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MALAGHAN INSTITUTE OF MEDICAL RESEARCH

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COVID-19 vaccine alliance formed

The Malaghan Institute and partners at the University of Otago and Victoria University of Wellington are leading efforts to secure a COVID-19 vaccine for New Zealand as part of the newly established Vaccine Alliance Aotearoa New Zealand – Ohu Kaupare Huaketo (VAANZ).

As part of the Government's COVID-19 vaccine strategy, details of which were announced by Prime Minister Rt Hon Jacinda Ardern at the Malaghan Institute in August, VAANZ has been tasked with establishing a national COVID-19 vaccine evaluation and development platform to screen, trial and accelerate the development of potential domestic and international COVID-19 vaccines.

Professor Graham Le Gros, VAANZ Programme Director, says the alliance is rapidly progressing New Zealand's capability and capacity to develop a COVID-19 vaccine, working with a range of local and international collaborators.

"We'll be making use of the abundant expertise and capability across the country and our global links to find the best vaccine options for New Zealand and our Pacific neighbours."

University of Otago's Associate Professor James Ussher, VAANZ Science Director, says the alliance has been formed following in-depth discussions with government as to the best approach to securing a COVID-19 vaccine for New Zealand.

"There are significant advantages of a national development and screening programme. Along with the obvious efficiencies, it gives us the scale needed to engage globally – with organisations like CEPI and big pharmaceutical companies – and will help develop local biotech capability to ensure we're best placed for future pandemics."

The alliance's funding pot has been boosted by philanthropic support to the Malaghan Institute, which as well as supporting the platform is accelerating the alliance's own vaccine research and development efforts.

"What we're looking at is an international landscape where COVID-19 vaccines are being developed rapidly for an emergency response, while others – the second generation vaccines we're developing here – are being designed with our increasing knowledge of immunity to SARS-CoV-2. These are ones, for example, that will provide lasting immunity, protect older and more vulnerable people, and can be scaled up and distributed easily and cheaply. At this stage, the more vaccines being researched and developed the better – it gives us choices.

"Vaccine Alliance Aotearoa New Zealand – Ohu Kaupare Huaketo is positioned to respond flexibly to changes in international developments, New Zealand's vaccine strategy, and vaccine candidates' progress. Our job is to help secure the safest, most effective vaccine – or vaccines – for New Zealand, as soon as possible."

IMAGE: Prof Le Gros with Rt Hon Jacinda Ardern and Assoc Prof Ussher

From the Director

It's a rare moment in history for science and biomedical research to come under such intense global scrutiny. The urgent need for a safe and effective COVID-19 vaccine has thrown both fundamental research and clinical development into the spotlight – two core pillars of our work at the Malaghan Institute. We are deeply aware of the responsibility we carry to help secure a cure for this global pandemic.

But our focus on this vital COVID-19 vaccine development has not hindered our existing, ongoing research programmes. Despite the disruption and uncertainty of recent months, our scientists have not skipped a beat and have continued to deliver quality, high-impact research. Of note, our cancer and gut health teams have progressed important clinical work as part of the ENABLE CAR T-cell clinical trial and the hookworm therapy clinical study, respectively. These are just two examples of community-driven research moving forward in challenging times and having an impact on the lives of New Zealanders.

Thank you once again for your support.

Prof Graham Le Gros
CNZM FRSNZ FRCPA (Hon)
Director

International vaccine expert joins Malaghan effort to secure a COVID-19 vaccine

The Malaghan Institute's expertise in vaccine development has been boosted further with the recent arrival of Dr Frances Priddy, former Chief Medical Officer and Vice President of Clinical Development at the International AIDS Vaccine Initiative in New York.

From early days researching the emergence of HIV in Africa and studying medicine in San Francisco during the height of the AIDS epidemic, to leading the International AIDS Vaccine Inititative, Dr Priddy has spent much of her career researching and developing clinical vaccines for infectious diseases. COVID-19 is her most recent challenge – and her expertise and experience will be vital in her new role as Clinical Director of Vaccine Alliance Aotearoa New Zealand – Ohu Kaupare Huaketo (VAANZ).

"Usually it takes around five years to take something from the lab and get it into the clinic," says Dr Priddy. "We, like everyone else in the world, are trying to compress this timeline as much as possible, ideally within two years. I would like to use my experience to help VAANZ accelerate promising vaccine candidates through the clinical process as quickly as possible.

"The other important goal for me is to make sure that the many resources here in New Zealand attract global interest and are used to evaluate international vaccine candidates. Already there are many candidates being trialled around the world, and there's no reason why New Zealand can't be involved in helping evaluate them. While we can't do efficacy studies – because thankfully New Zealand doesn't have enough COVID-19 cases – there's much we can be doing in terms of collecting safety and immunogenicity data, addressing vaccine hesitancy issues, and building knowledge around the vaccines under development.

I think trialling international candidates in New Zealand will go a long way to improving knowledge and acceptability of COVID-19 vaccines here. And it may enhance New Zealand's ability to have equitable access once these candidates have been proven safe and effective to use in humans."

MAIT cells and Mānuka honey – scientists uncover novel antibacterial mechanism

The Malaghan Institute and the Ferrier Research Institute have uncovered a novel way Mānuka honey helps stimulate the immune system to fight bacteria.

Honey is a complex natural product known to have strong antibacterial properties. Unlike regular honey which contains trace amounts of hydrogen peroxide as its main antibacterial component, Mānuka honey contains the molecule methylglyoxal (MGO). The amount of MGO in Mānuka honey gives Mānuka products its MGO rating.

It is the relationship between MGO and MAIT cells (mucosal-associated invariant T-cells), a specialised subset of immune cells found throughout the body, including the skin, that holds promise for Mānuka honey to boost the immune response to bacteria.

For the MAIT cells to turn on their bacterial-killing properties they rely on the presence of MGO, which is produced naturally in the body. The more MGO, the stronger the antibacterial response. However, it's not just locally-sourced MGO that can be used by MAIT cells.

"What we're exploring is this idea that an external source of MGO can enhance the activation and function of MAIT cells in the human body," says Translational Immunology Team Leader Dr Olivier Gasser. "Because MAIT cells need MGO to recognise bacteria, there's a limit to how much they can recognise at any one time. We think that perhaps the amount of MGO found in the body might be acting as a bottleneck in terms of our ability to fight bacterial infections in places like the skin.

"Can something like Mānuka honey, which contains MGO, be used boost the immune response to an infection? So far we haven't explored this in the context of human studies, but our published results are very encouraging."

> **"Can something like Mānuka honey, which contains MGO, be used to boost the immune response to an infection?"**

In practical application, honey has long been used as a wound-dressing due to its antibacterial properties, especially for burn patients where the risk of bacterial infection is high. As MAIT cells are found in high quantities in the skin, this research offers an opportunity to explore whether such dressings can be improved with Mānuka products.

The research is partly funded by the High-Value Nutrition Ko Ngā Kai Whai Painga National Science Challenge, with Mānuka Health donating Mānuka honey products.

Improving cancer immunotherapies through hypoxia-activated drugs

A recurring issue with many cancer immunotherapies is the difficulty of delivering the cancer-killing drug to the heart of a tumour.

The internal environment of a tumour can be very different from the rest of the body, which helps the tumour resist treatment. For example, many tumours are 'hypoxic,' or oxygen-poor. A lack of oxygen makes it hard for immune cells and cancer drugs to infiltrate a tumour, and on occasion even suppresses the immune response to the cancer entirely.

Dr Regan Fu, who recently completed his doctoral thesis with Professor Ian Hermans, is assessing immunotherapies in combination with the hypoxia-activated drug tarloxotinib. Through adding a hypoxic trigger that activates in the oxygen-poor intratumoral environments, higher doses of anti-cancer drugs can be delivered.

"Not everyone responds to immunotherapies like checkpoint inhibitors," says Dr Fu. "Many factors can prevent the generation of robust responses to these treatments. One of the factors is within the tumour microenvironment such as tumour hypoxia. In the hypoxic regions of the tumour, the function of most immune cells are suppressed, therefore preventing the treatment from working.

"By using a hypoxia-actived prodrug, the anti-cancer agent is delivered directly to the hypoxic zones of a solid tumour, where it then becomes active."

The added benefit of hypoxia-activated drugs is that they are much more tumour-specific, resulting in less damage to healthy tissues surrounding the tumour. Future work is planned to better understand how tarloxotinib interacts with the immune system, with the aim of moving towards clinical trials.

Brain energetics and neurodegenerative disease

Mitochondria are tiny 'batteries' that reside in almost every cell in our bodies. They play a vital role in providing cells with enough energy to function.

The energy produced by mitochondria in any given location in the body is, for the most part, measurable and predictable. Should the 'energetics' of a specific organ – such as the brain – change, that might signal something is going wrong and the organ is heading towards a disease.

Thanks to a Health Research Council of New Zealand Explorer Grant, Cancer Cell Biology Team Leader Professor Mike Berridge, with Professor Bart Ellenbroek and Dr Darren Day of Victoria University of Wellington, are investigating whether changes to mitochondria and energetics in the brain can serve as an early detection method for diseases like depression, autism and neurodegeneration, including Parkinson's disease.

"A consistent feature of these diseases is progressive loss of neural cells in particular regions of the brain," says Prof Berridge. "Dr Day has shown that mitochondrial gene expression is dramatically reduced in frontal cortex regions of the brain in a preclinical model lacking the serotonin transporter gene, Scla6a2, a model of depression.

"The results suggest that our mitochondrial gene knockout cells can potentially be used to develop a simple early detection test for depressive disorders, autism and dementia," says Prof Berridge.

What happens to cells with compromised mitochondria has been a hallmark of Prof Berridge's research for many years. His group were the first to demonstrate that healthy mitochondria

Professor Mike Berridge

can be 'donated' or transferred to cells with damaged mitochondria as a recovery mechanism. The project will build on this cutting-edge research, and explores whether mitochondrial dysfunction in specific cells is a reliable early predictor of certain neurological diseases.

"The ultimate aim of this two-year project is to develop a simple early detection molecular assay for Parkinson's disease based on loss of mitochondrial function in cells in the nasal cavity that are responsible for sense of smell," says Prof Berridge.

"These diseases can be initiated in sensing cells in the nasal cavity and slowly spread throughout the brain over decades via misfolded proteins, like those involved in mad cow disease. It's like a slow virus that moves from cell to cell."

Establishing a simple test for the presence of damaged mitochondria in olfactory cells could help in the early identification of brain diseases like Parkinson's, allowing better management of symptoms before brain function is compromised, and ultimately a better quality of life for those affected.

A message from our Head of Development

The Malaghan Institute wishes to acknowledge and thank Head of Development Jenny Sim who, after more than eight years, is moving on to the next chapter of her life. Jenny has been instrumental in building our philanthropy programme at the Institute – which underpins much of our research – and has nurtured strong and long-lasting relationships within and across our community.

"All support positively shapes the Malaghan Institute. Not matter what form, whether it be financial, advocacy or in kind, it is incredibly valued by all our staff.

In my time at the Malaghan Institute, I have really enjoyed seeing the next generation of families and supporters getting in behind the Institute. What started off as mum and dad supporters continues as we build on long-lasting relationships. I would also like to thank the Malaghan Friends.

As our advocates in the community, they are second to none and I have had the immense enjoyment and privilege of working side by side with them.

As I step down from my role as Head of Development, I wish to express just how grateful I am, and how lucky we are at the Malaghan Institute to have such a wonderful support base who really care about the Institute and its activities, and are totally engaged with what we're doing."

Thank you,
Jenny Sim

Jenny's replacement Laura Golland will start in mid November.

Freemasons New Zealand continue to back CAR T-cell research

Freemasons New Zealand have renewed their support of the Institute's CAR T-cell programme, pledging a further $600,000 over the next three years.

Freemasons New Zealand Grand Master Graham Wrigley says Freemasons New Zealand are proud to continue to support the Institute's work because it is practical research that will have real outcomes that have the potential to improve the lives of all New Zealanders.

"Freemasons New Zealand donate extensively to medical research programmes like this CAR T-cell research because they are a promising and effective way that we can do something tangible to help New Zealanders. Our support is motivated by the guiding principles that underpin Freemasonry, particularly compassion and love of, and support for, humankind."

Thank you to our partners

LEXUS · AG · WALKER HALL · crombie lockwood · KINETICS GROUP · MR MEDIRAY · SPY VALLEY · ThermoFisher SCIENTIFIC · FREEMASONS New Zealand · gbl · TB · BOLTON HOTEL · Acurity · SF Succession FIRST · JP JUST PATERSON · ZEPHYR CONSULTING

The Malaghan Institute wishes to acknowledge the support of the Health Research Council of New Zealand

hrc Health Research Council of New Zealand

Upcoming events 2020-21

Malaghan Month
In partnership with Just Paterson Real Estate
October 2020

Wilderness Foods Bay of Plenty Friends Charity Golf Tournament
Summerhill Golf Club
5 March 2021 | 10am

World Immunology Day
29 April 2021

Lexus of Hawke's Bay and Partridge Jewellers Charity Golf Tournament
Wairakei Golf + Sanctuary
29 April 2021

For more information about these events, please contact fundraise@malaghan.org.nz
04 499 6914 x 855

CHANGES TO DONATIONS: CHEQUES PHASING OUT

Please note that due to banking changes we will no longer be able to accept cheques after 31 May 2021. If you would like to set up a recurring or automatic payment please complete the automatic payment form included or give Beth Chesser a call on 04 499 6914 x826. More information is on our website **www.malaghan.org.nz/support-us/make-a-donation/**

Grants July – October 2020

We would like to acknowledge and thank the following Trusts and Foundations for their support:

Colin Williamson Charitable Trust
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DONATION METHOD

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**Please note, we are unable to accept cheques after 31 May 2021.*
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Or call **0800 MALAGHAN** (0800 625 244) to make a donation over the phone.

MALAGHAN INSTITUTE OF MEDICAL RESEARCH

Harnessing the power of the immune system.

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