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MALAGHAN INSTITUTE OF MEDICAL RESEARCH

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A return to normal: Clinical trials full steam ahead

While the COVID-19 lockdown period brought disruption to laboratory research at the Malaghan Institute, momentum is building across the Institute's clinical trials, signalling a welcome return to normal in our pursuit to harness the power of the immune system to improve human health.

"The rubber has well and truly hit the road," says Malaghan Institute Director Professor Graham Le Gros. "Our scientists are eager to really seize on what we've built over the years in the cancer, allergy, gut health and infectious diseases space."

ENABLE CAR T-cell cancer trial

"Much of our ENABLE CAR T-cell trial was paused during the COVID-19 lockdown period, consistent with other clinical activities," says Clinical Director Dr Rob Weinkove. "We are pleased to have resumed the ENABLE trial, including restarting the manufacture of CAR T-cell products, and the treatment and recruitment of participants. We continue to monitor the COVID-19 situation closely."

Alongside the ENABLE trial, the Freemasons CAR T-cell Research Programme continues to build on this groundbreaking technology to improve its efficacy and ultimately extend this treatment to other forms of cancer.

Hookworm clinical study

The Institute's study exploring the therapeutic potential of human hookworms was only slightly impacted by lockdown, thanks to the stringent protocol already in place for these types of clinical studies.

But post lockdown, things have stepped up a notch, with recruitment of a second round of healthy volunteers for the initial study, and our next phase of hookworm research starting in parallel, treating patients with the inflammatory bowel disease ulcerative colitis.

"Our aim is to investigate whether hookworms have preventative effects for people with early mild forms of ulcerative colitis, or can stop things getting worse," says Prof Le Gros.

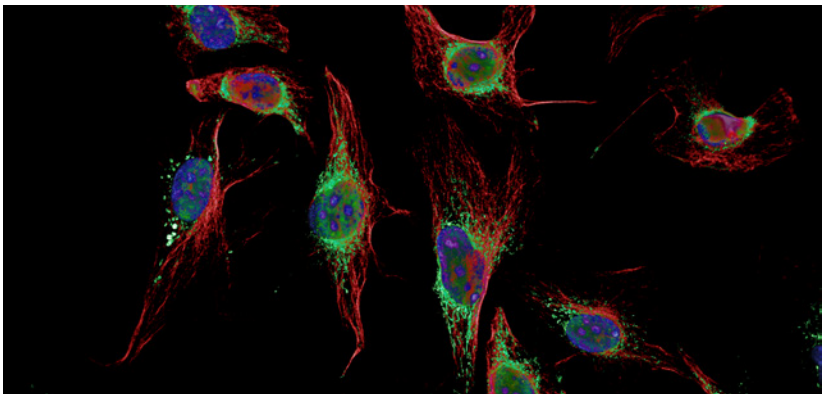
From the Director

I've had many conversations with supporters in recent weeks and the feedback is clear: while we all recognise the importance of developing a cure for COVID-19, we cannot afford to lose any of the momentum our scientific programmes have painstakingly built over the past several years.

I want to reassure our readers that we are doing everything we can to capitalise on your vital support, support that tasks us with finding new treatments and cures across cancer, asthma and allergy, gut health, brain health and infectious disease. Never has the value of medical research been more clear.

A COVID-19 vaccine remains the only assurance New Zealand has to return to some sense of normality on the global stage. Along with our collaborators, we're working hard with government to finalise details of our role in securing a vaccine for New Zealand and our Pacific neighbours, and I look forward to updating you on this in the very near future.

Prof Graham Le Gros
CNZM FRSNZ FRCPA (Hon)
Director



Molecule driving brain cancer cell survival could lead to future treatment options

Recent discoveries on why glioblastoma cells are resistant to treatment are offering potential new treatment options for patients suffering from this aggressive brain cancer.

Glioblastoma patients have poor survival rates, partly due to the cancer's unique ability to 'bounce back' from treatment. Malaghan Institute Research Associate Dr Melanie McConnell and her team believe this survivability may come down to a single molecule – BCL6.

"BCL6 is a molecule normally expressed by immune cells that makes up an important part of the adaptive immune response. For some reason, we're seeing this molecule turning up in brain cancer. It should never be there," says Dr McConnell, whose paper 'The oncogene BCL6 is up-regulated in glioblastoma in response to DNA damage, and drives survival after therapy' was recently published in *PLOS ONE*. The paper was also named paper of the week, ahead of around 600 papers across all fields of science the journal covers.

While BCL6 is necessary for a functioning immune system, having it appear in the brain is troubling. Dr McConnell and her team are investigating how this molecule ends up being expressed in the glioblastoma cells, as well as looking at possible therapies that block its function in the brain.

"There are a couple of emerging drugs being trialled in the States that block the function of BCL6 which look really promising," says Dr McConnell. "However, these have been developed for treating blood cancer, so we don't know yet if they'd translate to brain cancer. We don't know if these drugs can cross the blood-brain barrier. We also don't fully understand if the BCL6 expressed by glioblastoma looks and acts in quite the same way as the BCL6 expressed by the immune system. That's the focus of our research moving forward, to get a better understanding of BCL6 in the brain, how it's being expressed and whether stopping it is really enough to knock out tumours in glioblastoma patients."

ABOVE: Brain cells under the microscope showing BCL6 in green.

COVID-19: Potential vaccines in profile

As we finalise details of our role as part of the Government's COVID-19 vaccine strategy, we're progressing work with our collaborators on three potential COVID-19 vaccines, work that has been accelerated thanks to generous philanthropic donations, including from the Hugh Green Foundation.

VACCINE CANDIDATE 1: RECOMBINANT SPIKE PROTEIN

Self-proclaimed protein 'mechanic' Dr Davide Comoletti and his team at Victoria University of Wellington are creating copies of the spike protein on the virus' surface that give it its distinct 'corona' or crown-like appearance and are essential for the virus to gain entry to human cells. The aim is to create a vaccine that will stimulate the immune system to create antibodies against the spike.

Because these proteins are 'manufactured' rather than derived from a live virus, Dr Comoletti's team can make many variations of the protein and test them simultaneously, in order to determine which combinations stimulate the best immune response.

VACCINE CANDIDATE 2: INACTIVATED VIRUS

Professor Miguel Quiñones-Mateu and his team at the University of Otago, who were the first in New Zealand to isolate the COVID-19 virus in their specialised facility, are leveraging this unique 'IP' to develop another potential vaccine.

The team are growing and then 'inactivating' large quantities of the virus – treating the virus to eliminate its ability to replicate, yet preserve its structure. This offers a perfect, safe replica for the immune system to recognise and respond to.

" The New Zealand scientific community is really coming together" says Prof Le Gros. "It's fantastic. However, it's important to acknowledge that alongside New Zealand efforts, we are closely monitoring developments overseas, to source and evaluate any promising vaccines that could work for the New Zealand population."

VACCINE CANDIDATE 3: PAN-CORONAVIRUS

Working with international collaborators, Avalia Immunotherapies, led by Chief Executive Dr Shivali Gulab, is exploring whether a pan-coronavirus vaccine – that targets all coronaviruses not just COVID-19 – is a feasible approach.

Before any potential vaccine can make its way into human clinical studies, groundwork must be done to demonstrate it can stimulate an appropriate immune response. The Malaghan Institute's role is to take these candidates and explore which stimulate the best immune response – one that is neither too weak nor too strong. The next stage is to see whether the immune responses stimulated by these vaccines can successfully inactivate live COVID-19 viruses housed in the University of Otago's specialised PC3 laboratory, before eventually moving on to clinical testing and safety trials.

ABOVE: From top, Dr Davide Comoletti, Professor Miguel Quiñones-Mateu and Dr Shivali Gulab

Malaghan vaccine used to explore development of novel malaria treatment

How the immune system could be used to target the malaria-causing parasite plasmodium is part of a trans-Tasman project which has recently received nearly $1.2m funding from the Health Research Council of New Zealand.

Malaria is a global health issue that kills nearly half a million people each year according to the World Health Organization, with no effective long-term vaccines. The disease is caused by the plasmodium parasite that resides in the saliva glands of mosquitos and is transferred to humans when the mosquito feeds.

A crucial stage of the development of plasmodium occurs in the liver of infected humans, offering a potential inroad for developing a targeted immune response to this parasite.

Alongside the Ferrier Research Institute, the University of Melbourne and Avalia Immunotherapies, the Malaghan Institute for Medical Research has been working over the past three years to develop a simple vaccine design that could be manufactured efficiently and administered easily in at-risk countries.

"We know that our vaccine seems to create the right sort of environment to activate T-cells in the liver," says the Malaghan Institute's Deputy Director of Research Professor Ian Hermans. "When Prof William Heath at the University of Melbourne got wind of this he got really excited, as he'd been looking for ways to get a T-cell response in the liver for developing a protein-based malaria vaccine that targets the sporozoite stage of the plasmodium."

"Right now, we're taking a really broad approach to the question of how to create a malaria vaccine and trying to determine if it is feasible and what it might look like," says Prof Hermans. "We're a long way off human studies, but it's a really unique way of creating a vaccine, which is why this trans-Tasman collaboration is so exciting."

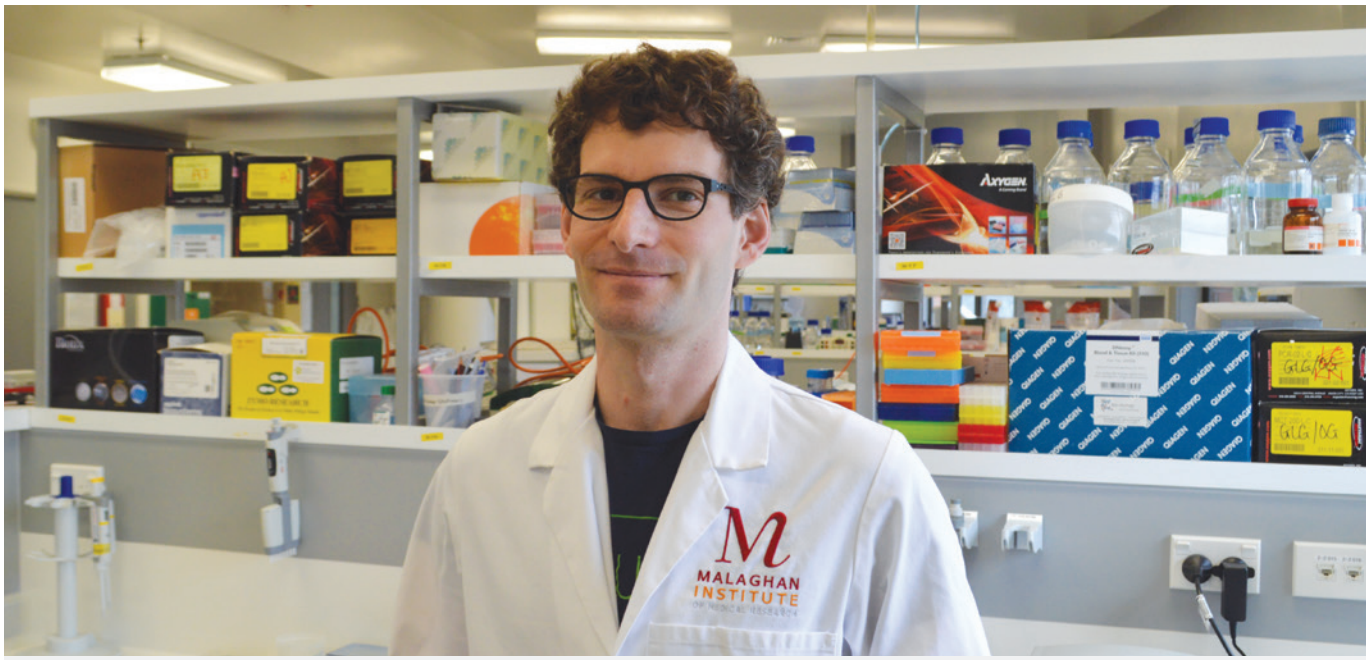
Head of Research Technology elected to global position

Malaghan Institute Head of Research Technology Kylie Price has been elected as Secretary for the International Society for Advancement of Cytometry (ISAC), recognising her expertise, passion and tireless efforts to boost the impact of cytometry as an advanced analytical research tool world-wide.

Kylie, who became the first New Zealander to be elected to the ISAC council in 2018, says she is driven to bring greater diversity and inclusion to ISAC, in order to increase the society's representation, membership and influence around the globe.

"It is a humbling experience being voted into such a position by my peers and I am really excited by the opportunity," says Kylie. "This year's election results are also a real positive for women in STEM, as for the first time in the Society's history four of the five council positions will be held by women. I am also proud to represent New Zealand and the Australasian region, to ensure we are not overlooked and that the international community is aware of the ground-breaking science and technological breakthroughs going on here."

Cytometry is a form of analytical technology that allows scientists to quantitatively analyse cells and cell systems in research. Supported by the Hugh Green Foundation, it is one of the key technology platforms at the Malaghan Institute, enabling our scientists to extract important information on how cells in the immune system behave and function in the context of disease.



Dr David O'Sullivan: the immune system and metabolic health

Cells need fuel in order to grow and function. Immune cells are no different. What we eat, and whether we're eating the right kinds of food, can affect how well the immune system works in the body.

To better understand how the immune system fuels itself – otherwise known as immune metabolism – the Translational Immunology team has recruited returning Kiwi scientist Dr David O'Sullivan.

Dr O'Sullivan completed his doctoral studies in multiple sclerosis research with Institute Research Associate Professor Anne La Flamme. Since then, Dr O'Sullivan has worked at both Washington University in the United States and at the Max Planck Institute in Germany, investigating T-cell metabolism and how different nutrients affect their function. Having returned to Wellington and the Malaghan Institute, Dr O'Sullivan is working with Translational Immunology Group Leader Dr Olivier Gasser to apply his expertise to our immune health research as part of the High-Value Nutrition National Science Challenge.

"I'll be working in the translational space looking at nutritional components or bioactive compounds from food groups and how these influence the immune cell metabolism and function," says Dr O'Sullivan. "Just like in the saying 'you are what you eat', what nutrients immune cells are exposed to influences their behaviour. We're trying to leverage bioactive compounds that are found in nutritional food products in a way that benefits immune cell function."

Thank you to our partners

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

Health Research Council of New Zealand

Upcoming events 2020

Hawke's Bay Research Update
Lexus of Hawke's Bay
16 September | 7pm

Hawke's Bay Friends of Malaghan Institute Charity Golf Tournament
Hastings Golf Club
30 October

Lexus of Wellington and Jarden Malaghan Institute Charity Golf Tournament
Royal Wellington Golf Club
16 October

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

Grants May – June 2020

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

Florence Petersen Leukaemia Trust

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Maurice Capstick Medical Trust

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The Thompson Family Foundation Inc

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Leaving a gift in your will to the Malaghan Institute is a personal and enduring investment in the future of biomedical research and discovery. All gifts in wills, whatever the size, mean a great deal to us and the longevity of our research.

You can help us shape advances in medical science and develop treatments that will benefit generations to come. If you would like more information on how to make a bequest to the Malaghan Institute, or would like us to advise your lawyer, please contact:

Jenny Sim | Head of Development
E jsim@malaghan.org.nz
P 04 499 6914 x 811

Please also get in touch if you have already made a bequest in your will, to let us thank you personally, involve you more in the Malaghan Institute today, and plan for the future.

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MALAGHAN INSTITUTE OF MEDICAL RESEARCH

Harnessing the power of the immune system.

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