

COVID-19:

Moving New Zealand towards a cure

The SARS-CoV-2 coronavirus is a pressing reminder of how vulnerable our society is to novel infectious agents. But Malaghan Institute Director Professor Graham Le Gros explains that infectious diseases are nothing new, and with the right investment in research and development, we can be well equipped to overcome this global pandemic and others to come.

"In recent decades we have all been privileged to live in a vaccine-protected world," says Prof Le Gros. "We have good awareness and effective tools to fight the important infectious agents out there like influenza, polio and measles. However, the recent

emergence of COVID-19 shows just how dynamic and destructive a new infectious agent can be to a susceptible host.

"Where we have been a bit remiss as a society, I believe, is that we tend to think we've conquered infectious diseases. We must always be prepared for the emergence of new infectious agents. There always has to be a strong investment in preparedness and capability to make new vaccines to combat new diseases," says Prof Le Gros.

"However, I have every faith that making an effective vaccine for this novel coronavirus is possible. What we can't yet predict is how long it will be until such a vaccine is

widely available. While there is plenty of news about work underway towards a vaccine, even the most optimistic predictions from top scientists put a safe and effective

"A vaccine is the only clear exit strategy that will allow New Zealand to return to normality"

- PROF LE GROS

vaccine that can be mass-produced at least 18 months away. In addition, there remain a few tricky aspects of the virus including how it infects people and hides from the immune system that science doesn't yet fully understand. What is essential

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From the Director



While New Zealand is navigating the challenges of COVID-19, it's important to remember that yes, these times are tough, but this is just a virus, nothing more nor less. The immune system is incredibly powerful at finding a way to deal with pathogens, and we will eventually come out the other side.

The Malaghan Institute is strongly advocating for action and clarity in securing a vaccine for New Zealand. We are progressing discussions with government, academics and industry to define a cohesive rapid response plan to ensure New Zealand is not left waiting to access vaccines from other countries and is well placed to respond to future virus outbreaks.

But we also remain absolutely committed to our core research programmes across cancer, asthma and allergy, infectious diseases, gut and brain health. We have not lost the momentum our supporters have given us over many years.

Thank you more than ever for showing faith in us.

Prof Graham Le Gros
CNZM FRSNZ FRCPA (Hon)
Director

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now is investment in research – global, collaborative research – to understand this virus, and for communities globally to follow public health guidelines to minimise the virus's impact.

The urgent need for New Zealand to be part of the cure

Many international organisations are hard at work making inroads towards a vaccine, but it is essential that New Zealand isn't complacent, waiting for a cure to arrive on our shores, says Prof Le Gros. That could spell disaster for our health and economy.

"While multiple vaccines are in development overseas, there's a growing concern among New Zealand scientists about the ability of manufacturers to scale up vaccine production to meet the needs of the global population."

"Most countries will almost certainly distribute new vaccines within their own borders before exporting to other countries"

- PROF LE GROS

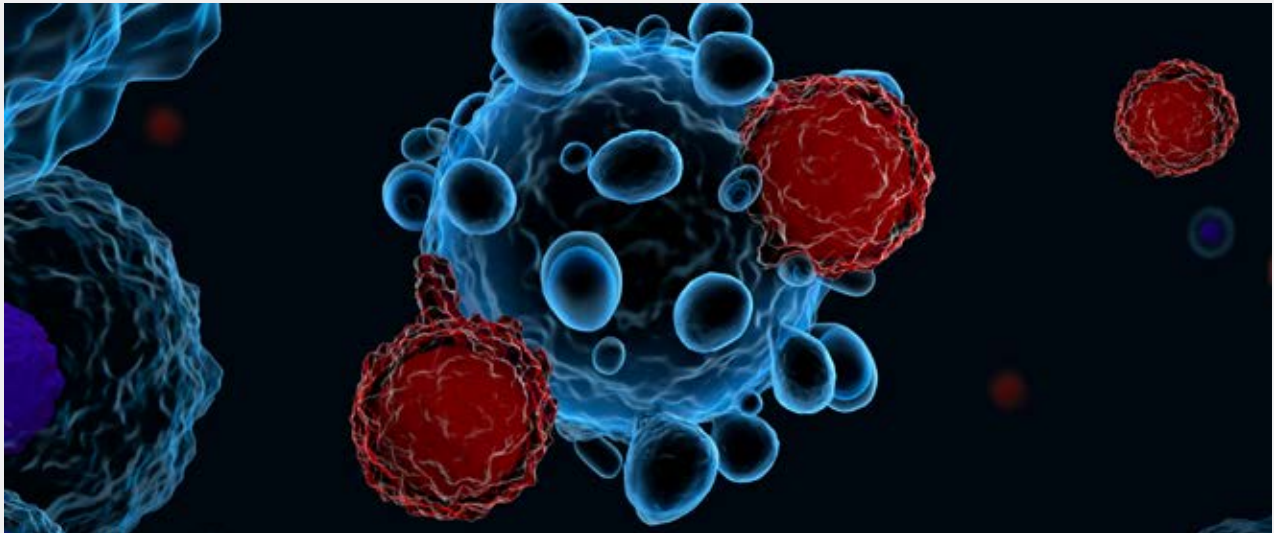


"Most countries will almost certainly distribute new vaccines within their own borders before exporting to other countries."

What this means is that New Zealand has to play an active role in finding, developing and manufacturing a vaccine, or risk being well down the pecking order to receive one.

Prof Le Gros and other top New Zealand scientists are calling for a national COVID-19 vaccine programme to ensure New Zealand is best placed to access an effective vaccine at the earliest opportunity. This would include assessing the best vaccine options internationally, progressing vaccine development with leading research institutions, government and industry, building capacity for vaccine production in New Zealand, and developing a plan for how it will be rolled out.

"A vaccine is the only clear exit strategy that will allow New Zealand to return to normality," says Prof Le Gros.



Taking CAR T to the next level

As New Zealand's first clinical trial of CAR T-cell therapy progresses, the Institute is looking to the future of this ground-breaking cancer therapy and ways to improve its effectiveness, reduce potential toxicities and extend it to other cancers.

The Institute's Freemasons CART -cell Research Programme was recently boosted with the return of Dr Rachel Perret, whose expertise in T-cell therapy will play an integral role in designing better CAR T-cells.

"My PhD research at the Malaghan Institute involved working on activating T-cells using dendritic cells at different stages of maturation"

- DR PERRET

Dr Perret completed her PhD at the Malaghan Institute 12 years ago, studying under Professor Franca Ronchese. After completing her doctorate, she spent several years

working with some of the world's top T-cell researchers in labs across Europe and the United States.

"My PhD research at the Malaghan Institute involved working on activating T-cells using dendritic cells at different stages of maturation," says Dr Perret.

"When I was looking for postdoctoral positions, I was interested in labs that focused on creating vaccines to stimulate T-cells. I ended up at the Ludwig Institute of Cancer Research in Switzerland under Dr Pedro Romero where I continued working on T-cells in preclinical models of cancer. Afterwards, I was lucky to secure a position in Seattle at the Fred Hutchinson Cancer Research Centre with Dr Phillip Greenberg, one of the pioneers of T-cell therapy."

Now back home again, Dr Perret is excited to begin working on CAR T-cells, pushing the envelope on this technology and whether it can be improved and extended to other types of cancer.

"We want to understand more about the way our CAR T-cells signal and function. While we have good evidence that they may be

effective in trial, there is much left to understand about what makes our CAR T-cells unique. This information

"We want to understand more about the way our CAR T-cells signal and function"

- DR PERRET

can help us design future strategies for making better CAR T-cells that have the possibility of being less toxic, survive better in patients and even target solid tumours."



ABOVE: Dr Rachel Perret

'Zooming in' on new confocal microscope

A new confocal microscope is a welcome addition to the Institute's Hugh Green Cytometry Centre, offering an exponential shift in the depth and quality of images produced by experiments.

The more information gained from an experiment, the more scientific value it has. Any advancement in technology helps create better, more sophisticated data per experiment. It's all part of creating a complete picture of what's going on within a body in order to find ways intervene in the context of disease.

In line with this, the new confocal is a significant leap in the quality of information gained in a single microscopic image. Unlike regular microscopes which examine only a single layer of tissues or cells, the confocal creates multiple layers of images at different depths, effectively creating three-dimensional images. To this end, the new confocal has a super resolution module incorporated, which means we will be able to resolve structures down to 120nm in size, which is about 16 times smaller than bacteria. These features combined, along with a vastly improved processing speed, exponentially expand our understanding of the immune system in the context of the tissue sections.

"The new confocal has necessitated a change in the way our scientists think about their experiments," says Kylie Price, Hugh Green Cytometry Fellow and Head of Research Technology. "Now we have the tools to ask really big picture questions and take a more holistic approach to big-data analysis."

Novel technique allows scientists to study parasitic infections one cell at a time

One of the primary challenges of studying the effect of parasitic infections on immune cells in the gut is the difficulty extracting and isolating immune cells. But a new technique developed by Postdoctoral Research Fellow Dr Johannes Mayer and other scientists at the Malaghan Institute, means we can now answer big questions about the interplay between parasites and the immune system.

"A big problem has been the difficulty extracting immune cells from an infected gut, as the infection causes very strong local reactions such as intense cellular slime production as it tries to flush the worms out," says Dr Mayer.

According to Dr Mayer, these reactions play havoc with the extraction process, making it extremely difficult to accurately isolate immune cell populations for study. However, after many months of experimentation, Dr Mayer and his colleagues within the parasitology team have developed a new method to reliably extract millions of immune cells from a single sample.

The technique involves three washes with EDTA (ethylenediaminetetraacetic acid), an agent to remove the mucus, lasting for 10 minutes. This is followed by 30 minutes in a solution of enzymes that help break down the tissue into individual cells, and then cell filtration.

"This allows us to study the individual immune cells for the first time," says Dr Laura Ferrer-Font, Staff Scientist within the Institute's Hugh Green Cytometry Centre. "We can then use spectral flow cytometry to look at many different types of immune cells all at the same time, and identify various changes to the immune system that take place throughout the course of parasitic infection."

"Now that we have found a way to extract immune cells from parasite-infected guts, we can start to answer

important questions about the immune response," says Dr Mayer.

"This technique will enable scientists to use powerful tools like single-cell RNA sequencing to study the immune response in different hosts. It may also help those studying inflammatory bowel disorders or food allergies to extract single cells from the gut for further investigation."



ABOVE: Dr Johannes Mayer

Dr Mayer was recently awarded the German Society for Immunology's Werner Müller Award recognising achievements in the field of immunology that can benefit the prevention, diagnosis or treatment of diseases in the developing world.

OPERATING UNDER LOCKDOWN

Navigating essential research during lockdown, Malaghan Institute scientists have had to adjust the way they work to stay safe while maintaining momentum with their important research.



DR ROB WEINKOVE | Clinical Director, Head of ENABLE CAR T-cell Clinical Trial

"While it was necessary to pause new recruitment to the CAR T-cell trial, follow-up of participants continues. The Freemason's CAR T-cell Research Programme team have been meeting regularly via remote conferencing, working on data analysis, developing new experimental plans and more. As we look towards cautious lifting of some of the COVID-19 restrictions, we expect to resume our laboratory research and ENABLE CAR T-cell trial activity."



DR ALISSA CAIT | Postdoctoral Research Fellow, Translational Immunology Team

"Because of the COVID-19 crisis, many companies around the world are providing free online content and resources. During lockdown I've been using the opportunity to test out bioinformatics tools that I otherwise would not have had access to or time to learn about!"



BRITTANY LEWER | Research Officer, Clinical Hookworm Study

"Because work on the hookworm study is essential, we've had to make adjustments on things like clinical visits. Luckily, standard laboratory protocol already promotes sterility and personal protective equipment, but we've stepped it up a notch. Once clinical samples are collected we now work to a single person per lab room – much quieter compared to the usual clinical study hustle and bustle! Regardless, this responsibility has tested our clinical study group and we have come together as a team to support each other and continue this important work, especially while not all of us are able to easily make it on-site."



YASMIN NOURI | PhD Student, Cancer Immunotherapy Team

"I was lucky in that I have my PhD literature review to write. Once I got into the swing of working at home this has been a good project to chip away at over the last few weeks. We decided that while I had the time, I might as well write it to publication standard and aim to send it to a journal once it's done. I really miss the lab and generating results but I'm grateful to have something productive to do in the meantime!"

Thank you to our partners



The Malaghan Institute wishes to acknowledge the support of the Hugh Green Foundation



Upcoming events 2020

Due to COVID-19, the Malaghan Institute has postponed future events and community engagement until it is recommended safe to do so by the New Zealand Government. Thank you for your ongoing understanding and support during this time.

Grants Nov 2019 – Apr 2020

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

David Levene Foundation	Infinity Foundation Limited	Pelorus Trust
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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
✉ jsim@malaghan.org.nz
☎ 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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