SCOPE 64
A MALAGHAN INSTITUTE PUBLICATION

MALAGHAN INSTITUTE OF MEDICAL RESEARCH

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Masters student Brittany Lewer, part of the Cancer Cell Biology team at the Malaghan Institute

Ankle-tapping cancer:

reducing therapy resistance in brain cancers

Cancer is particularly good at shrugging off whatever is thrown at it, ploughing on even as the severity of treatment is increased. How can we 'trip up' cancer so that treatment remains effectve, and the cancer does not 'get back up' again?

Therapy resistance has been a focus of research for both Professor Mike Berridge of the Malaghan Institute and research associate Dr Melanie McConnell at Victoria University of Wellington. Both teams have been working together to find out what makes cancer so resistant to treatment, and what we can do to counter its survivability – tackling this issue from two very different yet related approaches.

Prof Berridge and his team have been investigating the mechanisms that make cancer so resilient – and have discovered an entirely new biological principle from it. Published in 2015, the team found that cancers and tumours, once damaged, have the capacity to hijack mitochondria from neighbouring healthy cells which help them remain functional. Mitochondria are essential to cell life, providing the much-needed energy a cell requires to function. Without mitochondria, cells quickly die.

That cancer cells enlist healthy mitochondria from their surroundings when damaged gives insight into how cancer cells respond to the treatments designed to kill them. Finding ways to block this effect is a promising area of research for Prof Berridge and his team.

Meanwhile, Dr McConnell and her team have successfully identified a protein in brain cancer cells that appears to be essential for its survival. Called the BCL6 transcription factor, it is expressed by therapy and plays a vital role keeping brain cancer cells alive during even aggressive anti-cancer treatments. Dr McConnell's team have shown that when BCL6 activity is blocked, cancer cells quickly succumb to treatment.

From our Director

Thank you to everyone who has supported us this past quarter, your efforts have been motivating for the whole team.

Breakthroughs in therapy walk hand in hand with breakthroughs in discovery. While this cycle of development can sometimes take well over a decade to progress, the latest cancer therapy developments have shown that with real breakthroughs, new treatments can come to light in a much shorter period of time.

Within a single decade we have seen the emergence of a fundamentally new way of treating cancer that is providing real benefit to many people, and with it, the opportunity to develop this technology in New Zealand.

In addition, the Malaghan Institute is now transitioning into a period of major research and discovery of what we think will be a very exciting future. The Institute continues to push this cycle forward as we grow in strength of research and depth of capacity. I'm pleased to see some of the exciting research developments we're making in immunotherapy in this issue of *Scope*.

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CNZM FRSNZ FRCPA (Hon)
Director

Translational immunology leading the way with high value nutrition

Dr Olivier Gasser and Master's Student Anna Mooney

How can New Zealand companies leverage the relationship between food and our immune system to improve the health of consumers?

This is the question posed by Dr Olivier Gasser and the Translational Immunology team at the Malaghan Institute in collaboration with Plant & Food Research, as part of the High Value Nutrition (HVN) National Science Challenge.

People living in densely-populated urban environments are subject to much higher levels of air pollution than the general population, resulting in an increased risk of respiratory inflammation and disease. The goal of the HVN science challenge is to identify food and beverage products that can offer increased protection against inflammation caused by air pollution, and improve the effectiveness of vaccinations and the human immune system in the process. If Dr Gasser and his team can establish these relationships, it would create significant opportunities for the country's food and beverage sector.

The team presented the latest set of results of a preclinical trial at the annual HVN conference in early October, which will serve as a future platform for ongoing study into dietary interventions and immune response.

The next goal of the HVN programme is to secure funding to continue the research beyond 2019.

What do parasites have to say about allergic disease?

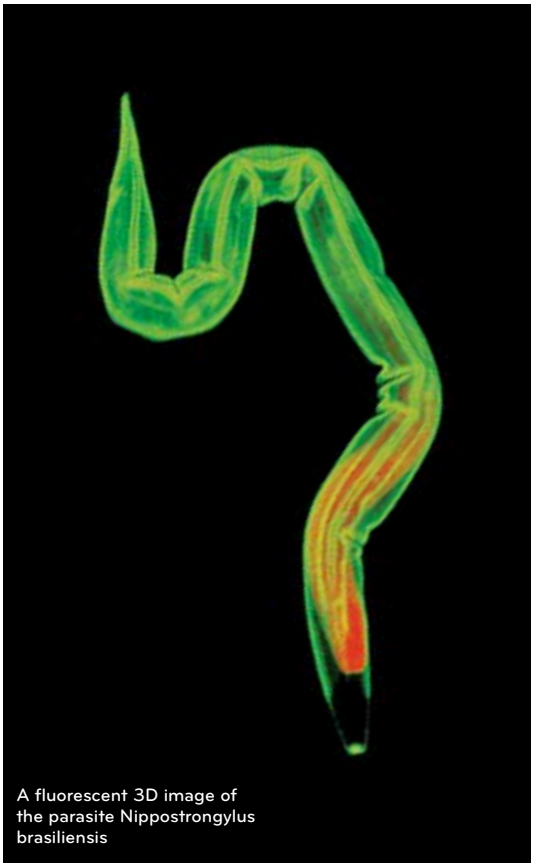
You wouldn't think a tiny helminth would have much to say about allergies, yet this is exactly the kind of parasitic worm Professor Franca Ronchese and the rest of her team at the Malaghan Institute are turning to for answers.

The process of developing an allergy happens long before you notice any symptoms. Yet from first encounter, an army of immune cells (known as Th2 cells) has already begun to form, lying in wait for the next time you're exposed, ready to launch an over-the-top counterattack to something that is harmless – otherwise known as an allergic reaction.

Parasites, such as helminths, are great at either stimulating or suppressing an immune response from their hosts. Studying what happens to the immune system when exposed to a parasite is giving the Immune Cell Biology team greater insight into the underlying mechanisms of asthma and allergy.

"The body is really good at inducing a strong Th2 immune response to parasites. This makes them good models to study," says Dr Connor, senior research fellow. "Th2 cells tell our body to activate physiological responses to rid ourselves of this parasite: things like increased mucus production, smooth muscle contraction and increased vascular permeability – symptoms that allergies and asthma share in common."

"We hope that these kinds of studies with parasites will help to identify targets that are involved in the initiation of the allergic immune response, so that it can be shut down and in some cases, turned off entirely."



A fluorescent 3D image of the parasite Nippostrongylus brasiliensis

New spectral cytometer is out of this world

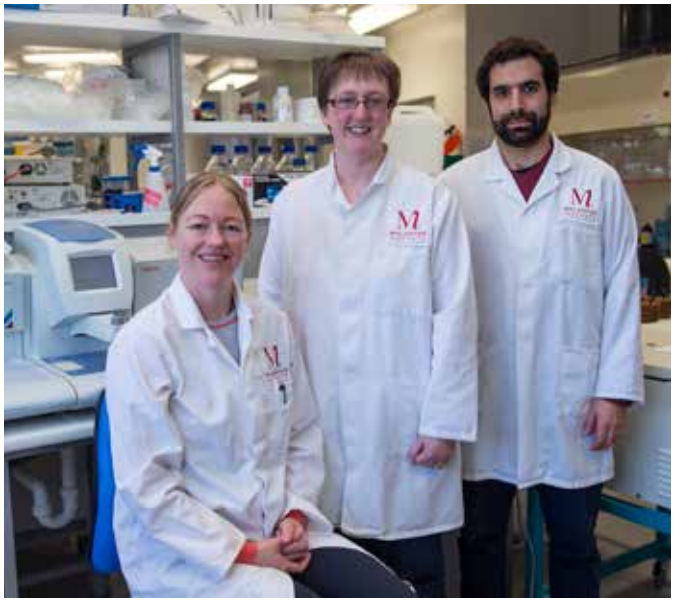
The Malaghan Institute is excited to welcome a new spectral cytometer to the Hugh Green Cytometry Core (HGCC) family.

Aptly named the Aurora, this machine is one of only four instruments of its kind in the world. The Aurora will dramatically increase the sophistication of detection carried out at the Institute and enable a greater level of experimentation.

"Flow cytometry is used to analyse and understand cells by tagging them with fluorescent dyes and then measuring a tiny portion of the emitted light. Unlike regular flow cytometry, a spectral cytometer takes the fingerprint of the whole emission spectrum for each fluorescent dye attached. This unique fingerprint will allow us to reliably analyse over 20 different parameters on a cell instantly with only three lasers – something we simply can't do with normal flow cytometry," says the Kylie Price, Head of Research Technology at the HGCC.

"We're really excited to start using this instrument," says Kylie. "In the future, we'd like to get the Aurora upgraded to five lasers, which would theoretically allow us to analyse 64 different parameters on a single cell at the same time. At the moment, what's holding this technology back is not the instrument itself, but that there haven't been enough new dyes created to fill up all of the possible combinations yet."

What makes this cell different from that one? Why is this cell so important? The more physical and biochemical features researchers can detect, the more questions scientists can answer about a cell or group of cells. Thanks to the Aurora, the Malaghan Institute will be able to pick out cells with much greater precision and accuracy than before, helping our scientists gain much greater insight into their precise nature.



The HGCC team: Kylie Price, Sally Chappell and Alfonso Schmidt

The private life of cells: seeing the big picture

Getting up close and personal with cells is a complicated task. Are the cells doing what we want them to do, when we want them to do it?

Many microscopic viewing techniques only let scientists peek at cells through very small windows of time. This makes it hard to get the full picture of what's going on in a cell's day-to-day life.

The IncuCyte S3, a recent addition to the Hugh Green Cytometry Core, is prying open this window and shedding new light on the private life of cells. Whereas most microscopes only offer a small snapshot in time, the IncuCyte S3 lets researchers observe individual cells for weeks, even months – spying on them as they carry out their functions, intended or otherwise.

This technology lets scientists like the Institute's senior research officer Astrid Authier look at whether our immune cells are correctly identifying and killing cells loaded with flu-specific peptides in the way we expect them to.

"It's the ultimate goal in terms of showing that the cells you're using are functionally capable of killing infected cells, which you can't see with other microscopic techniques," says Astrid. "With the IncuCyte S3 you can see the actual cells interact with each other in real time.

"This gives us an idea of how these cells function in real life. Eventually we'll expand it to look at cancer peptides and see if we can get cancer-specific cells to kill cancer cells in the same way."

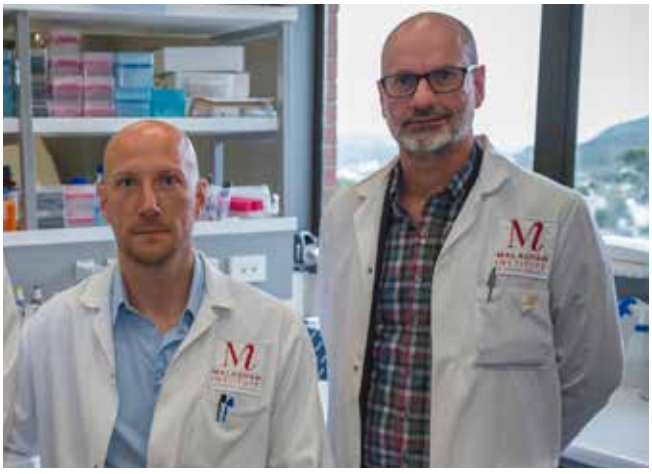
Senior research officer Astrid Authier

Cancer immunotherapy

The Cancer Immunotherapy programme has successfully completed the latest round of clinical trials of the novel melanoma vaccine therapy in development at the Malaghan Institute.

"The scientific manuscript describing the results of the Phase I trial has just been accepted in the journal *Cancer Immunology, Immunotherapy,*" says head of the Translational Immunology programme, Dr Olivier Gasser.

Leading on from the Phase I safety and dosage clinical trial, a research-based Phase II clinical trial is nearing completion. The results, which are scheduled to be collated and interpreted in the beginning of 2018, will provide a great deal of insight Prof Hermans and his team can use towards future work in this project.



Dr Olivier Gasser (left) and Professor Ian Hermans

Multiple sclerosis

Professor Anne La Flamme (right) with student Madeline White

The Multiple Sclerosis team has been working with Innate Immunotherapeutics, a New Zealand company that has developed a microparticle that could be used to regulate immune responses.

Their research is looking at how this microparticle harnesses the body's natural reparatory pathways by targeting very specific innate cell types, and how this might be used to repair neurons damaged by progressive forms of MS.

The results of the work have recently been submitted for publication following human clinical trials and an exploratory trial.

"We've been looking at how the microparticle affects disease in much larger populations and if there are any correlations with protection. This will help us identify those who may benefit from this treatment," says head of the MS team, Professor Anne La Flamme.

Malaghan Institute Research Updates: connecting science with the community

Throughout the year, the Malaghan Institute hosts a number of research updates across the country thanks to the generous support of the Institute's performance partner Lexus.

Recently, Lexus has hosted updates in Masterton, Auckland's North Shore and Hawke's Bay. Our leading scientists – including head of the Multiple Sclerosis programme, Professor Anne La Flamme, Research Fellow Dr James Baty and Director, Professor Graham Le Gros – covered a range of different research topics, presenting the latest developments at the Institute. Showcasing our unique story, strengths and opportunities as New Zealand's leading biomedical research institute, these research updates are one of the primary ways the Malaghan Institute connects and thanks our Friends, supporters and the wider community.

Attendees of the Malaghan Institute Research Update at the North Shore

Our people: Dr Laura Ferrer-Font

As the potential of immunotherapy grows, so must our team of specialised staff and researchers. Dr Laura Ferrer-Font recently joined the Malaghan Institute as a postdoctoral research fellow after completing her PhD in biochemistry and molecular biology at Universitat Autonoma de Barcelona (Autonomous University of Barcelona) in early 2017. She is excited to join our quest in developing world-leading cancer immunotherapies.

"I am very interested in treating cancer with immunotherapy. It is the main reason I was drawn to The Malaghan Institute. Here, the main belief is that many diseases are treatable by this approach and my own research only supports that. I personally want to investigate what is going on inside a tumour that makes it responsive or unresponsive to a certain therapy. Furthermore, I want to uncover the role of the immune system in current treatments, like chemotherapy."

In focus: Just Paterson Real Estate Ltd

One of the Institute's biggest supporters and advocates, Just Paterson Real Estate, has been supporting the Malaghan Institute for more than eleven years. This includes their annual 'Malaghan Month' promotion in the Wellington region.

In the lead-up to Malaghan Month, the Just Paterson team toured the Institute and our world-class facilities including the recently constructed GMP lab, which is a pivotal requirement in the manufacture and trialling of the new ground-breaking CAR-T cell cancer vaccine therapy set to be trialled in New Zealand late next year. The Malaghan Institute is immensely grateful for the ongoing and generous support of Just Paterson.

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

Malaghan Institute Friends Charity Golf Tournaments

20th November 2017 | Remuera Golf Club Auckland
SUPPORTED BY THE LEVENE FOUNDATION

27th February 2018 | Royal Wellington Golf Club

27th April 2018 | Wairakei Golf + Sanctuary

For further information contact: **Jenny Sim jsim@malaghan.org.nz**

Wellington Gala Fundraising Dinner – March 2018

For further information contact: **Charlie Holland cholland@malghan.org.nz**

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Research is our journey. Cure is our destination.

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