SCOPE 75
A MALAGHAN INSTITUTE PUBLICATION

MALAGHAN INSTITUTE OF MEDICAL RESEARCH

MALAGHAN INSTITUTE OF MEDICAL RESEARCH | NEW ZEALAND | WWW.MALAGHAN.ORG.NZ | AUG 2021

Equal protection for everyone:

COVID-19 vaccine clinical study launched

Not everyone responds the same way to a vaccine. Safeguarding our community from infectious diseases like COVID-19 means ensuring everyone is equally protected.

In early June, Vaccine Alliance Aotearoa New Zealand – Ohu Kaupare Huaketo (VAANZ) launched a COVID-19 clinical study at two sites in Rotorua and Christchurch to provide valuable information on how our uniquely 'Kiwi' population responds to the Pfizer-BioNTech COVID-19 vaccine.

The study, 'Ka Mātau, Ka Ora' (from knowledge comes wellbeing), aims to track and monitor participants' immune responses to the vaccine over the course of a year in order to inform the national COVID-19 strategy and ultimately enhance vaccine effectiveness and confidence in New Zealand.

"We want to confirm if the immune response in New Zealand is what is seen internationally," says the Malaghan Institute's Dr Fran Priddy, VAANZ Clinical Director.

"While the Pfizer-BioNTech vaccine has demonstrated efficacy and safety in pivotal clinical trials and real-world studies, it has not yet been studied in New Zealand," says Dr Priddy. "That's not to imply that we're at all worried that the vaccine is not going to be effective in populations here. Rather, we want to understand how New Zealanders' immune systems respond to the vaccine, particularly in populations likely at higher risk from COVID-19, such as Māori, Pasifika and the elderly."

Above: Malaghan Institute scientists across different research teams working on the Ka Mātau, Ka Ora study.

Dr Priddy says with vaccine safety already being closely monitored and evaluated in New Zealand and internationally, Ka Mātau, Ka Ora will focus on characterising immune responses.

"Studies done post-vaccination in other countries have shown lower antibody responses in some groups, such as the elderly and those with obesity.

"We don't know if this translates to reduced effectiveness, but it will be very hard to measure effectiveness unless we have a large outbreak. So measuring immune responses is the best proxy right now for us in New Zealand.

"I think the data from our study is likely to be confirmatory and supportive, and should make people feel more confident that the vaccine is going to work across Kiwi populations".

Continues inside >

From the Director

Our role at the Malaghan Institute, as New Zealand's infectious disease immunologists, is to ensure that New Zealand has the right tools and capabilities to create a strong, healthy and resilient population through better, more effective vaccines.

We are now coming to terms with the fact that the emergence of new infectious diseases, like COVID-19, will be an ongoing part of our future and that we will have to build the capability that enables us to be resilient to future global pandemics.

That means our research investigating how the immune system interacts and adapts to new infectious agents is an important cornerstone for the future health of New Zealand. The success of the recently developed mRNA vaccines has shown the impact deep investment and laser-sharp focus on scientific R&D has on meeting the health challenges of the future.

However, too many people have already lost their lives to COVID-19. We need to do more to provide the fence at the top of the cliff rather than the ambulance at the bottom.

Prof Graham Le Gros
CNZM FRSNZ FRCPA (Hon)
Director

Continued from front page

Dr Priddy says our 'COVID-naïve' population will also offer unique data to global research. "Vaccine immune responses may differ in populations with little prior viral exposure, as is currently the situation in New Zealand."

There are ways to increase immune responses to vaccines says Dr Priddy, so if the study identifies responses that may impact effectiveness, this could be addressed in the future by booster shots, different vaccination schedules, or different vaccine types.

> **"We know there is more to learn and this research is important to help identify and understand any difference in the immune response."**

Clinical immunologist Dr Maia Brewerton, who is a member of the Institute's Trust Board and Te Urungi Māori advisory board, says that Aotearoa is in an enviable position due to our elimination strategy and measuring specific immune markers offers a useful alternative approach to assess the vaccine response amongst our people.

"Māori and Pasifika have a greater burden of conditions like heart disease associated with more severe COVID-19 disease, however even after we account for these conditions, Māori and Pasifika are still at increased risk of developing severe disease. We know there is more to learn and this research is important to help identify and understand any differences in the immune response which can guide the optimal vaccine approach for our people," she says.

"During the influenza pandemics last century, Māori experienced higher death rates and I hope with knowledge from research like this we can prevent a repeat of this story for Māori as we journey into the uncertain future of this COVID-19 pandemic together – Ka Mātau, Ka Ora."

The Malaghan Institute is running Ka Mātau, Ka Ora in conjunction with Lakeland Clinical Trials in Rotorua, and Southern Clinical Trials in Christchurch.

Vaccines are the best, most effective way we can protect our loved ones from infectious diseases like COVID-19. However, we know that not everyone responds equally to the same vaccine. For most people, vaccines induce a strong immune response that protects them from a virus or disease. This isn't the case for everyone.

Factors like age, immune health and even the food we eat can influence how strongly, or poorly a persons' immune system responds to a vaccine. Several groups within the Malaghan Institute are tackling this very problem – whether by working to design vaccines that are better at stimulating the immune system, or uncovering how we can leverage diet to improve immune responses.

New research finds link between pH balance and allergic disease in the skin

New research by the Translational Immunology team has identified a key gene that, in the right acidic conditions, can stop T-cells from causing excessive inflammation in the skin.

T-cells are a type of immune cell that help recognise antigens – a key condition for initiating an immune response. Their main role is to cause inflammation to help fight an infection. For most people, their T-cells behave as they should. But for those with inflammatory conditions, often their T-cells activate or turn on when they shouldn't, kicking off the immune response and causing harmful inflammation. Ensuring that T-cells behave as they should, especially in the skin, is vital in preventing the development of inflammatory diseases such as eczema and psoriasis.

"There are many factors that determine whether a cell should activate," says Dr Gasser. "Things like temperature, the presence of chemical signals, salinity. The body's pH – or acid-base – balance is just one of many factors, but for T-cells in the skin it's an important one.

"Many cells, including T-cells, rely on the gene GPR65 to determine the pH of their environment. GPR65 codes for a protein that sits on the surface of the cell which feeds information back on how acidic or basic the surrounding environment is. For T-cells in the skin, if the pH is acidic, the protein sends signals back to the cell to suppress activation."

"We've found in both preclinical and clinical studies that for those with the defect in their GPR65 gene, their immune cells are blind to their extracellular pH environment, making it much easier for their T-cells to activate."

Healthy skin typically has a slightly acidic pH, around 5.5. However, it becomes more neutral (or basic) in diseases like atopic dermatitis, more commonly known as eczema. Many sufferers are prescribed skincare treatments for their conditions to reset this imbalance, lowering the pH of the skin to a more healthy range. This research supports this approach, suggesting that one of the reasons these skincare products work is by making it harder for T-cells to activate in the skin and cause the hallmark inflammation associated with these diseases.

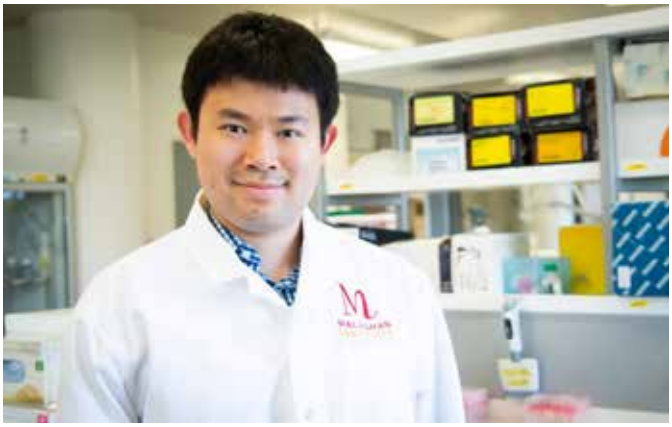
Moving forward, Dr Gasser and his team hope to explore this discovery further to determine exactly how GPR65 functions across different types of immune cells and whether this information can lead to new targeted treatments for atopic disease.

Chinese herbal medicine and its effect on our health

A novel clinical study is seeking to better understand the impact certain Chinese herbal medicines have on the immune system and human health, and whether they can be used as a potential treatment for a range of inflammatory conditions.

"While there is evidence that traditional Chinese herbal medicines have anti-inflammatory effects, the mechanisms underlying them are largely unknown," says Dr Jeffry Tang who is leading the study. Part of the New Zealand High Value Nutrition National Science Challenge, the Malaghan Institute is recruiting up to 25 volunteers to take an oral dose of indigo naturalis to investigate how immune cells in their blood change before and after taking the medicine.

Indigo naturalis, also known commonly as Qing-Dai, is a traditional herbal medicine, extracted from multiple Chinese herbal plants. It is currently available as an over-the-counter nutritional supplement. Previous studies in Japan have shown promise for its use as an alternative treatment for ulcerative colitis, an inflammatory bowel disease. However, little is known about how this herbal medicine influences the immune system and whether it can be applied across other inflammatory conditions.



"We want to know more about how natural herbal medicines like Qing-Dai can affect the ability of immune cells in the circulatory system to maintain a 'healthy' environment in the body," says Dr Tang.

"The success of this study will help inform us as to whether indigo naturalis holds the potential for further clinical studies to treat systemic inflammatory conditions such as obesity, metabolic syndrome and diabetes," says Dr Tang. "In addition, by better understanding the underlying science behind these traditional herbal medicines, we may be able to identify more natural products that have a similarly beneficial role."

Cytometry superstar appointed to international leadership programme

Malaghan Institute cytometry specialist and Deputy Manager of the Hugh Green Cytometry Centre Dr Laura Ferrer-Font has been appointed to the International Society for Advancement of Cytometry's Shared Resource Lab (ISAC SRL) Emerging Leader Programme. The four-year programme is designed to develop the next generation of leaders in the field of cytometry.

Flow cytometry is a state-of-the-art technology for cell analysis used at the Malaghan Institute, underpinning much of our research.

"Spectral cytometry enables us to deeply interrogate which cell populations are present and what these cells are doing in the context of the diseases we study," says Dr Ferrer-Font. "With advances in this technology we're getting unprecedented amount of information from each precious sample."

"I am really interested in high-dimensional full spectrum flow cytometry and its applications to new biological contexts. I've been involved in many different clinical and fundamental research projects, and I have expertise in developing and analysing multicolour high-dimensional panels to monitor immune responses across preclinical models and human clinical trials," she says.

"I am also passionate about cytometry education and I am keen to help build collaborations and networking opportunities to share tools and knowledge that will benefit other shared resource labs, the Malaghan Institute and the cytometry community in general."

The ISAC SRL Emerging Leadership Programme is designed to do exactly that; elevate talented individuals within the cytometry field to help promote education, application and operation of cytometry internationally.

"I am greatly honoured to become one of the new ISAC SRL Emerging Leaders for 2021-2024 and the first in New Zealand. The programme will offer me the privilege to connect with like-minded people from around the world and keep me and the Malaghan Institute up to date with the last advances and trends in the cytometry field."

John Carter: Trustee, friend, mentor and collaborator

It is with great sadness that we recently farewelled Associate Professor John Carter MNZM, Trustee and long-time collaborator and supporter of the Malaghan Institute, who died on 2 June 2021, surrounded by his family.

In his role his role as head of the Wellington Blood and Cancer Centre, John was an early ally in the Institute's first cancer immunotherapy trials in the late 1990s and has remained a close friend and colleague since, helping guide the Institute in transforming its research into the clinic. In 2003 he was appointed to the Institute's Trust Board and was recently appointed Deputy Chair.

Malaghan Institute Clinical Director and fellow haematologist Dr Rob Weinkove said that as well as being a deeply committed and relentlessly cheerful clinician, John was an enthusiastic supporter of research and teaching.

"John was instrumental in building the clinical haematology service in Wellington, particularly the bone marrow transplantation service. This, as well as his encouragement of research, helped to bring the very first cellular therapy trials to the Malaghan Institute. He remained a keen supporter of our research for decades, and was campaigning on behalf of the CAR T-cell programme in recent weeks. His commitment to patients, enthusiasm for research, dedication to teaching and development, laconic humour, and sage advice will be greatly missed."

Deputy Director and Cancer Immunotherapy Programme Leader Professor Ian Hermans said he'll always remember John's erudition.

"When asked to comment on anything, his responses were always well considered, clear, and always, always, respectful. There was also the endless enthusiasm – and the grin. It was only with John's energy and expert guidance that we conducted our first clinical trials. When we had issues, I'd often seek out John for advice. Those discussions always ended with a clear plan and a new sense of optimism. I'm sure many of us at the Institute have similar memories. He was a mentor to many – we'll miss him a lot."

Investigating the link between dendritic cells and allergic skin disease

The Malaghan Institute's Professor Franca Ronchese and Dr Maia Brewerton have been awarded a $1.2M Health Research Council Project Grant to investigate the link between dendritic cells and allergic disease in the skin. The three-year programme, which will compare inflammatory responses in healthy individuals with those suffering allergic disease, is part of wider Malaghan research to find new, more effective ways to treat skin disease such as eczema, and provide relief for those with debilitating allergic conditions.

Dendritic cells are a key immune cell of interest for allergy research, due to their role in initiating different kinds of immune responses. They patrol the body's tissues and organs, 'priming' the immune response as they pick up evidence of infection or dangerous interlopers and present this information as antigens to the rest of the immune system.

Prof Ronchese's Immune Cell Biology team will work with Dr Brewerton, a clinical immunologist, to better understand these cells' involvement in initiating allergic responses in the skin.

"Dr Brewerton will be helping run feasibility studies where we aim to use a 'blister' method to analyse skin dendritic cells from healthy volunteers and patients with inflammatory skin disease," says Prof Ronchese. "For now we just want to know whether we can gather enough material to conduct the study. If we do, we'll aim to expand it to a larger group of patients."

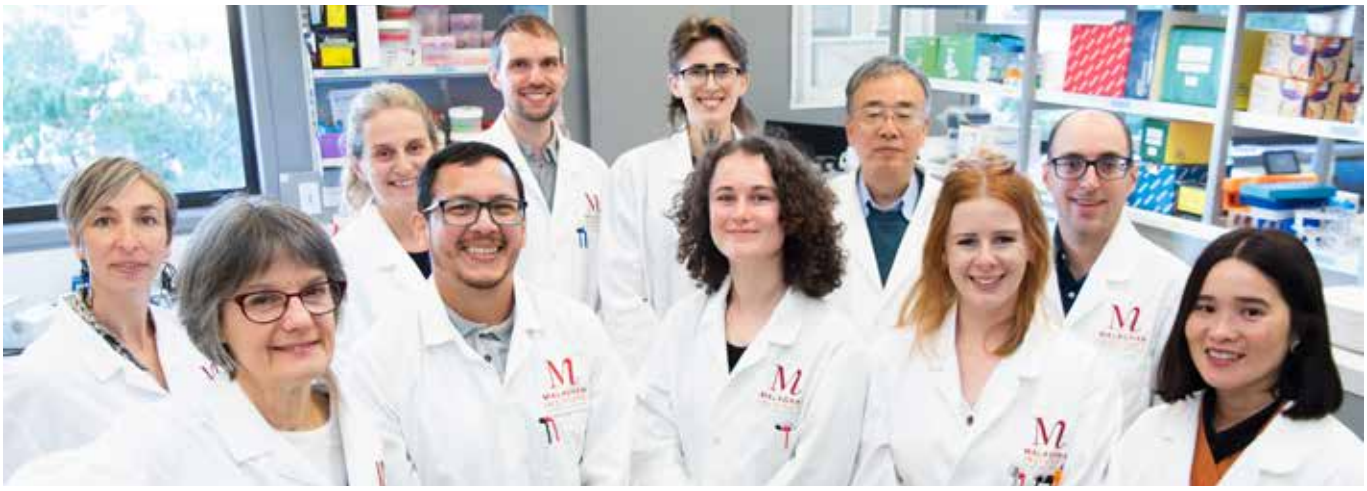
The feasibility study will provide valuable insight into the cellular and genetic differences that push a person's dendritic cells to initiating the allergic inflammatory response.

Immune responses can be either good or bad, depending on whether the response is to a threat (such as a virus) or something harmless (such as dairy products). Researchers believe dendritic cells are directly involved in the initiation of harmful immune responses leading to the development of allergies and inflammatory conditions. Understanding the triggers of this, and what signals nudge dendritic cells towards initiating allergies is one of the things this research will explore in detail.

And a naturally occurring signalling molecule – IL-13 – may be key to this.

"IL-13 is known to drive the allergic response when it comes into contact with immune cells, particularly in the lung," say Prof Ronchese. "However, our previous research has shown that at least for the skin, this isn't the case and in fact dendritic cells in the skin need a certain amount of IL-13 present in order to develop and function properly.

"We want to understand better how IL-13 changes the molecular makeup of dendritic cells and other skin cells when they are exposed to allergens. And we want to look at dendritic cells in patients with inflammatory skin disease such as eczema and psoriasis which is why the collaboration with Dr Brewerton is so important to finding new treatment options."



Immune Cell Biology team

Thank you to our partners

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

Reminder: cheques no longer accepted

We understand that the withdrawal of cheques by banks is having an impact on many of our wonderful supporters. There are a number of different ways you can make payment, if you would like to continue supporting our work, and our dedicated team is here to help you every step of the way.

- Make a credit card donation over the phone – please call the fundraising team on 0800 625 244.
- Make a credit card donation through the post using the donation form below.
- Donate online via our donation page www.malaghan.org.nz/donate.
- Make a donation directly into our bank account: 06-0507-0052635-30.
- Set up a regular monthly payment from your credit card using the form below.

And please do remember, we're here to help, so don't hesitate to contact us on 0800 625 244 or email fundraise@malaghan.org.nz.

Grants

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

The Clegg Family Charitable Trust
The Dines Family Charitable Trust
Dr Marjorie Barclay Charitable Trust
EM Pharazyn Charitable Trust
FH Muter Charitable Trust
Four Winds Foundation
Grassroots Trust Central Limited
Hugh Green Foundation
LifeBlood Trust
The Lion Foundation
McDonald Family Trust
New Zealand Community Trust
Nikau Foundation
Pelorus Trust
The Thompson Family Foundation Inc

TOGETHER WE CAN HARNESS THE POWER OF THE IMMUNE SYSTEM AND SAVE LIVES

NAME: .....

EMAIL: .....

ADDRESS: .....

I'd like to donate $ ..... to help accelerate the pace of research. **PHONE:** .....

☐ I would like information about leaving a gift in my will to the Malaghan Institute.

DONATION METHOD

☐ **Credit card**

Card number ..... Expiry ☐☐/☐☐

Name on card ..... Signature .....

☐ **Recurring monthly payment by credit card** First payment date: ☐☐/☐☐/☐☐

Online – www.malaghan.org.nz/donate

Electronic transfer – bank account 06 0507 0052635 30

The Malaghan Institute is a registered charity, no. CC 10357. Please call to inform us of your donation so we can send your tax receipt. Donations over $5 are eligible for a tax refund of up to 33%.

Or call **0800 MALAGHAN** (0800 625 244) to make a donation over the phone.

☐ I no longer wish to receive communications from the Malaghan Institute.

MALAGHAN INSTITUTE OF MEDICAL RESEARCH

Harnessing the power of the immune system.

T: +64 4 499 6914 | PO Box 7060 | Wellington 6242 | New Zealand | www.malaghan.org.nz | info@malaghan.org.nz