SCOPE 66
A MALAGHAN INSTITUTE PUBLICATION

MALAGHAN INSTITUTE OF MEDICAL RESEARCH

MALAGHAN INSTITUTE OF MEDICAL RESEARCH | NEW ZEALAND | WWW.MALAGHAN.ORG.NZ | JULY 2018

Breast cancer research to take aim at stronger, more effective vaccines

PhD Student Olivia Burn

The Malaghan Institute's cancer immunotherapy team has been given the green light to investigate better treatment options for breast cancer thanks to a joint Health Research Council, Breast Cancer Cure and Breast Cancer Foundation NZ grant worth up to $250,000 over the next two years.

The research, led by Dr Rob Weinkove, will focus on making cancer vaccines more effective, to ultimately improve survival rates from the disease.

"One of the major areas for improvement of existing cancer treatments is preventing relapse," says Dr Weinkove.

"In breast cancer, this can happen many years after someone's initial treatment for the disease. It's a devastating complication. Metastases – the spread of the cancer cells from the place where they first formed – can occur in various organs, but one of the most common is the bone.

The research builds on a collaboration with the Ferrier Research Insitute which has Breast Cancer Foundation NZ funding to develop synthetic breast cancer vaccines

"At the Malaghan Institute, we've been researching breast cancer vaccines in different combinations and conditions to try and create stronger protection across various organs. One of these vaccines seems to be quite effective at targeting the bone."

PhD student Olivia Burn is investigating whether this vaccine can create new immune responses that protect the body against breast cancer metastases long term.

"We want to know if these different vaccines protect different organs against breast cancer metastases that have HER2 – the target of the anti-breast cancer drug Herceptin.

By inducing a powerful immune response in local tissues at likely places where cancer might recur later in life, the ultimate goal of this research is to provide immunity from relapse in breast cancer patients.

From our Director

With the Health Research Council's recent announcement of continued funding for the Independent research organisations programme, I am in very positive spirits about the future of health research in New Zealand.

The funding will play a critical role in underpinning the core of the Malaghan Institute's strategic plan over the next three years, helping us meet our targets and goals to make real and verifiable contributions to improving New Zealanders' health and wellbeing.

Yet this achievement would not have been possible without the firm and unwavering support of our backers and philanthropic givers. Your support not only allows us to maintain our independence, but gives us the freedom to steer our research and expertise in new and exciting directions. This is crucial for us to deliver the greatest impact from the most promising areas of research internationally.

Thank you,

Prof Graham Le Gros
CNZM FRSNZ FRCPA (Hon)
Director

The allergy story hidden in our genes

Our genetic information tells a complicated story about our relationship with infections. Bacteria, parasites and allergens have been around as long as we have, influencing our immune system and the genes that control its workings.

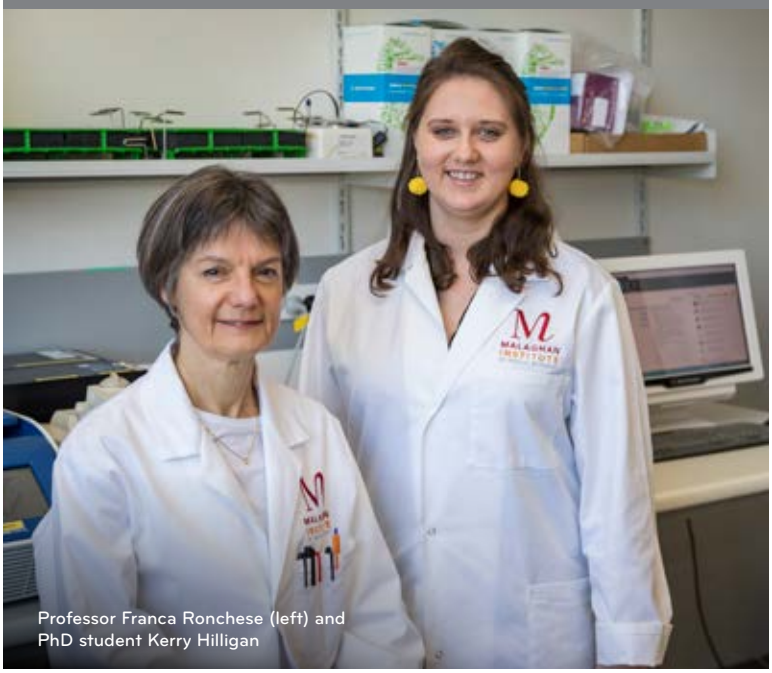
"We know that allergies tend to run in families, which means that genes that are passed down through generations must be involved," says Professor Franca Ronchese, head of the Malaghan Institute's immune cell biology team.

"However, there seem to be many different genes contributing to allergy, and the result is that the combined effect of all these genes together is difficult to predict."

Prof Ronchese says that because allergens seem to be hard for our body get rid of, they end up triggering the immune system in multiple ways. We can therefore track how the immune system responds by seeing which genes are stimulated during an allergic reaction.

"Interestingly, we find that the genes that are stimulated can be different depending on which allergen we use. For example, the work of PhD student Kerry Hilligan has demonstrated that certain key molecules (like TSLP and type 1 interferon) both act on the dendritic cells of our immune system, even if they have very different downstream impacts."

So, while an immune reaction to parasites or to eczema may look very different on the outside, there is a subtle commonality underpinning them. By watching how allergens interact with the immune system, we gain vital clues into how to manipulate this relationship for our collective benefit.



Professor Franca Ronchese (left) and PhD student Kerry Hilligan

Allergic disease research pays tribute to 30-year strong relationship

Senior research officer Melanie Prout (left) and Professor Graham Le Gros

The Malaghan Institute's allergic disease programme recently published a paper that honours an outstanding 30-year collaboration with Dr William (Bill) Paul at the National Institutes of Health in Washington DC.

"We were invited to publish some work in tribute to Bill," says Professor Graham Le Gros, leader of the asthma, allergy and parasitic disease programme.

"The purpose of the paper was to understand how a key hormone, IL-4 – which has long been associated with allergic disease – may actually control the development of the disease in the first place.

"It's a question I worked on with Bill, who was my postdoctoral supervisor between 1987 and 1989, but which we were never able to answer in his lifetime – partly because of the limits of technology back then."

Prof Le Gros says his research with senior research officer Melanie Prout found that IL-4 plays an important role in the skin with development of atopic dermatitis (eczema) – but not in other places like the lymph node. This provides direction on where to target anti-IL-4 therapies for them to be most effective.

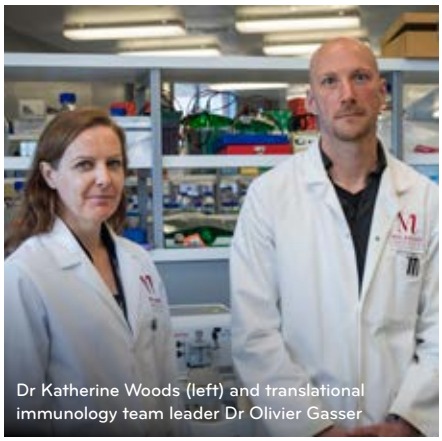
"The other significance of this paper is that it closes off a really important chapter in our 30-year relationship with Dr Paul. He has been a person whose support of all members of the scientific community is acknowledged and respected."

Research for Life funding enables in-depth look at MAIT cells

The translational immunology team at the Malaghan Institute has recently secured a Research for Life grant to look at how an obscure type of immune cell is activated and controlled.

Known as MAIT cells (mucosal associated invariant T cells), these immune cells are a relatively recent discovery in the field of immunology – having only been studied for the past decade or so. Several different subsets of MAIT cells exist, but their functions and how they're activated and controlled largely remain a mystery.

Dr Katherine Wood will be leading the research, which looks to answer important questions about how to manipulate these cells to activate and suppress the immune system.

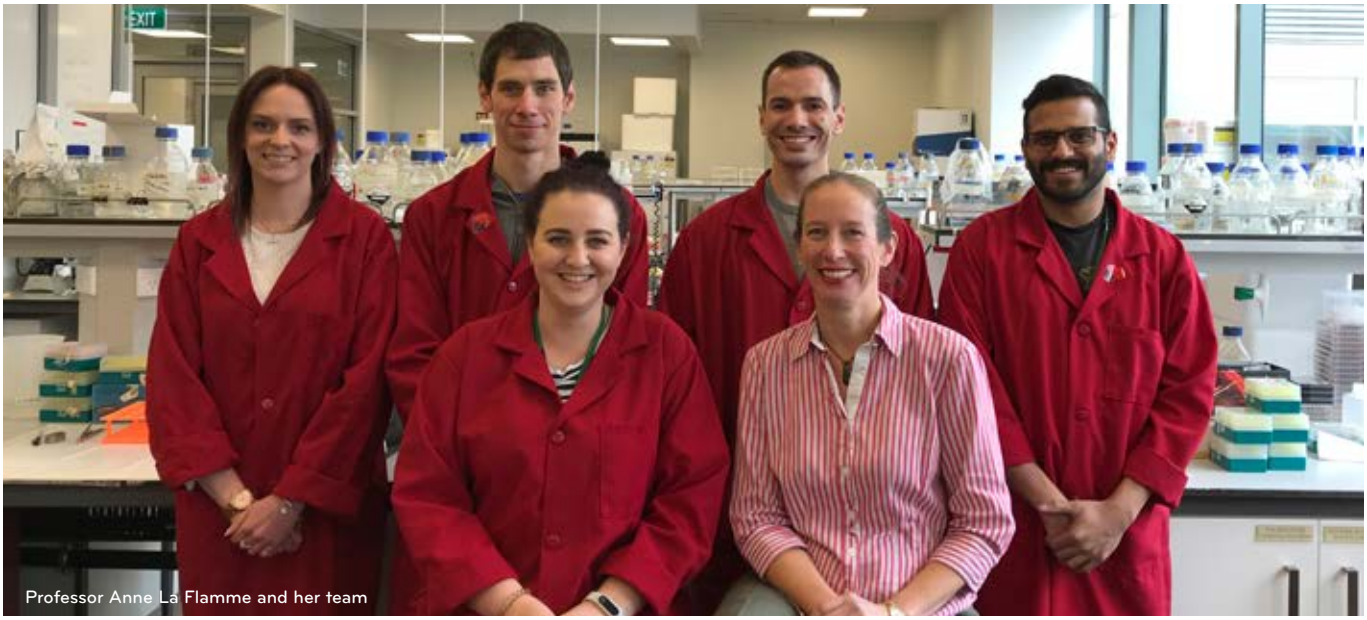


Dr Katherine Woods (left) and translational immunology team leader Dr Olivier Gasser

"It's quite a simple study looking at human blood," says Dr Woods. "Our aim is to isolate the MAIT cells and analyse them in different ways. Flow cytometry lets us look at specific activation markers on the MAIT cells and the new Seahorse technology lets us investigate the metabolics – what substrates are involved in activation. We should get some really clear information about different MAIT cell subsets, how and why they're activated, and what activates them.

Dr Wood says knowledge building is very important in this field because there's so much science doesn't yet know about why there are different subsets and why they behave differently.

"There may be a specific subset that is not acting in a way we want to – it's too aggressive and it contributes to allergy, or maybe it's suppressing other immune cells. If we know how each subset is activated and what it does once it's activated, we also know how to potentially block it, or alternatively boost it if we want to."



Professor Anne La Flamme and her team

Why do some people respond better to MS treatments than others?

A recent exploratory trial looking at the effect of the drug MIS416 on patients has found that the type of immune response induced from the drug plays an important role in determining its efficacy.

MIS416 is a microparticle developed by Innate Immunotherapeutics that has shown promise in regulating immune responses associated with multiple sclerosis.

"The trial ended up being really important in understanding how MIS416 could work and provide benefit – and what you need to get that benefit," says MS programme leader Professor Anne La Flamme. "We knew some people benefited more than others, but we didn't know why."

The answer, it seems, lies in the subtle differences between each patient's immune system.

What Prof La Flamme and her colleagues found was that the MIS416 drug targets myeloid cells, a subset of immune cells. The myeloid cells activated by MIS416 calm down the immune response and make their way into the central nervous system where they reduce the inflammation that leads to MS symptoms.

Because a patient's immune system plays a determinant role on the effectiveness of drugs such as MIS416, patients with a slightly different immune system profile had a less effective response to treatment.

"Understanding this will help future work in tailoring drugs or treatment options to the immune profile of MS patients. This will help to make treatments more effective and ensure that patients receive the best treatment for them," says Prof La Flamme.

This research was recently published in *Pilot and Feasibility Studies* and was a collaborative effort led by Dr Gill Webster (Innate Immunotherapeutics Ltd) with Prof Nancy Mayo (McGill University), Dr Dalice Sim (Otago University) and Prof La Flamme.

Spectral cytometry taking off with second Aurora

The Malaghan Institute's Hugh Green Cytometry Core team have had their hands full with the addition of a second Cytek Aurora spectral flow cytometer to the technology suite.

Having only recently acquired the first, the purchase of a second instrument was brought forward to meet demand.

"Demand for the Aurora has just taken off," says team member Sally Chappell, "so the second one couldn't have come at a better time. We'll also be upgrading both instruments soon to further increase capacity."

Part of the success of the Aurora lies in its ability to outclass traditional cytometers, including testing new and complex ways cells can be identified. For postdoctoral research fellow Dr Laura Ferrer-Font, being able to potentially carry out experiments she'd otherwise have to travel to Sydney to achieve will make a huge a lasting impact on her research.

The acquisition of the Auroras has been made possible thanks to the support of the Hugh Green Foundation.

David Downs: CAR-T recipient

David Downs, cancer survivor and self-proclaimed 'genetically modified organism', recently visited the Malaghan Institute.Over the last 18 months or so, David wrote a popular column in *Stuff*, recounting his efforts to beat cancer. From initial diagnosis to treatment, to travelling to Boston for cutting-edge CAR-T cell therapy, David's light-hearted yet deeply insightful column was closely followed by the nation, including the team at the Malaghan Institute.

With the Institute aiming to conduct New Zealand's first CAR-T cell clinical trials in the near future, David's successful journey was both an inspiration and affirmation of the CAR-T team's efforts.

During the visit, David made the generous pledge to raise $1 million towards the Institute's CAR-T cell work to help give Kiwis better access to this breakthrough treatment. You can find out more about the pledge at www.car-t.nz.

Dr Rob Weinkove (left) and David Downs

Technology head makes international strides in cytometry

Hugh Green Cytometry Fellow and head of research technology at the Malaghan Institute Kylie Price has become the first Kiwi to be elected to the International Society for the Advancement of Cytometry (ISAC) council.

The appointment recognises Kylie's tireless work over the past decade advocating for the use of cutting-edge cytometry in research and her ability to extend her expertise and influence internationally.

As part of the ISAC council, Kylie will work to further strengthen the ISAC's Shared Research Laboratories program and expand the availability of online and live cytometry education. Her appointment also acknowledges the Institute's commitment to using cutting-edge technologies to provide new discovery opportunities for New Zealand scientists.

Perpetual Guardian: Your legacy gift can benefit future generations

As seen in this issue, by leaving a gift to the Malaghan Institute in your will, you can help us develop treatments to benefit future generations.

Legacy gifts provide an essential financial foundation for us – and make a difference, no matter how big or small.

When considering leaving a gift in your will to the Malaghan Institute, we suggest consulting a financial advisor or solicitor who will give specialist advice on which option would work best for you and your family.

If you would like to talk in confidence with a professional, we are collaborating with Perpetual Guardian nationwide to provide a special service for our supporters who would like to learn more about making a will.

Perpetual Guardian are experts in preparing plain English wills to ensure your assets are distributed as you want them to be when you die. An up-to-date, well-drafted will avoids uncertainty, delay and cost.

For a confidential conversation about your options, please contact Rakesh Masalawalla on: **04 901 5430** or **rakesh.musalawalla@pgtrust.co.nz**. Alternatively, you can contact Jenny Sim at the Malaghan Institute at: **jsim@malaghan.org.nz**.

perpetual guardian

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

hrc Health Research Council of New Zealand

Upcoming community events 2018

North Shore Research Update at Lexus of North Shore | Wed 26 September
Please contact our Fundraising Administrator for more information
mweber@malaghan.org.nz or 04 499 6914 ext. 855

Hawke's Bay Research Update | Thursday 25 October
Please contact our Fundraising Administrator for more information
mweber@malaghan.org.nz or 04 499 6914 ext. 855

Malaghan Institute Hawke's Bay Golf Tournament, Hastings | Friday 26 October
Please contact our Head of Development for more information
jsim@malaghan.org.nz or 04 499 6914 ext.811

Malaghan Institute Auckland Golf Tournament, Remuera | Monday 19 November
Please contact our Head of Development for more information
jsim@malaghan.org.nz or 04 499 6914 ext. 811

Thank you to our partners

Performance Partner LEXUS

JUST PATERSON REAL ESTATE LTD NELSON · nichecom · ThermoFisher SCIENTIFIC · CQ Hotels Wellington · gbl PERSONNEL · HUGH GREEN FOUNDATION · KINETICS GROUP

Recent grants

April - June 2018

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

- Edith Rose Isaacs Estate
- Florence Petersen Leukaemia Trust
- Hugh Green Foundation
- Infinity Foundation Limited
- James Russell Lewis Trust
- Jennifer Smith Family Trust
- Pelorus Trust
- Rex & Betty Coker Foundation
- The Paddy Brow Charitable Trust

YES! I'D LIKE TO ACCELERATE THE PACE OF RESEARCH.

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** – Visa / MasterCard / AMEX / Diners

Card number ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ ☐☐☐☐ Expiry ☐☐/☐☐

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

☐ **Cheque** – Payable to the Malaghan Institute of Medical Research

Please return to PO Box 7060, Wellington, 6242

Online – www.malaghan.org.nz

Electronic transfer – Bank Account 06 0507 0052635 30

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

MALAGHAN INSTITUTE OF MEDICAL RESEARCH

Research is our journey. Cure is our destination.

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