNA interactions, multiwavelength analysis can be applied to numerous other fields, such as protein drug interactions or as a diagnostic tool. This therefore supports the potential for strong international collaboration and will highlight the innovative science New Zealand has to offer.

Ms Kelsi Hall and Ms Abby Sharrock were awarded partial support from the MWC to visit the Wilmer Eye Institute at Johns Hopkins University in Baltimore, USA, for two months. Both Kelsi and Abby are working on PhD projects with Professor David Ackerley involving the engineering and directed evolution of nitroreductase enzymes from bacterial species for future potential therapeutic uses. At the Wilmer Eye Institute they were able to access zebrafish disease models that they could use to test their evolved nitroreductase enzyme variants as well as training from experts. The data gathered from this trip is expected to lead to several future publications. The trip has also strengthened the collaboration between the Ackerley lab in Wellington and the Mumm Lab in Baltimore, and has since sparked additional collaboration between the labs in related research areas.

Dr Adam Middleton had a three-month placement in the laboratory of Prof. Sachdev Sidhu at the University of Toronto in Canada. Here, Adam learnt how to perform phage display, using both an already-established library and a new library he produced on site. The libraries are comprised of massive pools of ubiquitin variants (UbVs), which are presented on the protein coat of the phage. By the end of Adam's time he had isolated over

100 phage that each produce a different UbV. Adam is now validating and characterising the interactions of the UbVs to an array of target proteins, as well as setting up a parallel system in the laboratory at the University of Otago. Adam is now interacting with Dr. Alexander McLellan in Microbiology at the University of Otago, who is also using phage display, to discuss and share techniques and resources. Given UbVs can inhibit or enhance ubiquitin transfer, Alex believes this work may aid the understanding of the ubiquitin pathway, with the potential to provide leads for future drug design.

Dr Effie Fan attended the EMBO practical course on solution scattering from biological macromolecules in Hamburg, Germany. The course covered all aspects of state-ofart solution scattering experiments with lectures and hands-on beamline tutorials, as well as covering data collection, analysis, and model building, provided by the BioSAS group led by Prof. Dimitri Svergun and a number of speakers from across the globe. The structural information on biomolecules provided by small angle X-ray/neutron scattering (SAXS/SANS) experiments is powerful in understanding the molecular details and conformations governing the function and regulation of these molecules, which lies at the foundation of a number of projects within the MWC research programme, particularly in the area of developing new treatments for infectious diseases. During the course, participants visited the EMBL high brilliance BioSAXS beamline at the PETRA-III storage ring and the EMBL laboratory facilities at the German Electron Synchrotron (DESY). Effie's research samples were prepared and examined on site during the course, from which high quality SAXS data was obtained and processed for advanced modelling. The knowledge learnt during this course has been shared with several research groups in New Zealand who are interested in solution scattering through personal communications, meetings and social media. A seminar in 2019 will also be arranged through the Centre for Biodiscovery at the Victoria University of Wellington.

Ms Kristiana Santoso's PhD project involved synthesising various libraries of compounds in the search for new anti-tuberculosis drugs. Kristiana, supervised by Assoc. Prof. Mattie Timmer and Assoc. Prof. Bridget Stocker at Victoria University of Wellington, spent five days at the University of Otago, hosted by Prof. Greg Cook and his research team to test the 70 compounds she had synthesised. There, Kristiana tested the compounds against four different bacteria and learned how to conduct some of the assays and analyse the results. In addition to obtaining MIC values for the synthetic compounds, Kristiana also spent time with Dr. Kiel Hards on the biochemistry assays he had designed to see whether any of my compounds affected the respiratory system of mycobacteria, the bacteria that causes tuberculosis. The results were included in Kristiana's PhD thesis.

Associate Professor Paul Harris visited the laboratory of Prof Nicola Pohl at Indiana University in Bloomington, Indiana. Prof Pohl's laboratory is pioneering the use of flow chemistry to rapidly prepare biomolecules such as peptides, proteins, glycoproteins and oligosaccharides. Flow chemistry is the science of continually flowing reagents together at high flow rates, resulting in dramatically reduced reaction times, and high purity products, that can be isolated easily. Such techniques are now becoming the mainstay of



modern laboratories but can be too expensive for academic settings. Prof Pohl's approach is to build the apparatus "from the ground up", assembling each component (e.g. pumps and switching valves) and then to use simple computing languages e.g. Python to control the flow chemistry via a mini computer. This home built system is a fraction of the cost of a commercial instrumentation and more importantly, the simple design facilitates users to troubleshoot, fix and maintain on-site. During his stay, Paul assembled all the components needed for flow chemistry peptide synthesis, underwent training in the use of Python computer programming to automate the process from a remote computer and obtained several example programs to enable installation within the Maurice Wilkins Centre.

Mr Hamish Angus was given the opportunity to meet collaborators in Brisbane, after attending the 'Organoids are us' conference in Melbourne. Dr Jakob Begun, of the Translational Research Institute of Australia and his colleagues had experience with intestinal organoids, a model that is currently being developed by Hamish and others in the lab of Associate Professor Roslyn Kemp at the University of Otago. Both labs are working on introducing an immune cell component to intestinal organoid models – and the visit was a great opportunity for Hamish to put faces to names, present his data for feedback and to share some tips and tricks for culture techniques. Hamish plans to use the connections made and information gathered to improve the culture techniques back in Otago and push intestinal organoids forward as accurate in vitro models for the study of inflammatory bowel disease and intestinal cancer.

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 2018 this once again 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 2018:

- · Prof Catherine Bollard, Children's National, Washington DC, USA
- · Dr Thomas Cox, Garvan Institute of Medical Research, Australia
- · Dr Giles Yeo, Cambridge University, UK
- Prof Benjamin G. Davis, University of Oxford, UK
- · Prof Ke Ding, Jinan University, China
- · Dr Yury Goltsev, Stanford University, Stanford, USA
- · Prof Jose Martins, Ghent University, Belgium
- · Prof David J. Newman, NCI's Natural Products Branch, Frederick, USA
- · Prof Philippe Lambin, University of Maastricht, Netherlands
- · Prof Peng Li, Guangzhou Institutes of Biomedicine and Health, China
- · Prof Nicola L.B. Pohl, Indiana University, Bloomington, USA
- · Prof Des Richardson, University of Sydney, Australia
- · Dr Uli Schwarz-Linek, University of St Andrews, UK
- · Dr Debbie Williamson, Peter Doherty Institute for Infection and Immunity, Australia

International and national officials and delegations

In 2018, Maurice Wilkins Centre investigators hosted or participated in visits by the following officials and delegations:

· Consulate-General of China in Auckland Delegation, August 2018

Madam Erwen Xu, Consul-General

Mr Yewen Xiao. Vice Consul-General

Ms Mengjun Kou, Consul-Economic & Commercial Affairs

Mr Xin Tang, Consul

 Guangdong Provincial and Guangzhou Municipal Government Delegation, September 2018

Mr Xi Li, Member of Political Bureau of CPC Central Committee, Secretary of Guangdong

Mr Yezhou Guo, Vice Minister of International Department of CPC Central Committee (IDCPC)

Mr Guohui Wen, Deputy Secretary of Guangzhou Party Committee, Mayor of Guangzhou

Mr Yanxiong Zheng, Deputy Secretary-General of Guangdong, Director-General of Guangdong Policy Research Office

Mr Qiuyan Chen, Director-General of Guangdong Office of Leading Group of Foreign Affairs

Mr Jianrong Zheng, Director-General of Guangdong Department of Commerce

Mr Yufei Duan, Director-General of Guangdong Health and Family Planning Commission

Mr Xuefeng Ai, Vice Mayor of Shenzhen

Ms Dingding Du, Deputy Director-General of Bureau VII, IDCPC

Mr Hongjun Shangguan, Deputy Director-General of Protocol Bureau, IDCPC

Mr Huiling Zhang, Division Director of Guangdong Office of Leading Group of Foreign Affairs

Mr Guanghui Zhang, Secretary of Mr. Xi Li

Ms Liang Hu, Deputy Division Director of Bureau VII, IDCPC

Ms Ning Shen, Deputy Division Director of Bureau VII, IDCPC

Mr Rongshui Zhou, Deputy Division Director of Bureau VII, IDCPC

Ms Wei Wang, Deputy Division Director of Coordination Bureau, IDCPC, Interpreter

Mr Sheng Bi, Deputy Division Director of Protocol Bureau, IDCPC

Mr Jian Chen, Third Secretary of the General Office, IDCPC

Mr Donghai Qin, Director of Comprehensive Division I, CPC Guangdong Committee

Mr Tiehe Qin, Director of Internal Medicine Department, Guangdong People's Hospital

Mr Weixi Yang, Section Chief of General Office of Guangzhou Municipal Government

Mr Jing Zhang, Section Chief of Guangdong Foreign Affairs Office

Mr Lei Zou, Section Chief of Guangdong Foreign Affairs Office

· Guangzhou Institutes of Biomedicine and Health (GIBH) Delegation, October 2018

Prof Hongming Hou, Deputy Secretary of Party Committee, Secretary of Disciplinary Inspection Committee

Prof Donghai Wu, South China Institute for Stem Cell Biology and Regenerative Medicine

· National University of Samoa Delegation, November 2018

Prof Asofou So'o, Vice-Chancellor and President

Dr Satu Viali, Specialist Physician and Cardiologist

Dr Seuseu Tauati, CEO, Scientific Research Organization of Samoa

Dr Fiame Leo, Scientific Research Organisation of Samoa

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 public good funding

In 2018 Maurice Wilkins Centre investigators were awarded new grants worth more than \$45 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 \$14 million from the Health Research Council of New Zealand, \$5.5 million from the Marsden Fund and \$17 million from the Ministry of Business, Innovation and Employment Endeavour Fund.

New Zealand commercial funding

In 2018 Maurice Wilkins Centre investigators secured new funding of over \$500,000 from New Zealand companies to support research.

International funding

In 2018 Maurice Wilkins Centre investigators secured new funding of \$700,000 from international sources to support research.

Governance and management

Maurice Wilkins Centre Board

In 2018 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 2018; April, August and November. The Board reviewed and advised on strategy for international activities, a process for appointment of new principal investigators and engagement with Māori led research organisations. They also approved recommendations from the Flagship Review Committee for the allocation of resources to two new flagship programmes and from the March and August MWC Project Review Committees for allocation of resources to projects submitted for inclusion in the Flexible research programme. The Board continued to monitor progress of the MWC research programme through the year for compliance with the funding mandate and budget.

Management Committee

The MWC Management Committee consists of the following principal investigators; Professors Rod Dunbar (Director), Peter Shepherd (Deputy Director), Margaret Brimble, Bill Denny and Associate Professor Rinki Murphy (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).

Associate Professor Rinki Murphy was appointed to the Management Committee in July 2018 and brings both clinical and research expertise in the field of diabetes and metabolic disorders.

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 2018 and its focus was on the implementation of the 2018-2020 MWC Plan. This included managing the allocation of resources and set up of four reconfigured Flagship programmes and the initiation of two new Flagship programmes. The Committee ran processes to appoint new management and non-management principal investigators and a new process for appointment of Clinical Associates. The Committee continued to manage 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. Seven non-management Principal Investigators continued in this position in 2018; Professor Vic Arcus (University of Waikato), Professor Mike Eccles (University of Otago), Professor Gary Evans (Victoria University of Wellington), Associate Professor Shaun Lott, Associate Professor Rinki Murphy (to July 2018), Associate Professor Adam Patterson and Professor Cris Print (University of Auckland).

In 2018, four new non-management Principal investigators were appointed; Professor Debbie Hay and Dr Nikki Moreland from the University of Auckland and Professors Tony Merriman and Kurt Krause from the University of Otago.

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 Auckland on the 18th of June. The progress of the large-scale collaborative 'flagship' research projects was reviewed and future strategy for the research and outreach programmes was discussed.

The second forum, attended by principal and associate investigators, was held in Auckland on the 6th of December. At this forum investigators were updated on progress in 2018 and consulted on future strategy for the Centre.

Scientific Advisory Board and Clinical Advisory Board

The members of the Scientific Advisory Board (SAB) for 2015 to 2018 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).



Three new members were invited to join the SAB in 2018; Professor Adrian Harris (United Kingdom), Professor Mark Walker (Australia) and Dr Giles Yeo (United Kingdom).

Meetings of the SAB are generally held biennially and the next meeting is scheduled for March 2019.

Members of the Clinical Advisory Board (CAB) 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 did not formally meet in 2018 however the members of the CAB were consulted with during the preparation of guidelines for the new Clinical Associates membership category and several of the members have been actively advising the ongoing research strategy of the MWC at strategy for ain 2018.

Project Review Committee

The Project Review Committee convened twice, in March and August 2018, to review applications submitted in 2018 for inclusion in the Flexible Research Programme and make recommendations to the Management Committee and MWC Board on which applications to approve.

In March, the Project Review Committee consisted of 7 principal and 3 associate investigators from the University of Otago, Victoria University of Wellington and the University of Auckland. They reviewed applications for Categories 2 and 3 of the Flexible Research Programme.

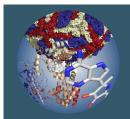
In August, the Project Review Committee consisted of 8 principal and 4 associate investigators from the University of Otago, Victoria University of Wellington and the University of Auckland. The committee reviewed applications for Categories 2 and 3 of the Flexible Research Programme.

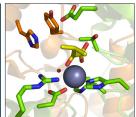
Flagship Review Committee

A Flagship Review Committee was convened and met on the 29th of March 2018 to review proposals submitted for new Flagship programmes. The committee consisted of 18 members, including 13 management and non-management principal investigators and 5 associate investigators.

The committee reviewed 5 applications for new Flagship programmes and made recommendations to the MWC Board for 2 of these to be funded.









Research Outputs

Publications

In 2018 research outputs from Maurice Wilkins Centre investigators included more than 460 peer-reviewed scientific papers published in international journals, and numerous patents granted, published or filed. Maurice Wilkins Centre contributed support to the following 92 scientific papers and reviews and 11 patents granted, published or filed.

Papers and Reviews

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Presentations

The significance of the research being done by Maurice Wilkins Centre investigators and their teams is demonstrated by more than 170 invitations to give international and national presentations in 2018. The presentations included invited lectures at conferences and seminars at academic institutions in Australia, Brazil, Canada, China, Croatia, Germany, Greece, Israel, Italy, Japan, Mexico, Norway, Portugal, Scotland, Singapore, South Africa, Tonga, the United Kingdom and the United States of America, as shown in the diagram below.



Presentation highlights

Significant presentations given by Maurice Wilkins Centre investigators in 2018 include:

- Distinguished Professor Margaret Brimble gave the keynote presentation "Nature's Medicine Chest: Opportunities for Synthesis and Drug Discovery" at the 24th Royal Australian Chemical Institute Organic Division Conference held in Perth, Australia. This talk was also presented at 11 other meetings, including the Royal Society of Chemistry Organic and Biomolecular Chemistry Symposium (Shanghai, China), XVIII Edition of the Ischia Advanced School of Organic Chemistry (Naples, Italy) and 29th International Carbohydrate Symposium (Lisbon, Portgual).
- Professor Dave Grattan was invited to give the keynote presentation "Prolactin and the maternal adaptation to pregnancy" at the Federação de Scoiedades de Biologia Experimental held in Campos do Jordao, Brazil.

- Professor Debbie Hay gave the plenary presentation "New Insights into Calcitonin Family and their Receptor Pharmacology" at the 9th International Conference on the CGRP Family of Peptides held in New Mexico, USA.
- Professor Emily Parker gave the keynote presentation "Twisting tails and curious channels - the Phosphoribosyltransferases" at the International Carbohydrate Symposium held in Lisbon, Portugal as well as the keynote presentation "Biosynthetic Enzymes: Tools and Targets" at BioCat's 2nd Annual Conference held in Oslo, Norway.
- Professor Cris Print was invited to give the plenary presentation "Genomics in Aotearoa, new opportunities for eResearch in NZ" at The NZ-China Non-Communicable Disease Research and Cooperation Symposium held in Shanghai, China.
- Associate Professor Rinki Murphy was invited to give the presentation "Genetics of diabetes and obesity for obstetricians and gynaecologists" at the NZ Society for Obstetrics and Gynecology Conference held in Tonga.
- Dr Nikki Moreland was invited to give a presentation on "Profiling complement and antibodies in ARF" at the Strep A Spectrum Meeting, hosted by Telethon Kids Institute, in Perth, Australia as well as the presentation "New diagnostics for rheumatic fever" at the Ideas to Life Conference held in Hangshou, China. Nikki was also invited to give the presentation "Tracking autoimmunity: role of serological assays and echocardiography" at the World Health Organisation consultation meeting on Group A Streptococcus Vaccines, held in London.
- Professor Greg Cook gave the keynote presentation "Tackling drug-resistant tuberculosis by targeting multiple components of mycobacterial bioenergetics" at the 17th Awaji International Forum on Infection and Immunity held in Awaji Island, Japan. Greg also gave two plenary presentations at the Australian Society for Antimicrobials, Antimicrobials 2018 held in Brisbane, Australia; "Targeting mycobacterial energetics to fight drug-resistant tuberculosis disease" and "Generation of new antimicrobials a metabolism centred strategy."
- Professor Bob Anderson gave a plenary presentation on 'Radiation chemistry insights on the hypoxia-selectivity of anticancer prodrugs' at the Association for Radiation Research conference in Belfast, UK.



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

- · A*STAR (Singapore)
- · Connecticut College (USA)
- Free University of Berlin (Germany)
- French National Center for Scientific Research (France)
- Hokkaido University Hospital (Japan)
- Instituto de Agroquímica y Tecnología de alimentos (Spain)
- · Kerchoff Klinink (Germany)
- Leibniz University Hannover (Germany)

- McGill University (Canada)
- · Medical University of Vienna (Austria)
- Menzies Institute for Health Research (Australia)
- · National Center for Protein Sciences (China)
- · National Defence Medical College (Japan)
- · Osaka University (Japan)
- · Qingdao University (China)
- Saarland University (Germany)
- · Shanghai Jiao Tong University (China)

- · University Laval (Canada)
- University of Applied Sciences Bonn-Rhein-Sieg (Germany)
- University of Hannover (Germany)
- · University of Pittsburgh (USA)
- · University of Sarghoda (Pakistan)
- University of Strasbourg (France)
- · University of Vienna (Austria)
- · University of Warwick (UK)
- · Yamaguchi University (Japan)

Continuing academic collaborations

North America

- · British Columbia Cancer Agency (Canada)
- · British Columbia Cancer Agency (Canada)
- Montreal Neurological Institute and Hospital (Canada)
- · University of British Columbia (Canada)
- · University of Ottawa (Canada)
- · Albert Einstein College of Medicine (USA)
- Arkansas State University (USA)
- · Binghamton University (USA)
- Brown University (USA)
- · Cedars-Sinai Hospital (USA)
- · Centennial Institute (USA)
- Cleveland Clinic, The Lerner Research Institute (USA)
- · Cornell University (USA)
- Emory University (USA)
- Fralin Life Science Institute, Virginia Tech (USA)
- · Georgia Institute of Technology (USA)

- Global Alliance for TB Drug Development (USA)
- Harvard University (USA)
- Icahn School of Medicine at Mount Sinai (USA)
- Indiana University School of Medicine (USA)
- · Johns Hopkins University (USA)
- La Jolla Institute for Allergy and Immunology (USA)
- Massachusetts General Hospital (USA)
- MD Anderson Cancer Center, University of Texas (USA)
- Mercer University (USA)
- Moffitt Cancer Center (USA)
- · National Institutes of Health (USA)
- · Northern Arizona University (USA)
- Penn State University (USA)
- · Phoenix Children's Hospital (USA)
- Rutgers University (USA)
- Sanford Burnham Medical Research Institute (USA)
- Stanford University (USA)
- Stony Brook University (USA)
- Texas A&M University (USA)
- University of Alabama (USA)
- University of Arizona (USA)
- University of California (USA)
- University of Chicago (USA)
- University of Colorado (USA)
- · University of Georgia (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 Southern California (USA)
- · University of Tennessee (USA)
- University of Texas South Western (USA)
- University of Texas Southwestern Medical Center (USA)
- University of Utah (USA)
- University of Virginia (USA)
- · University of Washington (USA)
- · Vanderbilt University (USA)
- Wake Forest University (USA)
- · Winona State University (USA)

South America

- · Federal University of Minas Gergais (Brazil)
- · Federal University of Sao Paulo (Brazil)

UK and Europe

- · Université Libre de Bruxelles (Belgium)
- University of Namur (Belgium)
- · Czech Academy of Sciences (Czech)
- University of Copenhagen (Denmark)
- · University of Eastern Finland (Finland)
- · Paris VI (France)
- · Pasteur Institute (France)
- · Université de Picardie Jules Verne (France)
- Braunschweig University of Technology (Germany)
- · Charite University (Germany)
- Hamburg University of Applied Sciences (Germany)

- Jacobs University (Germany)
- Johannes Gutenberg University (Germany)
- Max Planck Institute for Infection Biology (Germany)
- Max Planck Institute for Molecular Genetics (Germany)
- RWTH Aachen University (Germany)
- Technical University of Dortmund (Germany)
- University of Freiburg (Germany)
- · Vilnuis University (Lithuania)
- University of Leiden (Netherlands)
- · University of Maastricht (Netherlands)
- University of Oslo (Norway)
- University of Dundee (Scotland)
- · Estación Experimental del Zaidín (Spain)
- Karolinska Institute (Sweden)
- · Research Institutes of Sweden (Sweden)
- · Uppsala University (Sweden)
- École polytechnique fédérale de Lausanne (EPFL) (Switzerland)
- ETH Zurich (Switzerland)
- · Paul Scherrer Institut (Switzerland)
- Swiss Federal Institute of Technology (Switzerland)
- Aston University (UK)
- Defence Science and Technology Laboratory (UK)
- Essex University (UK)
- Queen Mary University of London (UK)
- · University of Cambridge (UK)
- University of Exeter (UK)
- University of Huddersfield (UK)
- University of Lincoln (UK)
- University of Liverpool (UK)
- University of London (UK)
- University of Manchester (UK)

- University of Nottingham (UK)
- University of Oxford (UK)
- · University of Southampton (UK)

Asia Pacific

- · Garvan Institute (Australia)
- Australian Institute of Marine Science (Australia)
- Australian National University (Australia)
- Children's Medical Research Institute (Australia)
- Edith Cowan University (Australia)
- · Garvan Institute (Australia)
- · Griffith University (Australia)
- Hudson Institute of Medical Research (Australia)
- · Latrobe University (Australia)
- Monash University (Australia)
- Murdoch Children's Research Institute (Australia)
- Peter MacCallum Cancer Centre (Australia)
- Queensland Institute for Medical Research (Australia)
- Telethon Kids Institute (Australia)
- The Peter Doherty Institute for Infection and Immunity (Australia)
- · University of Adelaide (Australia)
- · University of Melbourne (Australia)
- · University of New South Wales (Australia)
- · University of Newcastle (Australia)
- University of Queensland (Australia)
- · University of Sydney (Australia)
- University of Technology Sydney (Australia)
- · University of Wollongong (Australia)
- · Walter and Eliza Hall Institute (Australia)

- · Drug Screening Institute (China)
- Fujian University of Traditional Chinese Medicine (China)
- Guangzhou Institute of Biomedicine and Health (China)
- · JINAN University (China)
- Peking University (China)
- · Zhejiang University (China)
- · Indian Institute of Science (India)
- · Indian Statistical Institute (India)
- Pondicherry University (India)
- · Universitas Gadjah Mada (Indonesia)
- Universitas Padjadjaran (Indonesia)
- Kyushu University (Japan)
- · Nagasaki University (Japan)
- Okinawa Institute for Science and Technology (Japan)
- · RIKEN institute (Japan)
- · Korea Basic Science Institute (Korea)
- · Seoul National University (Korea)
- · Samoa Cancer Society (Samoa)
- Nanyang Technological University (Singapore)
- National University of Singapore (Singapore)
- · University of Medicine 1 (Southeast Asia)

South Africa

- · University of KwaZulu-Natal (South Africa)
- · Rhodes University (South Africa)



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 33 of this report. The Centre's investigators also act as consultants for a number of national and international companies.

In 2018 the expertise of Maurice Wilkins Centre investigators was sought by:

- · Abbott Diagnostics (USA)
- · Abcam (UK)
- · Allergan Pharmaceuticals (USA)
- · Auckland Clinical Studies Ltd
- · Auckland UniServices Ltd
- · Avalia Immunotherapies Ltd
- · AzurRx BioPharma (USA)
- · Bayer Animal Health NZ
- · Biotelliga Ltd
- · Caldera Health Ltd
- · Claridges Organic Ltd
- · Cancer Research UK (UK)
- · CoDa Therapeutics (NZ) Ltd
- · Canterbury Scientific Ltd
- · Comvita Ltd
- · Connovation Ltd
- · Convert Pharmaceuticals SA (Belgium)
- Dairy Goat Cooperative

- · Deosan NZ
- · EpiGen New Zealand
- · Gilead Sciences Inc (USA)
- · GlycoSyn
- · Hardie Health Ltd
- · Hikurangi Bioactives Ltd
- · Humble Bee Ltd
- · Intarcia Therapeutics, Inc (USA)
- · Ironwood Pharmaceuticals (USA)
- · Kea Therapeutics Ltd
- · Landcare Research NZ Ltd
- · Living Cell Technologies (Australia)
- Metavention (USA)
- MitoQ
- · New Zealand Pharmaceuticals Ltd
- · NZeno Ltd
- · OcuNexus Therapeutics Inc (USA)
- · Plant and Food Research

- · Quality Scientific Solutions LLC (USA)
- · Rain Therapeutics Inc (USA)
- · Roche Diagnostics (Switzerland)
- · SapVax LLC (USA)
- Sphingotec GmBH Ltd (Germany)
- · Syngenta AG (Switzerland)
- The Global Alliance for TB Drug Development (USA)
- · Union Therapeutics (Denmark)
- · Upside Biotechnologies Ltd
- · Upstream Medical Technologies Ltd
- · Wellington Zhaotai Therapies 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 Global Alliance for TB Drug Development.

Awards and honours

International and national honours awards to Maurice Wilkins Centre investigators, affiliates and students in 2018:

Royal Society of London Fellowship

Distinguished Professor Margaret Brimble was elected into the Royal Society of London, making her the first New Zealand female Scientist ever to be admitted. See highlight story for further information (page 9).

· George and Christine Sosnovsky Award

The UK Royal Society of Chemistry awarded MWC Principal Investigator, Distinguished Professor Margaret Brimble the 2018 George and Christine Sosnovsky Award in Cancer Therapy for her use of her novel chemistry platform to develop cancer vaccines.

British Pharmacological Society Fellowship

MWC Principal Investigator, Professor Debbie Hay, was elected a fellow of the British Pharmacological Society in 2018. Debbie gainied her PhD at the Imperial College London in Pharmacolgy, and now focuses her research on G protein-coupled receptors and their role as potential drug targets to treat a number of diseases and disorders.

Royal Society Te Apārangi Fellowships

MWC Investigators Professor Emily Parker from Victoria University of Wellington, and Professor Stephen Robertson from the University of Otago, were both invited to be Royal Society Te Apārangi fellows in 2018. Royal Society Te Apārangi aims to disseminate knowledge through supporting the research community, education and outreach. Individuals elected as fellows are recognised as leaders within their individual fields and within the New Zealand Scientific Community.

· Fullbright New Zealand Scholar Awards

In 2018, two MWC investigators were awarded the Fullbright New Zealand Scholar Awards, which help fund research at US institutions. Principal investigator Professor Tony Merriman, from the University of Otago, will conduct his research at the University of Alabama Birmingham to investigate the genetics involved in gout and urate control in African-American populations. Dr Bronwyn Kivell, an MWC Affiliate Investigator from Victoria University of Wellington, was awarded funds to research the development of superior pain and addiction medications at both Scripps Research Institute and Florida Atlantic University.

· James Cook Research Fellowship in Health Sciences

MWC Principal Investigator Professor Tony Merriman was granted the James Cook Research Fellowship to further his research on gout and other metabolic diseases, with particular focus on genetic variations in Māori and Pasifika populations.

· 2018 Thermo Fisher Scientific Award

Dr Peter Mace, an MWC Associate Investigator from the University Otago, was presented the Thermo Fisher Scientific Award at the 2018 Queenstown Research Week. This award acknowledges an accomplished scientist in molecular biology research.

· QMB Illumina Emerging Research Award

Dr Htin Lin Aung received the 2018 QMB Illumina Emerging Researcher Award. This is awarded to an early career researcher to acknowledge their accomplishments and efforts using molecular biology tools and techniques.

The Maurice Wilkins Centre also congratulates the numerous investigators and students who received local and institutional honours throughout 2018.

Summary

Broad category	Detailed Category	2015	2016	2017	2018
FTEs by Category	Principal investigators	1.70	1.72	1.75	1.72*
	Associate investigators	2.09	2.50	2.38	1.49*
	Postdoctoral fellows	7.29	13.98	14.80	8.89*
	Research technicians	0.57	0.63	5.28	4.80*
	Administrative/support	2.81	3.27	3.66	2.86*
	Research students	14.58	18.44	22.92	17.91**
	Total	29.04	40.54	50.79	37.67
Headcounts by category	Principal investigators	19	20	20	24
, 0,	Associate investigators	145	155	164	184
	Postdoctoral fellows	20	24	43	39
	Research technicians	2	4	15	28
	Administrative/support	7	5	8	7
	Research students	23	69	77	75
	Total	216	277	327	357
Peer reviewed research	Journal articles	84	93	95	92
outputs by type	Book chapters	1	1	2	1
	Conference Proceedings	9	-	-	-
	Total	94	94	97	93
Value of external research contracts awarded by source	Vote Science and Innovation contestable funds	2,831,00	2,350,770	2,658,865	4,680,00
	Domestic- other non-Govt	372,977	431,677	673,257	586,000
	Overseas	2,067,798	1,153,198	222,207	599,000
	Other	117,500	153,769	167,019	703,000
	Total	5,389,275	4,089,414	3,721,348	6,568,00
Commercial activities	Patent applications	4	10	16	9
	Patents granted	5	0	1	2
Students studying at CORE	Doctoral degree	21	58	66	70
oy level	Other	2	11	11	5
	Total	23	69	77**	75**
Number of students completing qualification by level	Doctoral degree	-	5	10	14
	Other	1	7	7	3
	Total	1	12	17	17
mmediate post-study	Employed in NZ	1	4	7	12
graduate destinations	Employed overseas	-	5	5	3
	Further study in NZ	-	-	2	2
	Other	-	-	1	0
	Unknown		3	2	0

^{*}In addition to the directly funded FTE in the above table in 2018, Principal investigators contributed to an additional 2.32 FTE in time only and 0.6 FTE was co-funded; Associate investigators contributed an additional 3.15 FTE in time only and 3.52 FTE was co-funded; Postdoctoral fellows, Research technicians and Administrative/Support staff had an additional 13.19 FTE, 4.81 FTE and 1.78 FTE cofunded respectively.

^{**}Research students had an additional 47.65 EFT co-funded from other sources.

Summary Financial Statement 2018

Funding summary for the year ended 31 December 2018

Actuals

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Funding received	
Tertiary Education Commision grant	7,082
Total funding received	7,082
Salaries and salary related costs	2,383
Overheads	2,489
Project costs	1,652
Travel	383
Postgraduate students	697
Total expenditure	7,604
Net surplus/(Deficit)	-522

This report covers the period from 1 January 2018 - 31 December 2018 and details funding received and fund distributed to collaborative partners of the CoRE.

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

In 2017 the CoRE carried forward a net surplus of 1,570. This surplus has been added to the 2018 income to fund the CoRE's research programme in 2018. The CoRE therefore has a net surplus of 1,048 that will be carried forward into 2019 to fund future expenditure of the CoRE.

Directory

Governing Board

Scientific Advisory Board

Mr Bill Falconer (Chair) Prof Peter Andrews (Chair)

Prof Conan Fee Dr Chris Cooper
Prof John Hosking Prof Suzanne Cory
Prof Jim Metson Dr Jilly Evans
Ms Maxine Simmons Prof David James
Prof Warren Tate Dr Warwick Tong
Prof Mike Wilson Dr Jeanette Wood

Principal investigators (management)

-		
Prof Rod Dunbar (Director) Prof Peter Shepherd (Deputy Director)	School of Biological Sciences Department of Molecular Medicine and Pathology	University of Auckland University of Auckland
Prof Antony Braithwaite Prof Margaret Brimble Prof Greg Cook	Department of Pathology School of Chemical Sciences Microbiology and Immunology	University of Otago University of Auckland University of Otago
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Prof Dave Grattan	Department of Anatomy	University of Otago
Prof Ian Hermans	Malaghan Institute of Medical Research	
Assoc Prof Rinki Murphy Prof Emily Parker	Department of Medicine Ferrier Research Institute	University of Auckland Victoria University of Wellington

Principal investigators (non-management)

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Professor Michael Eccles	Department of Pathology	University of Otago
Professor Gary Evans	Ferrier Research Institute	Victoria University of Wellington
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Professor Cris Print	Department of Molecular Medicine and Pathology	University of Auckland
Dr Nikki Moreland	Department of Molecular Medicine and Pathology	University of Auckland

Principal investigators (emeritus)

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Prof Garth Cooper	School of Biological Sciences	University of Auckland
Prof Peter Hunter	Auckland Bioengineering Institute	University of Auckland
Prof John Fraser	Faculty of Medical and Health Sciences	University of Auckland

Associate investigators

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Prof Bruce Baguley	Auckland Cancer Society Research Centre	University of Auckland
Prof Michael Baker	Department of Public Health	University of Otago, Wellington
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Prof Mike Berridge	Malaghan Institute of Medical Research	
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Dr Gib Bogle	Auckland Bioengineering Institute	University of Auckland
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Prof Colin Brown	Department of Physiology	University of Otago
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Assoc Prof Rebecca Campbell	Department of Physiology	University of Otago
Prof Richard Cannon	Faculty of Denistry	University of Otago
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Prof Lai-Ming Ching	Auckland Cancer Society Research Centre	University of Auckland



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Prof Christian Hartinger	School of Chemical Sciences	University of Auckland
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School of Biological Sciences

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Dr Shaoping Zhang

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Department of Anatomy

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Mr Mohinder Kaplish

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MAURICE WILKINS CENTRE FOR MOLECULAR BIODISCOVERY

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