Breathing easier – creating a vaccine for asthma

We were delighted to announce the patenting and publication of our novel vaccine therapy for asthma in October. This new technology was successful in a mouse model and has the potential to be applied to other allergic diseases.

Many years of hard work are ahead until this treatment could be a reality for the one in four children affected by asthma in New Zealand, but the result is a promising step forward.

Mountain running champion Melissa Moon, who had to manage pollen-related asthma throughout her 20-year career, is excited about the development.

“To have an asthma treatment would literally be a breath of fresh air! To be able to get through summer with energy instead of struggling to get out of bed in the morning, short of breath, would be wonderful.

“Asthma can be very challenging as an athlete, where every breath you take affects your performance. Some summer months I would be lucky and race well due to a low pollen count, but other summers I would have to stop racing when my body felt so fatigued and I was unable to get enough oxygen into my lungs”, she says.

“With my restricted oxygen uptake, I visualised myself training at altitude, telling myself how strong and fit I was going to be during the winter months when I could finally get a decent breath of air!”

Moon won the Empire State Building stair climb in 2010 and 2012, was twice world mountain running champion and was named 2001 Sportswoman of the Year. She is also proud to be a Malaghan Institute Ambassador.

“It has been very rewarding supporting the Malaghan Institute as an ambassador. I have felt privileged to be associated with the Run for Research (www.runforresearch.co.nz), which combines sport with medical research, to create as much awareness as possible.”
Dr Marjorie Barclay was a leader in life. She studied in Edinburgh, Vienna and Boston before returning to Dunedin where she worked for the Otago Hospital Board and lectured at the Otago Medical School. Dr Barclay pioneered diagnostic radiology, became the first female radiologist in Dunedin and was one of New Zealand’s first female hospital specialists.

In later life, Dr Barclay, an asthma sufferer, moved from Dunedin to Wellington, as she believed the bracing sea air would benefit her health.

Dr Barclay passed away in 1978 and a charitable trust was established in her name a decade later. Since 2000, the Dr Marjorie Barclay Trust has supported the Malaghan Institute’s asthma research. Her legacy of medical innovation lives on and we honour her memory as we celebrate our latest asthma research breakthrough.

Judge Paul Barber QSO, Chairman of the Trust, knew Marjorie well as a friend and as her lawyer.

“She suffered quite badly from asthma. The Trust is very pleased indeed with the way the Malaghan Institute furthers Marjorie’s objective regarding research into asthma and nervous disorders. She must be very pleased with, and proud of, the work carried out by the Institute with the assistance provided from her charitable trust.

“We appreciate the way we are kept meticulously informed as to the use of annual distributions from Marjorie’s trust by the Institute.”

Thanks to our supporters like the Dr Marjorie Barclay Trust, our research can make a real difference in improving the health and happiness of thousands of people affected by asthma.

I am often asked how we prioritise our research. The nature of science is that research begets research, with new questions thrown up regularly, each of which may be worthy of exploration.

Funding plays a big part in that decision-making and the $28 million of research grants we were awarded by the Health Research Council in June effectively shores up our cancer and allergic diseases research for the next seven years. It also enables us to progress these discoveries through clinical trials to see health benefits for the community realised.

However, this core funding is targeted for our mainstream programmes only and does not give us the opportunity to delve into more risky but potentially much more rewarding areas. Immunology is a new science and although we have many pieces of the jigsaw in place, we are still learning just how large and complex the picture actually is.

Our community support is as important as ever, providing us with the opportunity to explore new science and accelerate our research. With your partnership, we will grow the innovative, world-class science programmes that are beating our most challenging diseases.

Trustees from the Dr Marjorie Barclay Trust visited the Malaghan Institute in 2013.
The asthma vaccine story

The novel thinking behind the asthma vaccine has its genesis in a discussion between Associate Professor Ian Hermans and Professor Franca Ronchese, puzzling over results from their cancer vaccine research.

The pair had noticed that the dendritic cell-based vaccines were very effective at starting an immune reaction, but almost not active at all once the reaction was established. Perhaps the immune reaction was blocking the activity of the dendritic cells?

Later, Professor Ronchese realised that the observation could be useful in another context. It was a turning point.

“I wondered if this mechanism could be harnessed for asthma, where the dendritic cells are the ones that start the unwanted immune response, which leads to inflammation and the symptoms of asthma,” she explains.

The asthma vaccine, which is a chemically linked combination of adjuvant and antigen, was made by the Malaghan Institute’s chemistry collaborators at the Ferrier Research Institute. Linking the two components ensures they reach the target cells together and create a powerful, highly specific immune response.

The mice were sensitised to an egg-based allergen, immunised with the vaccine, then given the allergen to inhale. “We saw no inflammation in the immunised mice – it was a very exciting result.”

“What we think is happening is that we are directing the killer T cells to go and block the dendritic cells, so they stop sending out the wrong messages. It’s like taking out the generals of the enemy’s army in order to overpower it.”

Asthma – the facts

- New Zealand has the second highest rate of asthma worldwide
- Asthma affects 600,000 Kiwis and one in four New Zealand children
- Asthma’s economic burden in New Zealand is estimated at $800 million per year

THE SCIENTIST BEHIND THE RESEARCH

Ching-Wen Tang always wanted to be involved in medical research. One of a family of six girls growing up in Wellington, Ching-Wen and two of her sisters discovered a love of science at high school. One of those sisters, Shiou-Choot, also works at the Malaghan Institute.

“So many people are affected by cancer that I wanted to help find better treatments. I work in cancer immunotherapy here, so it’s perfect!”

Ching-Wen studied at the University of Otago with her sister, completing a Bachelor of Biomedical Sciences degree and a Master of Science.

In addition to her work on our cancer immunotherapy programme, Ching-Wen played a big part in the asthma vaccine research. Ching-Wen researches her methods and plans her lab work meticulously, well ahead of time.

“I did most of the experimental work to validate how the vaccine works, but there are still more questions than answers! That’s what makes science really exciting – there are so many things to discover and we work as a team to get there. “My sisters and I still love to get together to talk about our science and I like to explain my discoveries to my younger sister too. Then I have to try really hard to understand her when she talks about political science! That’s not my strength at all!”

Left to right: Associate Professor Ian Hermans, Professor Franca Ronchese and Professor Graham Le Gros.
Cancer immunotherapy update

Highlights from our cancer immunotherapy research programmes, led by Associate Professor Ian Hermans.

Some of our vaccine therapy researchers. From left: Dr Taryn Osmond, Dr Olivier Gasser, Cameron Field, Ching-Wen Tang, Associate Professor Ian Hermans, Gene Swinerd, Dr Lindsay Ancelet.

Melanoma vaccine
Our melanoma vaccine involves modifying blood cells from an individual so that they trigger immune responses to a protein found only in tumour tissue. The cells are grown and processed in the lab and returned to the patient. This vaccine is being tested in a Phase I clinical trial (which started in late 2013), to determine an appropriate dose for a larger study (scheduled for 2015), which will examine the size and the quality of generated immune responses.

Leukaemia vaccine
Patients suffering from leukaemia often respond well to chemotherapy, but some leukaemia cells commonly become resistant to the treatment and the disease recurs. In our preclinical work, we have shown that a vaccine targeting leukaemia can potentially be used to protect patients from a relapse once they are in remission after chemotherapy.

Brain cancer vaccine
There is no standard treatment for recurrent glioblastoma multiforme (GBM), the most common and most aggressive malignant primary brain tumour in humans. We have completed a Phase I clinical trial combining a cell-based vaccine with chemotherapy for patients with this disease. While manufacturing the vaccine from a patient’s own cells often proved difficult in this advanced disease setting, we found some evidence that the vaccines could induce immune responses. In light of these results we have been focussing on much simpler vaccine formats, which we hope to test in the future.

Synthetic vaccine
An alternative approach to cell-based vaccines is to use a completely synthetic ‘off-the-shelf’ design, which avoids the need to make an individualised vaccine from each patient’s blood. This fully synthetic vaccine (which also includes an adjuvant) is being tested using blood samples to check its effectiveness in humans. Some exciting preliminary results have been obtained.

What’s an adjuvant?
An adjuvant is a substance that is administered with a vaccine to enhance its effect by causing a greater response from the immune system.

Our cancer immunotherapy programme has been assessing an adjuvant called α-galactosylceramide (α-GalCer for short). It is a natural chemical that was discovered in a marine sponge but is now made synthetically. This adjuvant is included in our melanoma vaccine that is currently being tested in a clinical trial.

Novel adjuvants that differ slightly to α-GalCer are also being investigated. These compounds have been developed by our chemistry collaborators at the Ferrier Research Institute (in a research programme led by Dr Gavin Painter) and are being incorporated into our new synthetic vaccines.

In our most promising synthetic vaccine (which also appears to work in an asthma model), Dr Painter’s team used ingenious chemistry to link the adjuvant and the antigen. Once inside the target cell, the linked vaccine breaks cleanly into two, releasing both components to initiate a powerful immune response.
Just 20 years ago, DNA sequencing required elaborate sample preparation, batteries of specialised machines and deep pockets. That same process can now be performed in a few hours on a lab bench, using a device the size of a muesli bar.

The device, a miniature DNA sequencer called MinION, was developed by Oxford Nanopore Technologies and is being trialled at the Malaghan Institute by Professor Mike Berridge, Dr James Baty and bioinformaticist David Eccles. Our Institute is one of around 500 research laboratories worldwide that are trialling a prototype ahead of the release of a commercial version.

“It’s a very impressive device that changes almost everything about how sequencing is done,” says Professor Berridge. “Our ability to sequence DNA in a matter of hours was impossible ten years ago, meaning the speed at which we can ask questions and find answers has greatly accelerated.”

The device connects to a laptop via a USB and genetic sequences are read off as a sample travels through hundreds of tiny pores in the device.

“We don’t have to send samples of DNA away to be sequenced, but can do it here, in real time. MinION’s size, speed and convenience are revolutionary for the work we are doing.”

“When I started in medical research it was inconceivable that we could sequence even small DNA molecules, let alone a human genome consisting of three billion units. This DNA sequencer is helping us sequence and compare different mitochondrial genomes, which are small compared with nuclear DNA, with only 16,300 bases.

“We see applications for this device in aiding our understanding of tumour formation and metastasis. Although mutations in mitochondrial DNA occur with high frequency in human tumours, their role, if any, in the development of cancer is unclear. Understanding the development of cancer at this fundamental level could have far-reaching impacts on the development of new treatments.”

Above left: The micro-patterned surface of the MinION flow cell. Above right: The MinION device in use at the Malaghan Institute. Plugging directly into a laptop through a USB port, it is a self-contained device, delivering real-time genome sequence data to accelerate our cancer research.
We all work to accumulate wealth and security for our families. It’s important to know that everything you have strived so hard to achieve is there for your family in the years to come.

For many of our clients it’s not just about passing on wealth. It’s about realising ideals and hope for the future and cementing long-term values. At Perpetual Guardian we are experts at preparing plain English Wills. A Will is a legally binding record of your wishes that directly affects those close to you. This is how you 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.

Gifts provide an essential financial foundation for the Malaghan Institute. No matter how big or small your legacy, it will make a difference.

For a confidential conversation about your options, contact Jeremy Chaston on (04) 901 4405. Alternatively, you can contact Jenny Sim at the Malaghan Institute on (04) 499 6914, extension 811.

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