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Discovery points to the skin as

'ground zero' for allergic disease

A ground breaking discovery from the Immune Cell Biology team has shone a light on immune cells in the skin, suggesting they play a much larger role in the onset of allergies than first thought.

The discovery, published in *Nature Immunology*, throws into question the long-held belief that immune cells behave in the same way, regardless of where they are in the body, which has far-reaching implications for allergic and inflammatory conditions.

"Historically, we've assumed that a dendritic cell in the skin is virtually identical in form and function as a dendritic cell in the lung," says Professor Franca Ronchese, whose team led this research. "We're only just realising that's not the case, so in many ways we're playing catch up in terms of our understanding and implications in disease."

Dendritic cells act as 'lookouts' and play an important role in initiating and coordinating immune responses. Dendritic cells that live in the skin behave differently to dendritic cells anywhere else in the body, and what sets them apart might just be what's driving the formation of allergies – with the skin effectively 'ground zero' for the development of allergic conditions.

Above: The Immune Cell Biology team.

"This is the most important immunological discovery to come out of New Zealand in the past twenty years," says Malaghan Institute Director Professor Graham Le Gros. "It marks a milestone in fundamental immunology which will have far-reaching impacts in the design and development of immunotherapies that target allergic and inflammatory conditions."

Advancements in technology have played a key role in this shift, with recent improvements in analytical techniques enabling scientists to determine the subtle but significant differences that exist between cells of the same type.

For most people, these slight differences might not be significant, but for the development of allergies, they might make all the difference.

We are what we eat. Are we also what we put on our skin?

Our immune system isn't born inherently knowing what is and isn't good for you. Some things your body learns while in the womb and while breastfeeding. The rest, your immune system has to learn on its own – one encounter

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From the Director



I am encouraged by the high vaccination rates we are seeing around the country as New Zealand rallies together to fight this virus. It shows the compassion and care Kiwis share for our elderly, immunocompromised and vulnerable whānau. I'd also like to acknowledge the great sacrifices our Auckland community has made on behalf of the rest of the country in what has been an immensely tough and challenging time.

However, it's important to remember that even at 90% or greater vaccination rates, the fight against COVID-19 won't be over. Like polio or measles, this disease is not something we can tolerate in our communities, we need to continue to develop better vaccines and antivirals that provide even greater levels of protection and immunity to ultimately eliminate COVID-19. The Malaghan has a part to play in this, of which your support plays a critical role.

As we move into the festive season it's important to remember that when we vaccinate, we don't just do it for ourselves, we do it for our loved ones. I encourage you to continue to talk with those in your circles who may be concerned about the vaccine and reassure them that it is safe, it is effective, and it is the best tool we have to protect those we care about.

Prof Graham Le Gros CNZM FRSNZ FRCPA (Hon) Director

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at a time. Just like in real life, first impressions matter, and how you encounter something for the first time might make all the difference when it comes to developing or preventing allergies.

Take the food we eat, for example. Your gut, and the immune cells in the gut, have evolved to deal with all sorts of foods coming and going. It knows what 'food' looks like, so knows it's not a threat. But what if instead of encountering a



Dr Maia Brewerton

food through the gut, the skin is what makes first contact? The immune cells that live there might not get it right.

"What we put on our skin is crucial," says Dr Maia Brewerton, a clinical immunology consultant and collaborator for the Malaghan Institute's allergic disease programme. "There is increasing evidence that early life exposure of food through the skin may cause food allergy in susceptible individuals and delaying the introduction of high risk foods like egg and peanut butter in the infant diet increases the chance of developing a food allergy." She has seen first-hand just how devastating allergies can be for children and their families, and how difficult it can be dealing with severe allergies on a daily basis.

All too often, allergists see patients with severe allergies to food found in things like skin creams and soaps.

"When it comes to allergy, prevention is better than cure" says Dr Brewerton. "I think it's really important we consider what we're putting on our skin, particularly when we're very young or our skin barrier is damaged."

With the *Nature Immunology* paper showing how immune cells in the skin are dancing on a hair-trigger, Prof Ronchese and Dr Brewerton both recommend that parents make sure their children aren't unnecessarily excluding important items from their environment or their diet, and think twice about the products they put on their child's skin.

"Your body can't learn what is good for it if it's never encountered it, and perhaps we need to consider the manner in which we introduce these materials to the body," says Prof Ronchese.

Or, as Dr Brewerton puts it, "food is for your mouth, not your skin."

This is a condensed version of the original article. To read the full article head to our website or find it on our Facebook page.

New partnership to scale up CAR T-cell cancer treatment



Left: Dr Rob Weinkove demonstrating the LONZA Cocoon[®] to Hon Dr Megan Woods, Minister of Research, Science and Innovation. Right: Inserting a cell culture cassette into the Cocoon - credit LONZA.

The arrival of state-of-the-art automated cell therapy manufacturing technology in September launched a new era for our CAR T-cell therapy programme.

The new technology marks the creation of a new company – BioOra – formed between the Malaghan Institute and Bridgewest Ventures NZ to automate the manufacture of this revolutionary immunotherapy with a vision of delivering it at a fraction of current costs.

Malaghan Institute Clinical Director Dr Robert Weinkove says an automated, closed-system method of manufacturing CAR T-cells, using LONZA Cocoon[®] technology, will enable the Institute to shorten manufacturing times and increase the number of trial participants. BioOra will provide contract manufacturing services to the Institute for future CAR T-cell clinical trials.

"We are planning a series of CAR T-cell manufacturing and clinical improvements to our clinical trial programme – including automated manufacture – to improve patient experience and widen availability."

Initially two Cocoons are being installed at the Institute, one for research and development funded by donors, with the number of Cocoons being increased over time.

"We now have an opportunity to scale-up CAR T-cell manufacture, with the goal of improving both affordability and availability of this potentially life-saving therapy in New Zealand."

A Mild Touch of Cancer

"I came back to New Zealand and everybody's saying to me, gosh is this ever going to come to New Zealand ... and I said, no way, we're far too small a country, there's no way New Zealand's ever going to have the science, the research, the know how to do this sort of thing. And then I got a phone call..."

Following the success of David Downs' column and book, director Annie Goldson has now brought his unique story to the screen, in a powerful tale of survival, generosity, science and hope.

A Mild Touch of Cancer follows David's journey with non-Hodgkin lymphoma, the CAR T-cell therapy that saved his life and his tireless efforts helping others negotiate their own cancer journeys. It offers a unique view of our efforts to make CAR T-cell cancer therapy available to more New Zealanders.

It is currently screening (free to view) on SkyGo, and after its run at the NZ International Film Festival, will stream in feature length on Neon.



A screenshot from the New Zealand made documentary, A Mild Touch of Cancer, featuring cancer survivor David Downs.

Ka Mātau, Ka Ora: COVID-19 clinical study update

VAANZ Clinical Programme Manager Brittany Lewer gives an update on the Malaghan Institute's Ka Mātau, Ka Ora (from knowledge comes wellbeing) study.

We began enrolment in June and have now completed the 300-participant enrolment, with strong participation in Māori, Pasifika and elderly populations, and those at high risk due to comorbidities.

Participation in the study lasts for one year. We are now collecting all the early samples and have begun sending these to numerous national collaborators for testing. Our priority is to determine the immune responses of our key populations to the Pfizer-BioNTech vaccine in the short period after the vaccination and comparing this to international data.

We're supported by the clinical sites in Rotorua and Christchurch and most importantly by the commitment of our participants in the study. We are eager to see the longer term results in the new year.



Brittany Lewer (second from right) with scientists working on the Ka Mātau, Ka Ora study.

mRNA vaccines: how they work

Until recently, developing a vaccine was a time-consuming and costly process, involving the production of inactivated or weakened virus or viral proteins. It required a lot of trial and error to make these 'artificial' proteins look as close to the real thing as possible – a process scientists would have to repeat each time a virus mutates and changes its structure.

mRNA circumvents this iterative process and instead use our own cells to make the vaccine.

The process works so well because our cells already have all the machinery they need to build perfect copies of proteins. All we need to supply is the instructions. Because these instructions only code for a small part of a virus, there's zero chance that our cells will accidentally make the real thing.

Nestled in the nucleus, at the centre of our cells, is our DNA. It contains the instructions to produce most of the building blocks, or proteins, that make up our body.

However, DNA never ventures out of its position within the fortified nucleus. Instead, it sends out a tiny messenger molecules – mRNA – which contain only the relevant instructions for our cells to make particular proteins. This intermediate messenger is required because the machinery for making proteins lives outside the nucleus. Once the information in the mRNA is read by the cell and made into a protein, it's no longer needed and breaks down.

Because viruses are also made of proteins, by presenting the body with an mRNA molecule encoding a portion of the virus, like a spike on its surface, we can get a cell to produce copies of this protein, which then get picked up by our immune cells that can now begin the process of recognising and generating immunity. To make a new vaccine, all we need is to know the genetic code of the virus, a process that takes only a few hours. Once we know the code we can determine which bits will work best for a vaccine and generate a matching mRNA sequence.

All up, it takes only a couple of days and very few resources to have a brand new vaccine, compared to sometimes years using the traditional method. Once it's gone through the safety testing, billions of doses can be made and distributed from a single lab.

"The process works so well because our cells already have all the machinery they need to build perfect copies of proteins. All we need to supply is the instructions."



Recent accolades for Malaghan Institute scientists



PROFESSOR MIKE BERRIDGE

Shorland Medal from the New Zealand Association of Scientists, recognising major and continued contribution to basic or applied research that has added significantly to scientific understanding or resulted in significant benefits to society.



DR KERRY HILLIGAN

Royal Society Te Apārangi Fellowship to conduct research on how exposure to different germs impacts the likelihood of developing allergies and autoimmune diseases.



DR TOM MULES

Health Research Council Career Development Award to investigate intestinal barrier dysfunction which has been associated with a wide array of diseases, including inflammatory bowel disease, colon cancer, obesity, fatty liver disease and dementia.



DR DAVID O'SULLIVAN

Marsden Fund Fast-Start grant to investigate the impact of fever on our immune response.



DR NATHANIEL DASYAM

KiwiNet Emerging Innovator programme to support him to translate his research in CAR T-cell therapy.

Thank you to our partners











KINETICS







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



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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.

Please support our research today.

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. With your support we can gain a deeper understanding of how our immune system works to help us create better, lower cost treatments for New Zealanders in need.

To donate, simply scan the QR code, or visit donate.malaghan.org.nz

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



Best wishes to our supporters this festive season!

All support, big and small, holds a special place in our hearts at the Malaghan.

A big thank you to all the support we've received this year from our amazing community, foundations and trusts. Your support is what keeps our research independent and pushes us forward to make real, long-term impacts on the health and wellbeing of New Zealanders.

Happy holidays!

Our online fundraising platform is live!

We're excited to share our new online community fundraising page – Raise for Research!

We all want to find better treatments and cures for disease, and now you can be part of our fundraising journey. Our amazing scientists have the passion and drive, but it takes everyone to help transform these discoveries into lifesaving cures.

You can find everything you need to set up, run and manage a fundraiser for the Malaghan Institute – from fun runs to bake sales – and 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 if you need help setting up your event.

Happy fundraising!



donate.malaghan.org.nz/raise-for-research

Harnessing the power of the immune system.