



From left to right: Professor Franca Ronchese and Dr Lisa Connor

Our immune system's 'teachers' are still full of surprises

All scientific discoveries around dendritic cells are both exciting and fundamental, because without them, our immune system would be unable to fight disease or infection.

These cells are found in any body tissue, and especially those regularly exposed to the outside world – the skin, airways and, via our food, the gut. They can reach between and around other cells to form an immune 'filter'. "Dendritic cells can initiate or turn off immune responses. Fundamentally, their job is to educate our immune system on what to react to and what to ignore" explained Prof Franca Ronchese, leader of our Immune Cell Biology programme.

Prof Ronchese has been studying dendritic cells for several years, to understand – at a cellular and molecular level – how they respond to environmental changes, in order to trigger allergies. "Even today, we don't understand the causes of allergic responses, just their symptoms" says Prof Ronchese.

In the team's latest paper, published in the prestigious Journal of Experimental Medicine, they explored the response of dendritic cells to two allergens – one from a parasite called *Nippostrongylus brasiliensis*, and dibutyl-phthalate, a chemical plasticizer implicated in allergies in children.

Key to this research project's success was the use of "omics", or 'big data'. To understand how dendritic cells respond to allergens, the team identified and compared every molecule produced by healthy and "allergic" dendritic cells, creating a list of hundreds of changes. "Handling this vast amount of data is a challenge in itself, requiring the use of biostatistics and large computers, to store, process and visualise the data," explained Prof Ronchese.

Their surprising results showed that while the overall immune responses to both the chemical and the parasite allergen were similar, the mechanism behind it was very different. "This is the first time such a study has been carried out," Prof Ronchese said. "We expected to see more similarities than differences, but that was not the case. This is an initial step on a complex scientific path. There is still a lot to discover and understand about allergies!"

From our Director



In today's world, it can be hard to find positive news. I am delighted that we will celebrate the International Day of Immunology on April 29th. For me, immunology represents the future for human health. I believe that as our knowledge of the immune system grows, it will lead us to ground-breaking treatments, for many diseases. Here in our labs, we've recently seen that tweaking just a few insignificant molecules of the immune system could cure specific skin diseases such as atopic dermatitis.

But meeting the broader challenges of immunology requires a truly global effort, which is why we collaborate internationally.

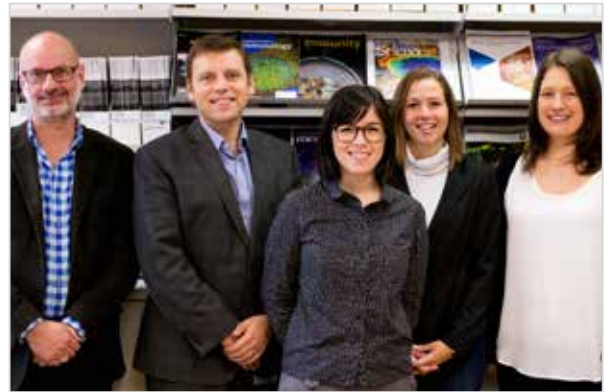
We are also about to explore new cancer immunotherapy treatments here in New Zealand through a collaboration with an international biotech group Hunan Zhoatai Medical Group. Our aim is to give New Zealand's patients early access to potential new cancer therapies. The importance of this work was brought into perspective, when we received the sad news that Dr Jim Watson, a long-time former trustee of the Malaghan Institute, had passed away from prostate cancer. I'd like to take this opportunity to urge you all to stay up-to-date with your cancer checks. Early diagnosis saves lives.

I hope you are proud of the work we are doing. Without the longstanding backing of you, our donors we would not be in the position that we are today. With your help, we'll get ever-closer to a new generation of therapies that will improve the lives of millions.

Thank you

Prof Graham Le Gros
CNZM FRSNZ FRCPA (Hon)
Director

Driving the next generation of cancer immunotherapy treatments in New Zealand



From left to right: Professor Ian Hermans, Dr Robert Weinkove, Lucy Pearce, Dr Giulia Giunti, Bethany Andrews

Professor Ian Hermans, Vaccine Therapy Programme Leader, and Dr Robert Weinkove, Wade Thompson Clinical Research Fellow and Clinical Director of the Human Immunology Lab, are establishing a research group in collaboration with Hunan Zhoatai Medical Group that will bring cutting-edge new cellular therapies into New Zealand. This research involves a breakthrough area of oncology called CAR-T cell immunotherapy.

In this transfusion-like therapy, some of the patient's own immune cells, the 'T cells', are modified to express a specific receptor – a chimeric antigen receptor (CAR) – in order to redirect them against cancer cells. "The approach works differently to vaccines, which aim to boost someone's own immune response," explains Dr Weinkove. "Here, we're directly altering the immune cells themselves to target them."

Central to the success of this new translational research is the expertise and knowledge of our team in good manufacturing practice (GMP) – international regulations for the production of medicinal products. "Our collaborators have developed an exciting pipeline of CAR-T cell therapies, our role is to make changes to the way they are manufactured and trialled, so that it fits with what's regarded in the Western regulatory environment as 'best practise'," Prof Hermans explained.

For us at the Malaghan Institute, the driving motivation behind this project is the impact that it could have on the lives of New Zealanders. "For some leukaemias, more than half of people treated with CAR-T cell therapies have remained in remission for years without any other treatment," Dr Weinkove said. "This is preliminary data, and we still have questions about the longer term effects, but as a clinician, I am extremely excited about the potential of CAR-T cell therapies."

Gut Health research programme will now be led by Dr Olivier Gasser

It is with a mixture of sadness and pride that we said farewell to Dr Elizabeth Forbes-Blom, who has moved to Switzerland to join the elite Nestlé Research Centre. Dr Forbes-Blom started her career at the Malaghan Institute with a postdoctoral fellowship, and she went on to undertake ground-breaking research, while successfully building our expertise in gut health. We are delighted to announce that our now extensive gut health programme will continue under the stewardship of Dr Olivier Gasser, newly appointed leader of the Translational Immunology team. Dr Gasser joined the Malaghan Institute from Basel, Switzerland in 2011 to become a Senior Research Fellow in our Vaccine Immunotherapy programme.

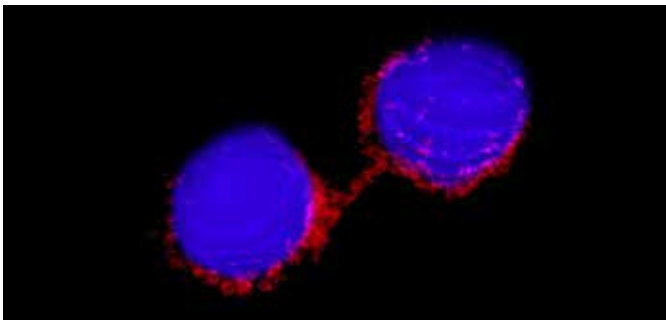
He and his research group will ensure that our research efforts will remain a key pillar of the High-Value Nutrition National Science Challenge. In particular, the group's research will focus on novel mechanistic aspects of the human immune system, which, because of the link to cancer, inflammatory and infectious diseases, could have an immediate impact in the field of immune health.



Dr Olivier Gasser

As a leading expert on the link between the immune system and metabolism, Dr Gasser also has a clear vision of where he wants to take the group "The field of immune metabolism has exploded recently. We have a unique combination of tools and expertise that could see us become major players in that area. Long-term, the lessons learned could help us to manage metabolic diseases like obesity and diabetes. And they could have even wider implications than gut health. I'm excited about what's to come."

Is mitochondrial transfer a player in bone marrow transplantation?



Erythroblast bridging in normal human bone marrow smears stained with E-cadherin (red) and the nuclear DNA stain, DAPI

"Using our cancer model, we showed that a damaged cell could collect fresh mitochondria from the host organism – there was a transfer of DNA," said Dr Melanie McConnell, Malaghan Institute Research Associate and Senior Lecturer at Victoria University. The team soon realised that a similar situation occurred in bone marrow transplants. There, a patient is given therapies to suppress the growth of abnormally proliferating cells, before receiving replacement bone marrow from a donor. The result is that a transplant recipient could be left with two different types of mitochondrial DNA – their own, and that of the donor.

Using the differences between these mitochondrial DNA—there are about 40 base differences between any two humans – Prof Berridge and his research group aim to investigate whether genes travel between cells in order to replace those damaged in bone marrow transplants that include cancer. Eight donor-

Our Cancer Cell Biology researchers are undertaking a study that Group Leader, Professor Mike Berridge describes as "a world-first". They are investigating whether DNA can transfer between cells damaged in bone marrow transplants.

recipient pairs will be involved in this ground-breaking study. Samples of each participant's bone marrow will be taken before, and again three months after transplantation. The aim of this is to examine whether any donor mitochondrial DNA markers are present in the recipient's bone marrow.

In parallel, the team will investigate mitochondrial transfer in mice that have been treated with radiation – similar to that used in cancer treatment – which induces damage in the bone marrow. "We work with mouse models as it allows us to carefully design our experiments," explains Prof Berridge, "...and to probe for genetic differences, we are using DNA sequencing and bioinformatics."

Combined, these studies will provide a unique insight into the mechanism behind DNA transfer, and may have an impact on future treatment choices.



From left to right: Dr Natalie Pujol and Dr Jonathan Ewbank

A tiny worm and our understanding of human diseases

Since January, the Malaghan Institute has been home to two visiting researchers from France's prestigious Centre d'Immunologie de Marseille-Luminy. Drs Nathalie Pujol and Jonathan Ewbank have brought with them their great expertise on a tiny nematode worm called *C. elegans*. Their knowledge of the genetic and cellular processes of this worm has been proven to be of the utmost value to understand similar processes in humans.

"The labs here are world-class, which allows us to run unique experiments. I'm enjoying spending so much time at the bench!" said Dr Ewbank. For Dr Pujol, this visit is all about collaboration, "The mutual exchange of ideas is key to advancing science. Merging our long-standing experience of nematode genetics and cell biology with the Malaghan scientists' understanding of the immune response to parasitic worms provides a new and unique direction for this exciting collaborative research."

Our technology helps to understand Dendritic Cells

Professor Franca Ronchese and her team have made an exciting discovery around dendritic cells that is helping to unravel the complex nature of the immune response to allergens. The type of dendritic cells mentioned are very unique and not many people are aware of their presence just yet. We required nine markers just to be able to identify them, before our Influx technology was used to sort a pure population of these cells out for genetic analysis. It was a combination of flow cytometry and genomics that led to this new discovery.

The Great New Zealand Trek: 9 Years of support for our Multiple Sclerosis research

With an impressive 238 participants taking part this year, it's been another successful stage of the Great New Zealand Trek (GNZT). Professor Anne La Flamme, who leads our Multiple Sclerosis (MS) research programme also participated in the trek, having done so since 2010. Her 12-year-old daughter Josephine joined her this year for the first time.

"Thanks to the ongoing support of the GNZT we are able to pursue novel and cutting-edge ideas in our scientific discoveries," says Prof La Flamme. The key achievements in our MS research have been in identifying several new therapeutic strategies to treat progressive MS and seeing them undergo clinical trials.

Kitty Johnson, a trustee and the organiser of the GNZT stated, "Professor Anne La Flamme's engagement and the research team's ability to probe new never-before- seen medical research is what makes it exciting and fundamentally important at the same time."



From left to right: Josephine, Hepa Paewai and Professor Anne La Flamme



Employee Spotlight

Dr Giulia Giunti
GMP Manager (CAR-T Cell project)

I joined the Malaghan Institute at the beginning of this year and I am leading the design and validation of one of our GMP (Good Manufacturing Practice) laboratories to bring a new cellular therapy, called CAR-T Cell to production. I am also responsible for adapting the CAR-T cell manufacturing protocol to Western regulatory standards.

Overall I have 7 years' experience working on similar projects in United Kingdom and in the United States.

The biggest challenge with setting up this project is to adapt the manufacturing protocol for a new cellular therapy as it was developed overseas to different regulatory standards.

Community Research Updates

A Community Research Update held in Wellington in early March this year, gave some of our supporters an opportunity to meet with the Institute's Director, Professor Graham Le Gros, research team leaders and senior science staff before hearing about the Institute's latest research programmes and intentions for expansion.

A similar Community Research Update was held in Christchurch later in March, kindly hosted by Lexus of Christchurch. All enjoyed both events and we hope to organise more Community Research Updates to acknowledge and share our achievements and aspirations.

Malaghan loses two loyal supporters

All involved with the Institute were saddened by the recent loss of two long term supporters, Dr Jim Watson CNZM and Judge Paul Barber QSO.



Dr Jim Watson

Dr Watson, Auckland, was a pioneer of biotechnology in New Zealand who was appointed to the Malaghan Trust Board in 1993, a position he held for 23 years. He held several governance and management roles in Medical Research, his most recent was co-founding the prostate cancer company Caldera. Dr Watson was a valued mentor to the scientists at the Institute and will be sadly missed.



Judge Paul Barber

Judge Barber, had a very illustrious law career in Wellington and thoroughly enjoyed his profession which included acting on several Tribunal's and Authorities. He also served as Chairman of the Dr Marjorie Barclay Charitable Trust which are great supporters of Professor Graham Le Gros and our Asthma research programme.

Events

Charity Auction and Dinner

Rotary Club of Port Nicholson in Wellington have once again chosen the Malaghan Institute as one of two recipients at this year's Charity Auction and Dinner to be held on

Friday 19 May 2017 | Intercontinental Hotel, 6.30pm.

Tickets **\$85 per person** or
\$850 for a table of 10 people.

Please email rossi.fogel@gmail.com or phone **021 730 773** to book your tickets for an evening of wonderful food, wine and company.

Recent grants

November 2016 – March 2017

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

Infinity Foundation Limited
Albert (Pat) Devine Charitable Trust
Carol Tse (No 2) Family Trust
Helen Graham Charitable Trust
Jennifer Smith Family Trust
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Research is our journey. Cure is our destination.