



Dr Lisa Feldman and Associate Professor Patries Herst

## American neurosurgeon chooses New Zealand

The Malaghan Institute is hosting American neurosurgeon Dr Lisa Feldman MD, the recipient of a prestigious William P Van Wagenen Fellowship. Dr Feldman is a clinician and researcher in the Department of Neurosurgery at Virginia Commonwealth University, in the State's picturesque capital Richmond – one of the oldest cities in America. The subject of her year-long research is, 'Perfluorocarbons as an Adjuvant treatment for Brain Radiation Therapy.'

She says, "Perfluorocarbons (PFCs) are a very interesting liquid. They carry eight times more oxygen than blood. Investigators have looked at their applications; ranging from as a blood substitute in the 1980s, when people feared HIV infection through blood transfusion, to maximising patient's oxygen level after severe wound trauma, until they can get to surgery, to maximising safe diver decompression avoiding the so-called 'divers bends'. This Fellowship allows me to investigate PFC use in improving treatment for glioblastoma – an extremely

challenging brain cancer, while living in a country which I first visited over ten years ago and have wanted to return to since."

Dr Feldman expands on her proposal, "Rapidly growing tumours have unusual blood vessels, which leaves the tumour tissue with a lower concentration of oxygen than surrounding tissue; this hypoxia which makes tissues resistant to radiation therapy. I want to find out if injected PFCs increases oxygen delivery to glioblastomas and increase their radio sensitivity. If so, it could lead to a better targeted treatment for a disease which at present has a poor outlook. I am also being supported by my Principal Investigator, Associate Professor Patries Herst, Department of Radiation Therapy, University of Otago, Wellington and Dr Melanie McConnell, Senior Lecturer School of Biological Sciences, Victoria University of Wellington (Co-Principal Investigator), and Carole Grasso, Senior Research Officer at the Malaghan Institute.

OUR RESEARCH  
World class

OUR PEOPLE  
Global impact

YOUR SUPPORT  
Our inspiration

# From the Director



*2016 marks 50 years since a group of far-sighted New Zealanders set the course for fully independent medical research to be carried out here.*

There are too many people to thank in this short message but I hope throughout the year we will honour those that have helped to make us what we are; a first-class medical research facility with our eyes firmly fixed on the diseases that matter most to New Zealanders.

Fifty years is not the destination point, as the timeline to the right of this page illustrates. No one knows what the timeline will look like in the next 50 years, but if I were a betting person I would predict a rapid acceleration of events and significant breakthroughs; and this acceleration to become more pronounced. We now have sophisticated tools and greater understanding of diseases because of the work carried out during the last five decades.

Our independence enables us to make use of international collaborations and incorporate this in to our own work. Our supporters understand this and we are so very grateful. We are unique, born in Wellington, still in Wellington but for all New Zealanders.

Professor Graham Le Gros

- 1966 — Institute first conceived November
- 1986 — Name change to Malaghan Institute of Medical Research
- 1997 — First preclinical demonstration that a vaccine made from Dendritic cells and protein fragments delayed the development of cancer
- 1998 — Conducted one of the world's first Dendritic cell anti-cancer vaccine trials
- Professor Graham Le Gros' discoveries support the hygiene hypothesis as a factor in a broad range of diseases
- 2013 — Cancer immunotherapy named the "worldwide scientific breakthrough of the year" by *Science*
- Phase I Melanoma Clinical trial commences
- 2014 — Malaghan Institute discovery of novel asthma vaccine approach in animal model
- 2015 — Professor Mike Berridge co-leads a team which first demonstrate mitochondrial DNA movement between cancer cells and healthy cells in an animal model
- Phase II Melanoma Clinical trial commences
- Formation of *Avalia Immunotherapies*<sup>[1]</sup> company to progress synthetic cancer vaccine technology
- 2016 — World-first study of possible link between gut microbiome community type and influenza vaccine response
- 50th Anniversary of the Malaghan Institute

[1] Note there are not yet any clinical trials underway using the synthetic vaccine technology

# Rachel Perret

## – Seattle-based, Malaghan trained



Professor Franca Ronchese and her former student Dr Rachel Perret

Dr Rachel Perret recently returned to the Malaghan Institute to deliver a seminar on her current post-doctoral work at the Fred Hutchinson Cancer Research Institute, or Fred Hutch, in Seattle.

Almost ten years ago Rachel was a PhD student in Professor Franca Ronchese's group, investigating the potential of 'memory' immune responses to sustain the body's fight against cancer. Today the Christchurch-born scientist says she is still a detective, but an even more focused one; on the hunt for the best T cell receptor (TCR)-based immunotherapy for Acute Myeloid Leukaemia (AML), a rapidly progressing form of cancer of the blood and bone marrow.

AML has a poor survival rate of around 25 percent measured at five years after diagnosis, with treatment outcome highly dependent on age and disease type. Current therapy consists of two phases of chemotherapy and/or radiation, which attempt to completely eliminate the high numbers of cancerous white blood cells. Patients with high-risk genetic mutations and/or chemotherapy-resistant tumour cells may additionally receive a bone marrow or stem cell transplant, if a good donor match can be found. Unfortunately, although these treatments frequently lead to initial remissions, they can be extremely toxic to the patients and cancer relapse rates are high. "There is a huge unmet need for safer and more effective therapies for AML, and targeted immunotherapy holds great promise for eliminating cancer without the severe side-effects of chemotherapy," says Rachel. "The Philip D. Greenberg laboratory of immunology enables me to search for new AML-specific immunotherapies among an essential type of cancer-killing immune cells; T cells."

The nature of Rachel Perret's work reflects the breadth of research globally into how we can stimulate the immune system to fight cancer. She is using a carefully optimised experimental system to seek out 'high affinity' TCRs, which are cancer-seeking molecules on the outside of the T cells that can be used as finely honed immunotherapy tools.

The surface of a T cell has thousands of these receptors, which rapidly scan huge numbers of potential target antigens on the surface of cells. Immunology research has progressed to the extent that Rachel is able to select 'safe' antigens that are abundant on tumours but not on normal cells, and to identify the antigen-specific TCRs with the greatest affinity i.e. the best chance of recognising and killing cancer cells. This is a semi-personalised therapy as the antigen and TCR combinations selected have to match the tumour and immune type of the patient (in a similar way to how donor and patient tissue types have to be matched for transplantation). The availability of this kind of therapy is currently very restricted, with only small numbers of patients eligible for treatment.

According to Rachel, "If we produce novel high affinity TCRs for ~seven of the most common immune/tissue types, we will have the potential to produce off-the-shelf therapies that could offer new, safer, targeted and effective treatments to over 90 percent of AML patients. This strategy may be used in combination with bone marrow transplantation or as a stand-alone therapy to hopefully deliver much-needed cures to patients who have run out of options from standard existing therapies." When Rachel was at the Malaghan Institute she was the recipient of a Research Grant from proud supporters Beverley and Harry Romanes.

# The PhD club

*In the last few months we have said goodbye to several staff members armed with newly conferred Doctorates, but the 'pipeline' to train New Zealand scientists at this advanced level continues. The attraction for students to complete their PhDs while working at the Malaghan Institute remains strong. As of April we have five PhD students, with a sixth to be confirmed.*

The time needed to complete a Doctorate varies between people but is usually between three and four years. Malaghan students typically spend time at the end of their studies visiting international collaborators or institutions which is where cancer researcher Connie Gilfillan is at present; with a schedule of visits to Switzerland, UK, Dublin and The Netherlands programmed. Connie featured in last April's Scope newsletter.

The next student expected to complete is Karmella Naidoo, the Nikau Foundation Scholar. She is working to further understand the immune events that drive allergic inflammation in the skin. This allergic disease typically starts in infancy and results from an inappropriate immune response to innocuous substances such as house dust mites or pollen. Karmella, who is a popular speaker for visitors and tours to the Institute, hopes her findings will identify new targets for the treatment and prevention of eczema.

Kerry Hilligan who won first prize at the Wellington Health and Biomedical Research Society 'New Investigators Meeting' last year, follows Karmella. Her work is focused on understanding the subtypes of skin Dendritic cells (DC) and their ability to recognise different classes of pathogens (i.e. bacteria, fungi or parasite), as well as arm T cells with an appropriate response. She hopes this information will assist with managing the burden of infectious diseases by allowing for the development of preventative strategies, such as vaccines, that specifically target the appropriate DC subtype.

The growing international excitement about using the power of the immune system to target cancer cells provides the rich research landscape for our latest confirmed PhD students. University of Otago graduates Olivia Burn, and Joshua Lange, the Peter Lapsley Scholar, are both studying in the Malaghan Institute's Vaccine



From left to right Karmella Naidoo, Connie Gilfillan, Joshua Lange, Olivia Burn and Kerry Hilligan

Therapy Programme. Each student has chosen one of two populations of immune cells (gamma delta T cells and mucosal associated invariant T (MAIT) cells respectively) to investigate them for an even stronger anti-tumour response. The two populations of cells share important characteristics with natural killer T (NKT) cells, but are much more common in humans than in animal models. The greater numbers of these cells populations, often referred to as 'innate-like T cells', represent a powerful source of the signals required for triggering T cells to function, and both Joshua's and Olivia's studies hold great potential.

*A complete list of our PhD and Masters students, their research topics and their supervisors, can be found on our website.*

# Why I support the Malaghan Institute

By Gail McLean

*The McLean family journey with the BIG C started nearly four years ago when my son, 11 at the time, fell over at school sports day and hurt his ribs. Instantly a jet black bruise appeared the size of a piece of steak! A visit to the doctors ended with us being sent straight to hospital where after a blood test we were told he probably had Leukaemia and would be admitted to hospital for further tests.*

After a bone marrow biopsy we were told it wasn't Leukaemia but a rare blood disorder called Aplastic Anaemia, a condition where the immune system attacks the bone marrow. After the first round of treatment failed another bone marrow biopsy was performed sixteen months later; we were then told things had changed and our son was developing Acute Myeloid Leukaemia, an aggressive form of Leukaemia. Within a few of months we were in Starship Hospital having a bone marrow transplant (January 2014). Thankfully he has made a full recovery and is currently in remission.

I've been fortunate enough to visit the facilities of the Malaghan Institute and learn about the amazing work they do. One of their research programmes is developing a cancer vaccine where the immune system is switched on and attacks the cancer cells. The same principle applies to Asthma where the immune overreacts; they are looking to turn it off.

If the Malaghan Institute is successful with the vaccine, bone marrow transplants could become a



thing of the past. We are, and always will be eternally grateful for the conventional treatment and fantastic after care our boy received, which has saved his life. But after spending three months in Starship watching him being pumped with chemo and a cocktail of other drugs and seeing first-hand the side effects that come with that, I will do whatever I can to support the fantastic work the Malaghan do to make this vaccine a reality.

I'm not a strong runner at all, more of a shuffler really, but I trained to run the 10km at the Cigna Round the Bays to raise much needed funding for this research. My son is now almost 16 now and he also ran with me. He said to me "Mum, if I can help stop one kid going through what I went through with the transplant it will be worth it".

That's why I care. You never think it will happen to you but when it happens to your kids it feels 10 thousand times worse and you wish it was you. Thank you to everyone who supported me and supports the Malaghan Institute.

