



## Stopping infections at the door

Designing vaccines  
that target immune  
cells in the mucosa

### WHAT'S INSIDE

PhD student receives  
Māori Cancer  
Researcher Award

New funding to boost RNA  
research into vaccines and  
other healthcare treatments

Kiwi-made Covid-19 booster  
vaccine offers 100% protection  
in preclinical study



## From the Director

It is always a privilege to share the many activities and achievements of the Malaghan Institute that have been made possible thanks to our supporters like you.

As we publish our first issue of Scope for 2023, it is important to remember that it's a challenging time for the many New Zealanders who are going through hardship. Floods, the lasting impacts of the pandemic and a cost of living crisis – we are feeling the pressure on a number of fronts, and face a great deal of uncertainty over the next few years. Yet, perhaps in spite of all this, our recent annual appeal saw people giving to the Malaghan Institute more than ever before, backing what we're doing to truly change health outcomes for all New Zealanders. We are truly humbled by your support.

Your support sends us a clear message that we need to knuckle down and get on translating our research into better vaccines, cancer therapies, treatments for allergic and inflammatory diseases and more. You can read about some of these developments in this issue, developments that have been made possible thanks to support in our community.

Yours sincerely,

**Professor Graham Le Gros | Director**  
CNZM FRSNZ FRCPA (Hon)

## Stopping infections at the door

### Designing vaccines that target immune cells in the mucosa

New research has identified that MAIT-cells, a type of immune cell found in mucosal tissues, are a promising target for future vaccines, with the potential to create stronger, more protective immune responses against pathogens at the site of infection.

Many infectious agents, including those that cause the flu and Covid-19, typically gain access to our body through similar pathways, most commonly through the nose or mouth. In response, our bodies have evolved strategies to help prevent unwanted organisms gaining internal access through these entry points. One way is to line these entryways with viscous, sticky fluid to trap unwanted organisms and hold them in place to then get mopped up by the immune system. These sticky mucus layers are found in many different sites around the body, not just the nose but in the lungs and intestines as well.

Because of their proximity to incoming infections, the immune cells located in and around the mucosa are the cells we most want to train to identify and remove harmful organisms – through vaccination – yet our current vaccines don't prioritise these cells.

The Malaghan Institute's vaccine evaluation team, led by Dr Lisa Connor, have plans to change that. They've spent several years developing and testing a new form of vaccine, one that is administered to, and specifically targets, the upper airways (nose and lungs) and the immune cells living there. What's more, rather than an injection, these vaccines could be delivered via nasal spray.

"Mucosal vaccines are vaccines that are administered into the mucosal tract, such as the respiratory or digestive system," says Kaitlin Buick, a PhD student at the Malaghan Institute and Te Herenga Waka – Victoria University of Wellington and co-author of the paper. "For example, a vaccine that is inhaled or swallowed instead of the typical





▲ Dr Theresa Pankhurst, co-author. Cover: Kaitlin Buick (left) and Dr Lisa Connor

needle injection. Mucosal immune responses can provide additional defence against respiratory viruses, including influenza and Covid-19.”

The immune cells that live in the mucosa have uniquely adapted to deal with oncoming threats. These specialised immune cells make perfect targets for vaccines, as these are the cells that are best positioned in the body to recognise and quickly respond to an infection. Additionally, antibody-producing immune cells in the mucosal tissue secrete a type of antibody called IgA that has the job of neutralising harmful pathogens in the mucosal surfaces of the body, which helps prevent infections. However, traditionally vaccines are administered intramuscularly – an injection into the arm. As such, they do not typically activate an immune response in the mucosa, and therefore do not provide the same level of protection against infections that target mucosal surfaces.

Developing mucosal vaccines has presented multiple challenges. The vaccine needs to overcome the physical barriers of the mucosa, such as the mucus layer, but also needs to be safe to prevent damage to the delicate lung structure.

“The aim of giving a mucosal vaccine is to build up a strong immune response against the pathogen throughout the body, but importantly, at the locations

in the body where pathogens can invade. Vaccines injected into the arm give strong immune responses that circulate around the body but can be limited in generating protective immune responses in those more vulnerable mucosal sites, thus giving the pathogen slightly more time and opportunity to infect us.”

Published in *Cell Reports*, the team’s research showed that MAIT-cells, a type of mucosal-associated immune cell, makes a promising target for mucosal vaccines.

“We included an ingredient in our vaccine that targets and activates a specific immune cell in the lung called a MAIT-cell. When this ingredient was given through the nose along with parts of SARS-CoV-2 or influenza viruses, it activated the mucosal immune system by helping other immune cells do their job better without causing excessive inflammation and damage.

“The results suggest that MAIT cells could be a promising target for mucosal vaccines that can protect against respiratory infections like COVID-19 and influenza,” says Kaitlin.

“There continues to be growing research into mucosal vaccines due to their potential benefits and there are current preclinical and clinical trials ongoing, some of which include mucosal vaccines for SARS-CoV-2. So while there is work yet to be done, there are positive steps forward to develop mucosal subunit vaccines.”

# PhD student receives Māori Cancer Researcher Award

Malaghan PhD student Danielle Sword is one of two Māori cancer researchers awarded funding by Te Kāhui Matepukupuku o Aotearoa (the Cancer Society of New Zealand) and Hei Āhuru Mōwai (Māori Cancer Research Leadership Aotearoa) to help address health inequities.

Danielle, who is undertaking her University of Otago PhD within the Malaghan Institute's CAR T-cell programme, will look into improving the mechanisms of CAR T-cells in the laboratory and investigate te ao Māori perspectives on CAR T-cell therapy from patients, their whānau, and the researcher.

"I would like to see our whānau have a better chance at fighting against cancer. This Māori Cancer Researcher Award means I can pursue a PhD that will utilise both Western Science and Mātauranga Māori to explore the emerging cancer treatment CAR T-cell therapy and its potential impact on Māori," says Danielle.

"I am very humbled and proud to be awarded this scholarship. The support from Hei Āhuru Mōwai and the Cancer Society with this kaupapa gives me more confidence in my mahi as a wāhine Māori scientist and researcher."

Dr Jonathon Koea, Māngai for Hei Āhuru Mōwai, says "These awards demonstrate what can be achieved by mainstream and Kaupapa Māori NGOs working together to grow the Māori research workforce and answer research questions of relevance to all New Zealanders."

Tumu Whakarae of Te Kāhui Matepukuku o Aotearoa Lucy Elwood adds: "The Māori Cancer Researcher

**"I can pursue a PhD that will utilise both Western Science and Mātauranga Māori to explore the emerging cancer treatment CAR T-cell therapy and its potential impact on Māori."**



▲ Danielle Sword

Awards demonstrate our commitment to advance Māori aspirations in cancer research. We hope that with these awards, we can change the underrepresentation

of Māori researchers in the cancer space and reduce health inequities."

The other recipient of the award is Grace Young (University of Otago) for her

PhD research into developing a better treatment for triple-negative breast cancer, which is fatal to many patients.

This type of cancer is prevalent among young women in New Zealand, and in particular Māori women.

# INTERNATIONAL CONNECTIONS

## MALAGHANITES ABROAD



**DR YASMIN NOURI**

Walter and Eliza Hall Institute of  
Medical Research, Melbourne

“My project will be looking at CAR T-cells that target multiple antigens in a single brain tumour. Unlike blood cancer, which can be effectively cleared in most cases by just targeting one protein on the cancer cell surface, brain tumours are a lot ‘messier’. Within one brain tumour, cells often look very different to each other, so we need to be strategic about targeting several proteins on their surface. We are basically giving the CAR T-cells more than one flag to look out for that signals to it that that is a cancer cell and should be killed.

“In the later parts of my project, I may also look at combining the CAR T-cells with other treatments to increase the efficacy of the CAR T-cells. Eventually, I will be bringing this work back to the Malaghan to further our CAR T-cell therapy research in the area of solid tumours.”



**DR THERESA PANKHURST**

Babraham Institute,  
Cambridge, UK

“I’m currently working in the Linterman Laboratory at the Babraham Institute thanks to my Te Urungi Churchill By-Fellowship. I will be investigating germinal centres – an immunological structure formed in lymph nodes following an infection – and their responses to mRNA vaccination in mice, how this changes with age and potential modulations we can make to mRNA vaccines to improve aged germinal centre responses. I will also be researching how human secondary tissues change across the lifespan.

“We are hoping to better understand how mRNA vaccines alter the quality of immune responses and germinal centres in ageing, and also to test new mRNA vaccines including specific ingredients that have potential to improve germinal centre responses and antibody production in older bodies.”



**DR OLIVIA BURN**

Icahn School of Medicine,  
Mt Sinai Hospital, New York

“I’ll be working in Assistant Professor Amaia Lujambio’s Liver Cancer Laboratory. I will be utilising her state-of-the art liver cancer models to assess whether our novel mRNA vaccines, which we have found induce strong immune responses in the liver, can be used to treat liver cancer.

“I am particularly interested in whether administration of the vaccine can enhance the anti-tumour responses induced by drugs already available in the clinic, such as the immune checkpoint inhibitor drug Keytruda. Unfortunately, liver cancers are among the most commonly-diagnosed and least-survivable cancers in Aotearoa New Zealand, with notably higher occurrence and death rates in Māori. I hope to use this research to support the commercial development of an mRNA vaccine platform for liver cancer with the ultimate aim to improve liver cancer outcomes for all New Zealanders affected by this disease.”



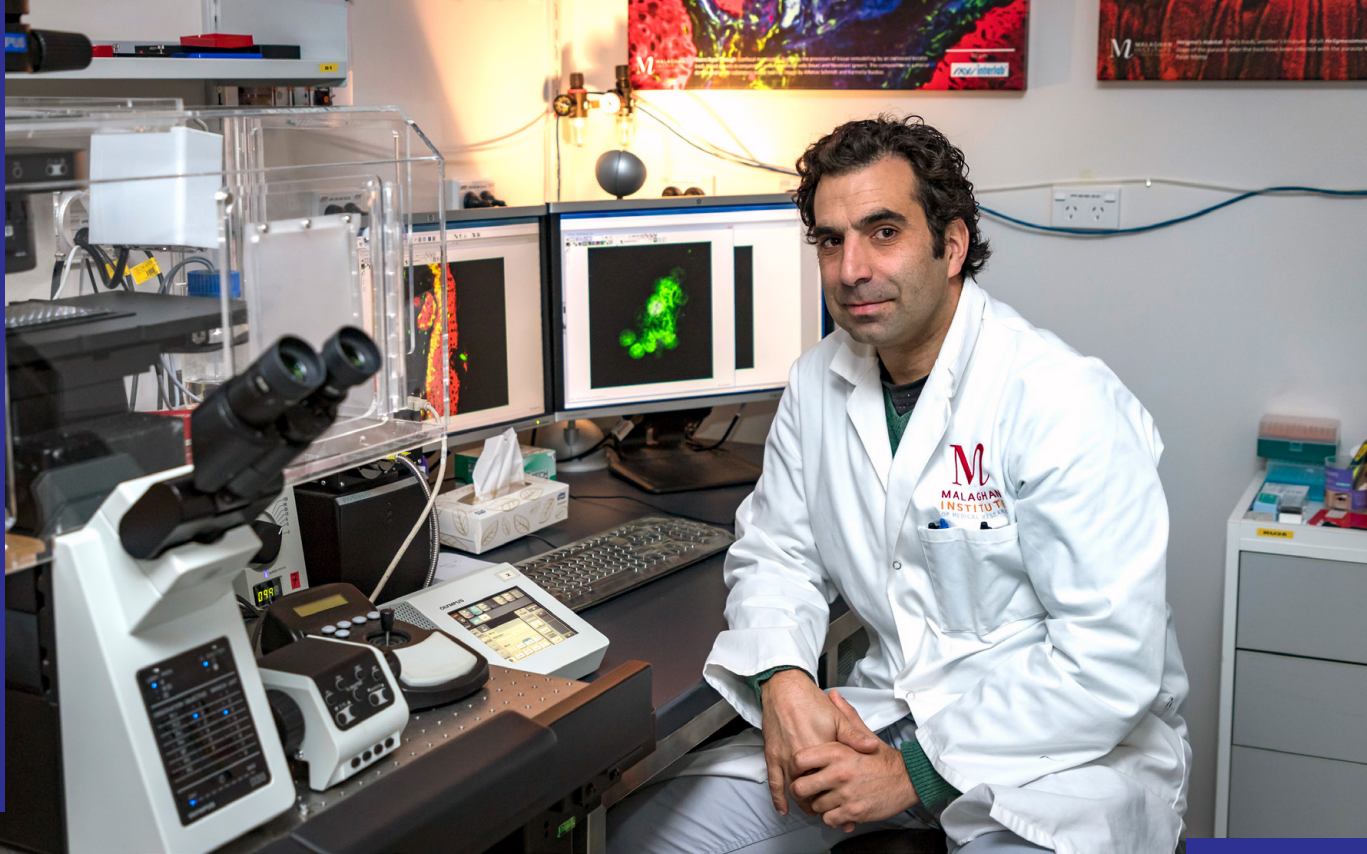
**DR KERRY HILLIGAN**

National Institute of Allergic  
and Infectious Diseases,  
Washington DC

“After completing my PhD at the Malaghan Institute, I spent four years at the National Institutes of Health in the United States under the mentorship of Dr Alan Sher. It was such an incredible experience being at the epicentre of science in the US, particularly during the COVID-19 pandemic where I got to see first-hand how the mobilisation of resources and assembly of minds to work on a common problem could be so effective.

“As immunologists working on infectious diseases in the lung, my colleagues and I were perfectly positioned to pivot our research into the study of SARS-CoV-2 and investigate what constitutes a protective immune response against COVID-19. Our findings that previous infection of the lung can protect against severe COVID-19 in preclinical models is really exciting and will form the basis of my work now that I am back at the Malaghan Institute.”





## MALAGHAN MICROSCOPY EXPERT AWARDED ADVANCED DIPLOMA

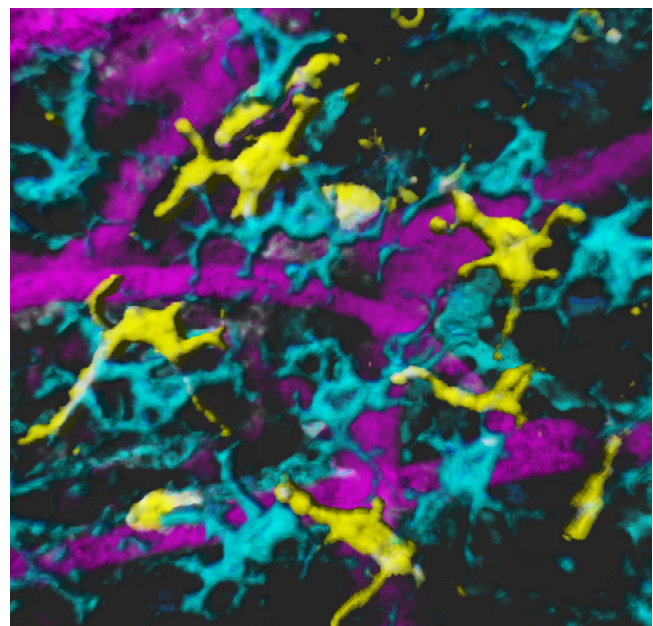
Malaghan bio-imaging specialist Alfonso Schmidt has received a diploma from the Royal Microscopical Society, adding another feather to his cap and expanding the institute's expertise in microscopic imaging.

"I had an amazing opportunity to undertake this flexible study to improve my knowledge in optical microscopy.

"The diploma was also an opportunity to develop professional relationships in the microscopy field through its mentorship, which in my case was with Graham Wright who is Director of the Agency for Science, Technology and Research in Singapore. He's an incredible person and was a great mentor for me during the diploma," says Alfonso.

"The whole experience was great for both my personal growth and professional development as a bio-imaging specialist. It's brought new skills and techniques that I've learned to the Malaghan Institute which will help me to continue to support our scientists and research here."

Microscopy is one of the key technology platforms our scientists use at the Malaghan to gain a deeper understanding of the immune system and its relationship to our health. By understanding how cells, tissues and organs interact with each other, we are able answer big questions about how the immune system works and make new discoveries.



▲ Microscopic image: 'The Front Line'

A three dimensional skin reconstruction – we can see blood vessels (pink) surrounded by two kinds of epidermal immune cells – dendritic epidermal T-cells (yellow) and Langerhans cells (cyan). Both immune cell populations play a complementary and vital role in monitoring and protecting the body as a first line of defence against invaders. Image captured using Olympus FV3000 confocal microscope and 3D rendering using IMARIS software.

# International deal for CAR T-cell therapy joint venture

Wellington Zhaotai Therapies Limited, a joint venture between the Malaghan Institute and Hunan Zhaotai Medical Group, has entered a multi-million dollar commercial deal with leading international pharmaceutical company Dr. Reddy's Laboratories Ltd for an exclusive license to its unique CAR T-cell technology in India.

Wellington Zhaotai Therapies was established in 2017 to take Hunan Zhaotai's novel CAR T-cell technology to the global market. In 2019 after further development at the Malaghan Institute, a phase I safety trial, ENABLE, got underway in New Zealand. Results of the trial are due to be published in the coming months.

Malaghan Institute General Manager Mike Zablocki, who is a Director of Wellington Zhaotai Therapies, says the deal validates the technology we've developed is attractive to the pharmaceutical industry and that the safety and efficacy clinical data generated in the New Zealand trial has given Dr. Reddy's confidence in our CAR T-cell product.

"This is great news, but early days in terms of commercialisation or financial benefit back to the Malaghan Institute as a joint venture partner – we'll still need funding for the next phases of development of our CAR T-cell therapy in New Zealand. The value of the deal is over 20 years so while the initial income is enough to support the ongoing business activities of Wellington Zhaotai Therapies, it won't represent a cash windfall for the Malaghan Institute," says Mr Zablocki.

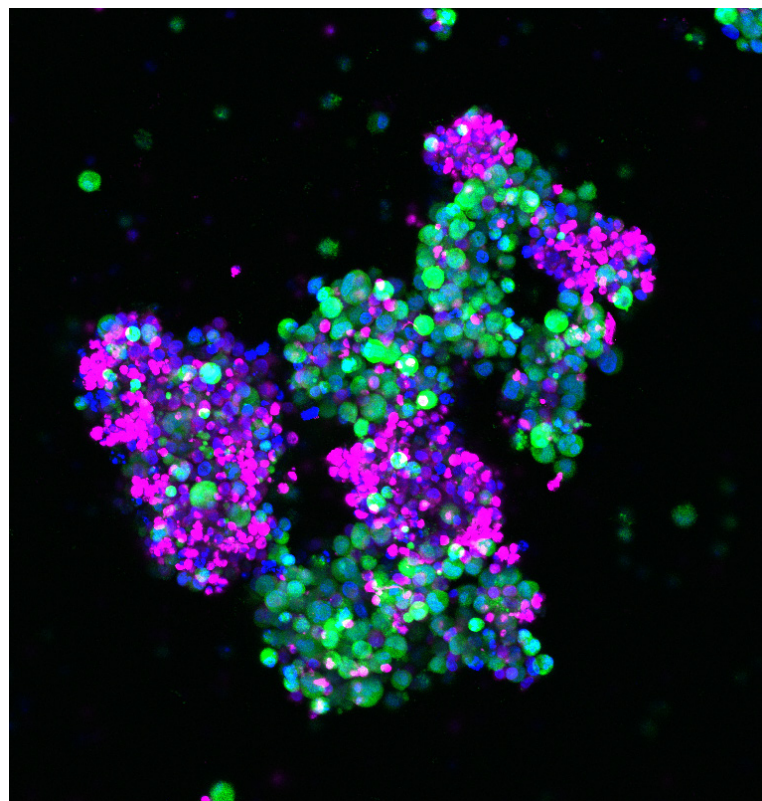
"That said, if Wellington Zhaotai Therapies does achieve its goal of becoming a globally successful biotech then the financial return to the

Malaghan Institute could be significant and will contribute towards future trials and research. And of

course, the Malaghan Institute retains the license for New Zealand for the therapy – so we can stick to our guns of making it cost-effective and accessible here."

Wellington Zhaotai Therapies' novel CAR T-cell construct has a unique, patented co-stimulatory domain which produces stronger anti-cancer activity in the laboratory than existing second generation CAR T-cells, which may provide a more effective treatment for patients. Preliminary clinical data

**"To develop a product through clinical trials to global licensing is no mean feat. This is a significant milestone for a New Zealand biotech."**



▲ CAR T-cells in action. Pink CAR T-cells, manufactured at the Malaghan Institute, are shown attacking a clump of green blood cancer cells. As the cancer cells die they turn blue.

also suggests an improved safety profile, with fewer side effects than competing CAR T-cell treatments.

Wellington Zhaotai Therapies Executive Director Peter Lai says the agreement is an inflection point for Wellington Zhaotai Therapies and reflects the successful partnership between the two research teams in New Zealand and China.

"The agreement gives Dr. Reddy's exclusive license to trial and commercialise the construct in India, but also signifies a strategic partnership

that could potentially extend to other countries and other cell therapies," says Mr Lai.

"The deal is also a positive reflection on New Zealand's science ecosystem and the support of the New Zealand Government for New Zealand's first CAR T-cell clinical trial. To develop a product through clinical trials to global licensing is no mean feat. This is a significant milestone for a New Zealand biotech."



# NEW FUNDING TO BOOST RNA RESEARCH INTO VACCINES AND OTHER HEALTHCARE TREATMENTS

Te Herenga Waka—Victoria University of Wellington and Waipapa Taumata Rau, University of Auckland, have been named as co-hosts of a government-funded Ribonucleic Acid (RNA) Development Platform. The platform is supported by the Malaghan Institute of Medical Research and the University of Otago, with Professor Kjesten Wiig of the Malaghan Institute and Professor John Fraser of the University of Auckland as the interim co-directors of the platform.

RNA technologies played a key role in the development of COVID-19 vaccines and this breakthrough has created significant opportunities for the technologies to be used in novel therapeutics, diagnostics, and vaccines. These technologies will also have application in other fields, including animal health and agriculture.

Initial funding of \$500,000 is being provided to the RNA Development Platform to prepare a seven-year research plan. This plan will be supported by a further \$69.5 million over seven years to support capacity- and capability-building in the sector.

The platform will bring together RNA researchers from around the country.

Victoria University of Wellington's Vice-Provost

(Research) Professor Margaret Hyland says that the University is excited by the possibilities that jointly developing RNA technologies with our partners offers, working towards enhancing New Zealand's resilience.

"This platform will bring together experts from across different organisations, here in New Zealand and internationally, and build the end-to-end capability of RNA technologies—from the lab right up to full-scale production."

Professor John Fraser, Dean of the Faculty of Medical and Health Sciences at the University of Auckland, and interim co-director of the platform agrees that results will come from a partnership approach that sees some of



▲ Professor Kjesten Wiig

New Zealand's leading research institutes and companies working to a shared goal of building this important technology in Aotearoa New Zealand.

Interim co-director Professor Kjesten Wiig from the Malaghan Institute says RNA technology presents a significant opportunity for New Zealand to supercharge

its thriving biotech sector and become a leader in the development of novel RNA therapeutics.

"We believe that we are at

the beginning of a step change in medicine—the RNA technology used in the COVID-19 vaccines is as disruptive and revolutionary as penicillin and computers."

The University of Otago's Deputy Vice-Chancellor (Research and Enterprise), Professor Richard Blaikie, says the university is pleased to be a part of this exciting new initiative.

"Through the pandemic we demonstrated as a research community our ability to work together to quickly provide novel solutions for the health sector or industry—this new platform puts this on an enduring footing for RNA research."



# Kiwi-made Covid-19 booster vaccine offers 100% protection in preclinical study

A preclinical study evaluating a Kiwi-made Covid-19 vaccine – Kiwi Vax – has shown its unique formulation induces a safe and highly effective immune response to SARS-CoV-2 variants of concern, making it a promising booster vaccine candidate.

Published in *iScience*, the study findings show that Kiwi Vax, developed by Vaccine Alliance Aotearoa New Zealand – Ohu Kaupare Huaketo (VAANZ) as part of the Government's Covid-19 vaccine strategy, is highly immunogenic, robustly expressed, and has a strong stability profile. The vaccine was independently tested at the National Institutes of Health in the United States and at the University of Melbourne.

"These findings not only show we have developed a promising booster vaccine candidate, but that we have the expertise, capability and experience within New

Zealand to make our own vaccines – something that stands us in good stead for future pandemics," says the Malaghan Institute's Professor Kjesten Wiig, Executive Director of VAANZ.

"Covid will be with us for many more years to come, so having safe and effective booster options, particularly for vulnerable populations, will help keep more people safe from the virus."

Kiwi Vax is a protein-based vaccine which works in a similar way to many traditional vaccines, using genetic information from the virus's distinct spikes.

Dr Lisa Connor, head of VAANZ's Vaccine Evaluation team says their subunit vaccine combines two different parts of the spike protein – the receptor binding domain and the N-terminal domain. These specific regions have been identified to contain 'hot-spots' that trigger potent immune responses against critical areas of the SARS-CoV-2 virus required for infection.

"Kiwi Vax has a unique set of attributes – its clean design does not attract extraneous immune responses, and it is designed to be specific to the virus. It elicits a broad antibody and T-cell response to all variants of concern, including Omicron, providing complete protection

against disease and preventing the virus from replicating in mice exposed to it.

"The immune response generated by the vaccine is also very durable and long-lasting and results to date indicate that Kiwi Vax is stable at refrigerator temperature for several months and at room temperature for at least one month. These are important advantages over current vaccines," says Dr Connor.

With philanthropic funding, the Malaghan Institute is planning to take Kiwi Vax through to a local phase I safety clinical using internationally-recognised GMP accredited New Zealand vaccine manufacturer, South Pacific Sera.

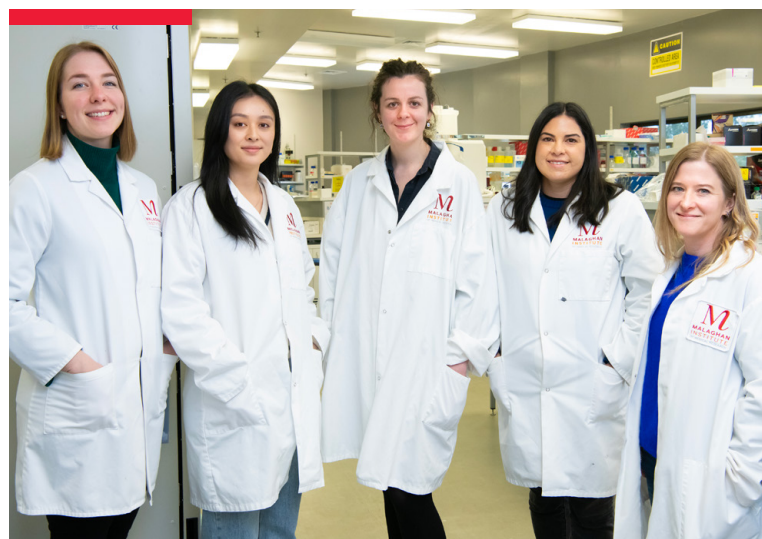
Professor Wiig says preclinically, Kiwi Vax is looking promising as a new potential COVID-19 vaccine

booster vaccine, but human clinical trials are required to confirm efficacy.

"We'd need a significant industry, philanthropic or

government partner to progress to later-stage clinical trials and regulatory approval. But wherever this lands, what we've set out to achieve here has been achieved. We've proven that New Zealand has the expertise and skills to develop a novel and effective vaccine against a pandemic virus and have built the capability, knowledge and connections to lay the foundations for New Zealand's response to future pandemics."

**"We have the expertise, capability and experience within New Zealand to make our own vaccines – something that stands us in good stead for future pandemics."**



▲ VAANZ Vaccine Evaluation team

# Farewell to Dan Williams and John Beattie

We are saddened to have recently lost two stewards of the Malaghan Institute.

Distinguished Trustee Dan Williams died at home in Plimmerton on 14 April. Dan served on the Malaghan Institute's Trust Board from 2005 and chaired the Board's Audit and Risk and Investment Committees until his retirement in 2020. He was recognised as a Distinguished Trustee in 2021.

As partner at accounting firm Deloitte and its predecessors over half a century, Dan was a strong leader for our finance team and adviser to Trustees, ably shepherding the institute through many years of growth.

Malaghan Institute Head of Finance David Lin says Dan's thoughtful insights and careful stewardship of our resources helped the institute remain financially stable and continue important work in medical research.

"Dan's commitment to our mission went far beyond his financial expertise, however. He was a tireless advocate for our cause and devoted countless hours to the institute. His passion for our work was infectious, and he inspired everyone around him to give their best."

Trustee of more than 30 years John Beattie died peacefully on 22 April, surrounded by his family.

As an executive of Brierley Investments Limited, John was integral in helping resuscitate the Malaghan Institute following the stock market crash in 1987, helping pull together a rescue package designed to financially underpin the institute and widen its support in the community. As part of this, Brierley Investments made a commitment to sponsor the institute for five years, but did so for many more.

John played significant roles within the Board and as a Director for related commercial entities, including Wellington Zhaotai Therapies Limited, set up to advance CAR T and other cell therapies.

"John was totally passionate about creating better opportunities in healthcare through research. Despite his long tenure, he could always be relied upon for creative and fresh thinking and for grasping any opportunity for the institute that arose. His energy and commitment will be sorely missed," says Malaghan Institute General Manager Mike Zablocki.

We extend our love and sympathies to Dan's and John's families.



DAN WILLIAMS



JOHN BEATTIE



## Back in the community!

We are so grateful to have such an incredible community backing us. By supporting the Malaghan you are helping to make disease a smaller part of our lives – thank you!

It has been such a fantastic start to the year as we continue to enjoy getting back out in the community, helping to raise awareness of our research, as well as the vital funds required to accelerate our research and bring better treatments and cures to New Zealanders. Thanks to you, our incredible supporters, our recent annual appeal raised a record amount of over \$350,000.

A special thank you to our anonymous match funder, who matched \$100,000 worth of donations. We know the best way to say thank you for all your support is to put our all into changing the game for people living with disease. You can count on us to do exactly that!



**LAURA GOLLAND**  
Head of Fundraising



▲ We had a fantastic day recently at the stunning Summerhill Estate Golf Course and Recreation Area in Papamoa hosted by our amazing Bay of Plenty Friends of the Malaghan Institute. A special thank you to our sponsors Lexus New Zealand, Wilderness Foods and of course the golfers who came out in force to support our research. (From left) Bay of Plenty Friends of the Malaghan Institute Chair Kimberly Mitchell, Pauline Caddigan & Hilary Fraser.



▲ A huge thank you to team March for Myeloma who across the month of March raised over \$8000 to support our cancer research. Led by Colin, who has lived with multiple myeloma for several years, and his wife Paula, the team are strong supporters of the Malaghan and understand the need for gentler, kinder cancer treatments in New Zealand.



TO FUNDRAISE FOR THE MALAGHAN INSTITUTE  
AND SUPPORT OUR LIFE-SAVING RESEARCH, VISIT

**[donate.malaghan.org.nz/raise-for-research](https://donate.malaghan.org.nz/raise-for-research)**

Here, you can find everything you need to set up and manage a fundraiser for the Malaghan Institute – from fun runs to bake sales – your fundraising efforts will help us get that much closer to breakthrough treatments for disease. As always, our fundraising team are here to help, so please reach out to [fundraise@malaghan.org.nz](mailto:fundraise@malaghan.org.nz) if you need help setting up your event.

# Together we can harness the power of the immune system and save lives.

People we love are suffering and dying from diseases we don't know enough about. But we do know the immune system holds the key to prevention, treatment and cures. By supporting the Malaghan Institute you are providing hope to those living with disease now and in the future.



## DEEPER UNDERSTANDING

We research to understand how to use the immune system to fight disease.



## BETTER TREATMENTS

We develop new immunotherapies to more effectively treat disease.



## FAIRER ACCESS

We are committed to taking our research into the community to provide treatment options for all.



TO DONATE, SIMPLY SCAN THE QR CODE, OR VISIT

**[donate.malaghan.org.nz](https://donate.malaghan.org.nz)**

You can also give our friendly fundraising team a call on 04 499 6914

## THANK YOU TO OUR PARTNERS

