SCOPE 67
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MALAGHAN INSTITUTE OF MEDICAL RESEARCH

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# Down with Cancer

David Downs

**Cancer survivor and self-declared 'genetically modified organism' David Downs launched the Down with Cancer fundraising campaign in September. David is on a mission to raise $1 million for the Malaghan Institute's ground-breaking CAR T-cell therapy programme and give New Zealanders early access to potentially life-saving treatment.**

In January 2017, the businessman, author, comedian and public speaker was diagnosed with non-Hodgkin lymphoma. After 12 rounds of chemotherapy, he was told he had less than a year to live.

Fortunately, David was accepted into a clinical trial for CAR T-cell therapy in the United States. A revolutionary new approach to cancer treatment, CAR T-cell therapy harnesses the body's immune system to fight cancer cells. It involves modifying a patient's immune cells (T-cells) in the laboratory, to redirect them against cancer cells. The modified T-cells are then returned to the patient, where they can attack and destroy cancer cells. The treatment David received in the United States sent his cancer into complete remission.

After returning to New Zealand, David visited the Institute to share his experience and find out more about our own CAR T-cell therapy clinical trials and research programme. Inspired by what he heard, he pledged to raise $1 million to help bring the treatment to New Zealand.

Led by clinical director Dr Rob Weinkove, the Institute's CAR T-cell therapy team is currently focused on ensuring the trial meets New Zealand's strict regulatory and safety standards, to ensure it will be as safe for patients as possible.

David's Down with Cancer campaign kicked off with a flurry of media activity, including in the Dominion Post, on Stuff, the New Zealand Herald, Idealog, Mike Hosking Breakfast and TV3's The Project. David will be speaking at a range of events across the country to encourage Kiwis to get behind the cause. For more information on the campaign and to get involved, visit www.downwithcancer.nz.

# From our Director

In the final issue of Scope for 2018, I would like to take a moment to reflect on the tremendous support the Malaghan Institute has received in this landmark year.

The year has been a stand-out example of the impact committed individuals and organisations can have on improving the health and wellbeing of our communities. Alongside the fantastic and cumulative support of individual donors, we have received significant backing from trusts and foundations who recognise the Malaghan Institute's unique position to advance biomedical discovery for the benefit of all.

The passion and commitment of David Downs and the overwhelming public response to his Down with Cancer campaign is encouraging reaffirmation of Kiwis' strong desire to bring globally-significant medical advancements to New Zealand. It gives us courage that we are working towards a goal that is supported, both financially and in spirit, by New Zealand.

Thank you.

Prof Graham Le Gros
CNZM FRSNZ FRCPA (Hon)
Director

# Award-winning research by multiple sclerosis team

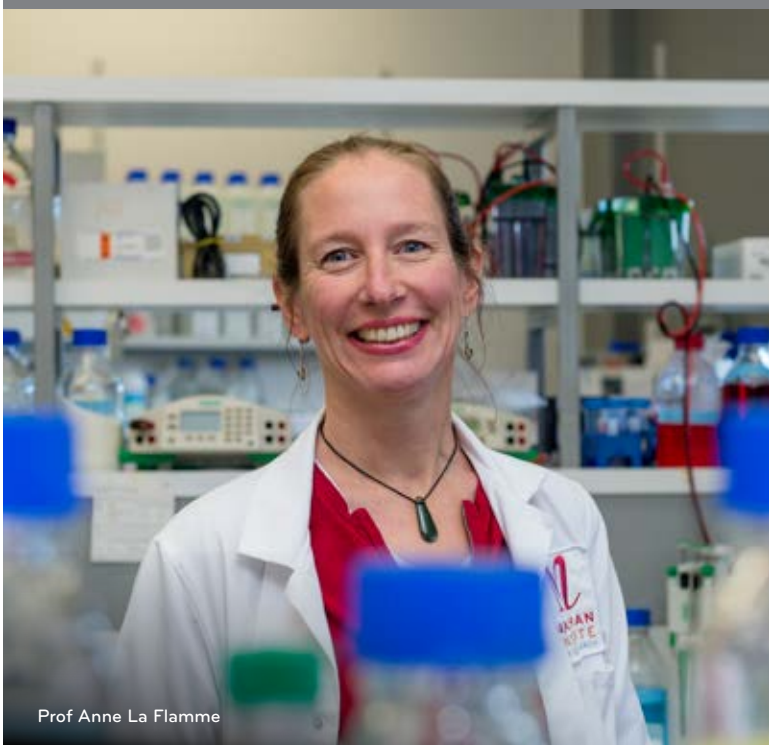
Research into a type of white blood cell by the Malaghan Institute's multiple sclerosis team has received international recognition by the journal *Immunology & Cell Biology*.

The team's paper, 'Glatiramer acetate treatment normalised the monocyte activation profile in MS patients to that of healthy control' was named runner up publication of the year by the journal's editorial board.

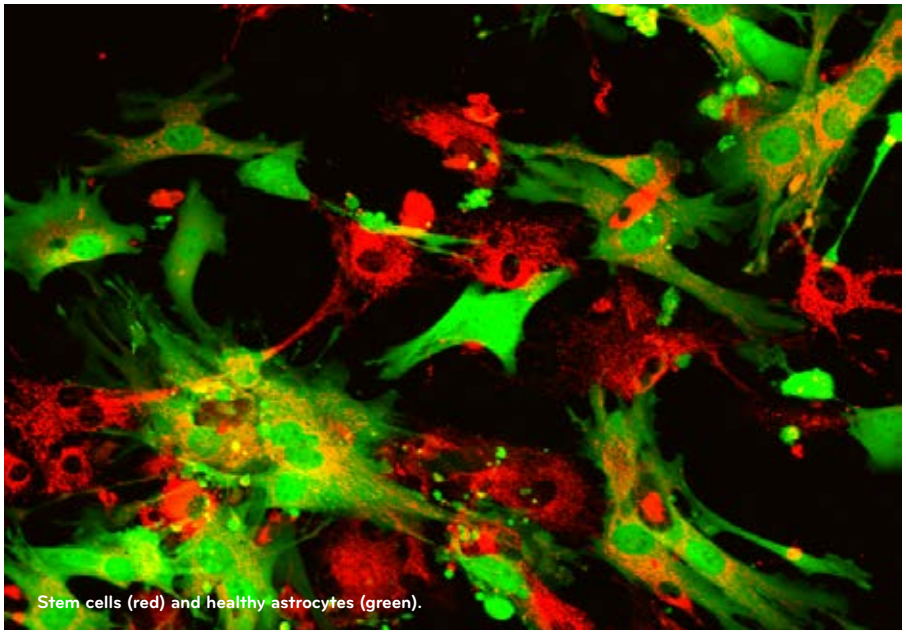
"For this paper, we looked at monocytes – a type of white blood cell that affects MS – in the blood of MS patients," said MS team leader Professor Anne La Flamme. "What was really interesting was comparing what monocytes look like in MS patients versus healthy subjects – and what happens when you treat MS patients with glatiramer acetate, a common therapy drug for relapsing-remitting MS.

"What we found was that these monocytes look completely different. But, when MS patients are treated with glatiramer acetate, it appears to alter monocyte activation. When you look at them again, these monocytes look like those from a healthy subject, not an MS patient."

"No one knows quite how this drug works in MS – but this research provides evidence that this monocyte alteration is one of the ways glatiramer acetate is modifying the immune system in a positive way."



Prof Anne La Flamme



Stem cells (red) and healthy astrocytes (green).

# Cell sacrifice in the line of duty

What happens when you deprive a key brain cell such as an astrocyte of its essential energy-generating components? That's the question Dr Melanie McConnell and her brain cancer biology team at the Malaghan Institute asked in a recently-completed research project, funded by the estate of Desley Mackey. Originally looking at the role mitochondrial transfer plays in brain biology, what the team discovered was far more unusual, and has real implications for treating neurodegenerative disease.

"Astrocytes are a type of brain cell that support neurons to function properly," says Dr McConnell. "We originally developed an astrocyte cell line which could be deprived of its ability to make energy, to look at how these cells might be supported under stressful conditions."

"What we found has intrigued the wider brain research community. We knew that cells communicated with each other, but we didn't realise that this could extend to whole cells 'sacrificing' themselves. In particular, we saw stem cells fuse with the stressed astrocytes to restore the health of these critical brain cells."

Deteriorating astrocyte function plays an important role for diseases such as Alzheimer's, Parkinson's and motor neuron disease. By showing a new way stem cells work to support other cell types like astrocytes, Dr McConnell and her team's work is shedding light on how certain stem cell therapies may work in preserving brain function during disease.

Dr Melanie McConnell

## How the skin influences the gut during an allergy

Cross-talk between the skin and the gut has been a focus of research for the translational immunology team. A recent project has been looking at how molecules produced in the skin during an allergic response influence the gut and the gut's sensitivity to an allergen.

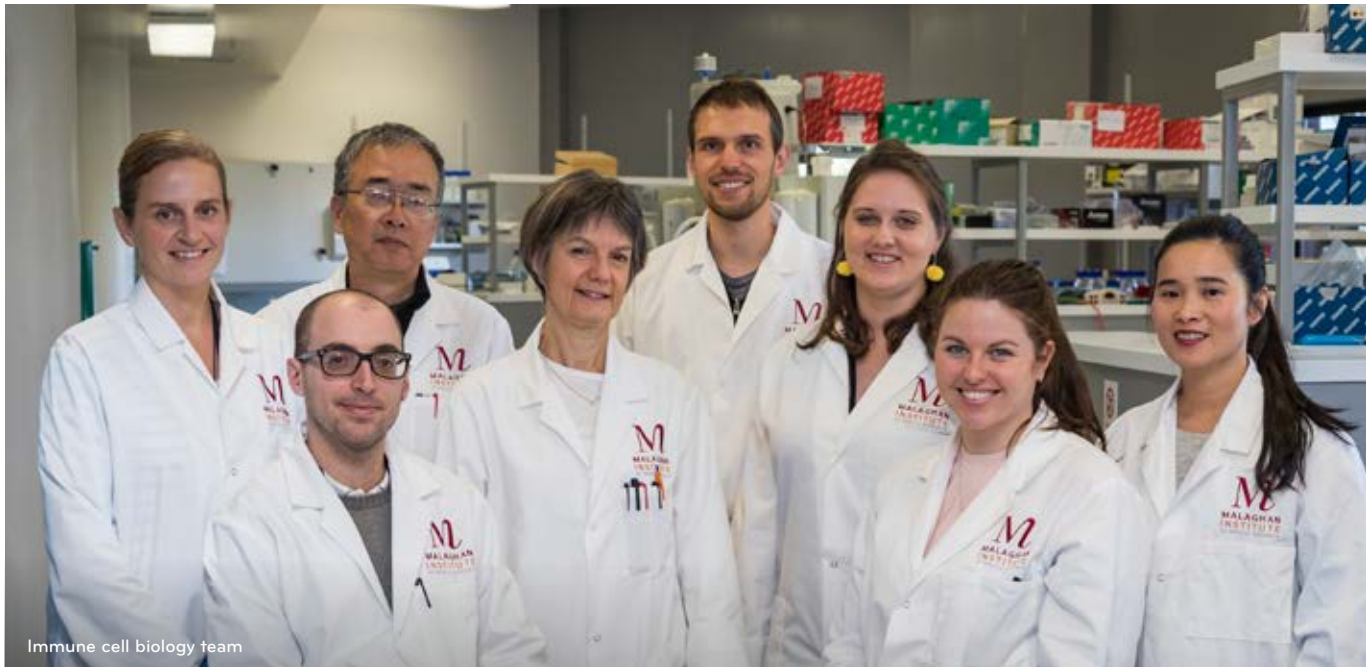
Dr Katherine Woods explains: "Alarmins are molecules secreted by many cells, in response to an allergen. For skin cells, these alarmins signal a barrier breach – a typical result from exposure to an allergen where the integrity of the skin is compromised. The alarmins then spread around the body, including places like the gut where it goes on to influence the local immune cells."

How much of an influence alarmins such as the molecule TSLP (thymic stromal lipoprotein) have on the immune system in the gut, and how it may affect allergies, is something Dr Woods and the rest of her team are investigating thanks to funding from the Dairy Goat Co-operative.

"We're looking at TSLP in detail to see whether it plays a role in accelerating allergies and cross-talk between different organs."

Dr Katherine Woods

OUR RESEARCH



Immune cell biology team

# HRC funding big picture research into dendritic cells

With more than $1 million in funding over the next three years, the Health Research Council is backing a major research project looking at molecular characterisations of dendritic cells during different immune responses.

Led by Professor Franca Ronchese, her immune cell biology team will be investigating what makes a dendritic cell 'prime' an unwanted allergic response. While the team have spent a lot of time understanding what happens to a dendritic cell during an allergic response, they still have an incomplete picture. Dendritic cells are also responsible for inducing a response to fight a bacterial or viral infection, so have a vital role in proper immune function.

"We've already collected a lot of data looking at this, but we're finding it's not enough – there are so many changes that it's impossible to tell which ones are relevant and which aren't," says Prof Ronchese. "We need to look at the bigger picture and what happens to dendritic cells in other situations in order to understand what makes an allergic response different to an antiviral response."

The HRC grant, which secures an additional research fellow for the team, will allow them to dive deeper into the genes stimulated in dendritic cells during different immune responses. By generating and analysing substantial amounts of data, the ultimate goal is to find and isolate the genes responsible for the development of allergies.

OUR PEOPLE

## Dr Philip George: Clinical research fellow

Joining the Malaghan Institute earlier this year as a clinical research fellow, Dr Philip George is playing a vital role in the Malaghan Institute's CAR T-cell therapy clinical programme. Previously a Haematology Registrar in Leicester in the United Kingdom, Dr George brings his wealth of clinical expertise to help set up and manage this New Zealand-first trial.

Dr George's current focus is preparing for the trial from a regulatory perspective, ensuring it will meet all ethical, safety and risk-management standards. He is also working with clinical staff at Wellington Regional Hospital, where patients enrolled in the CAR T-cell therapy trial will be treated.

Once the CAR T-cell therapy clinical trial is underway, Dr George will be directly involved in patient treatment and the day-to-day care of patients who have undergone this revolutionary cancer-fighting therapy.

Dr George's role has been made possible thanks to the funding from the Florence Petersen Leukaemia Trust.

# Harvard collaboration looking at genes that cause asthma

Jodie Chandler and Prof Graham Le Gros

Malaghan Institute PhD student Jodie Chandler recently returned from a research trip to Harvard Medical School in Boston where she spent six weeks working in the Benoist-Mathis Laboratory, tracing the origins of allergic diseases like asthma.

"I was working on a cutting-edge research technique called ATAC-seq (Assay for Transposase-Accessible Chromatin using sequencing)," says Jodie. "ATAC-seq can be used to figure out how transcription works by looking at which segments of DNA are unpacked at a given time – meaning which genes are available for transcription."

For cells to express genes and carry out their function, DNA first needs to be unwrapped from its tightly-wound coil before being transcribed into strands of RNA. These strands are then translated into proteins, the building blocks that make cellular functions possible. Traditionally, researchers have focused on RNA to understand which genes are currently active in a cell. However, stepping back and looking at which segments of DNA are available for transcription and why helps give researchers like Jodie insight into their development in relation to disease.

"In the case of allergic diseases like eczema, we know that the production of the molecule IL-13 is associated with its development. We hope that by finding out how the transcription of genes that code for IL-13-producing cells are regulated, we might be able to trace it back to its precursor origins and hopefully stop eczema developing in the first place."

While Jodie, whose PhD is supported by the Colin Williamson Charitable Trust, still has to sort through all the data generated during her time in Boston, she's optimistic her team will be able to fill in many of the blanks associated with allergic disease – both here and internationally.

"This work connects us with the global network of leaders in asthma research" says Professor Graham Le Gros, team leader and supervisor for Jodie's PhD. "Not only has Jodie's time in Boston brought relevance to our work, it has also enabled us to keep contributing to the global effort for a cure."



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

hrc Health Research Council of New Zealand

# Upcoming Events 2018 - 2019

**Malaghan Institute Wellington Friends Cocktail Evening with Lexus of Wellington | Guest speaker David Downs | Wednesday 7 November 2018**

**Malaghan Institute Auckland Friends Golf Tournament, Remuera Golf Club | Supported by the David Levene Foundation | Monday 19 November 2018**

**Malaghan Institute Bay of Plenty Friends Golf Tournament, Summerhill Golf Club, Papamoa | Friday 8 March 2019**

**Malaghan Institute Wellington Friends Golf Tournament, Royal Wellington Golf Club | Supported by FNZC and Lexus of Wellington | Monday 18 March 2019**

**Malaghan Institute Taupo Friends Golf Tournament, Wairakei Golf + Sanctuary | Thursday 28 March 2019**

Please contact our Head of Development for more information about these events: jsim@malaghan.org.nz or 04 499 6914 ext. 811

# Recent grants July - Sept 2018

**Albert (Pat) Devine Charitable Trust**

**Florence Petersen Leukaemia Trust**

**Humphry Bayly Charitable Trust**

**Infinity Foundation Limited**

**Jennifer Smith Family Trust**

**The Lion Foundation**

**The Margaret Ann Tibbles Charitable Trust**

**The Dr Marjorie Barclay CharitableTrust**

**The Nick Lingard Foundation**

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Research is our journey. Cure is our destination.

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