

scope

Innovation - the key to medical breakthroughs

Renowned early 19th century French chemist and microbiologist Louis Pasteur once said "chance favours the prepared mind". While serendipity plays an important role in scientific breakthroughs, it is the ability to recognise the potential of a chance discovery and turn it into something useful and innovative that exemplifies a truly great scientist.

Scientists at the Malaghan Institute of Medical Research strive to be at the forefront of innovation and creativity, and in this issue of Scope we showcase our asthma research programme as an example of this. We also discuss how our scientists are using techniques learned through researching cancer to study a rare disease that has no known cure, and how they are applying their knowledge of therapy-resistant cancer cells to the development of treatments for neurodegenerative diseases.

In doing so, our scientists are challenging the way we currently treat certain diseases and offer practical solutions for how we might improve these therapies in the future.

"The Malaghan Institute and its supporters seek to ensure that the combination of 'chance and prepared minds' is backed up by a world class laboratory infrastructure and a commitment to translating discoveries into meaningful outcomes."

Prof Graham Le Gros, Director.



Malaghan Institute Immunologist Prof Franca Ronchese, whose cancer research has opened the door to a potential immunotherapy for asthma.

TB vaccine reveals new approach to treating asthma

While establishing his asthma research programme at the Malaghan Institute in the mid-1990s, Prof Graham Le Gros observed that certain types of bacterial lung infection could actually halt the development of asthma in mice. This pivotal discovery made the front cover of the prestigious New Scientist magazine and has led to a new form of therapy that could revolutionise the way we treat asthma.

For parents of children who suffer repeated severe asthma attacks, life is a daily battle. Asthma is the consequence of an overactive immune system, causing inflammation in the lungs. The steroid inhalers that are used to treat the disease work by reducing the inflammation in the lung so it is easier to breathe. However, there is growing concern regarding their long-term use.



Three year old Dylan Carson who is affected by asthma. His mum Jacqui, who works at the Malaghan Institute, welcomes the news that an asthma vaccine is being developed, providing another treatment option for parents of asthmatic children.



It has been proposed that the recent increased prevalence and severity of asthma, particularly among children, is a consequence of the Western world's obsession with cleanliness. The so-called 'Hygiene Hypothesis' suggests that some people react to harmless environmental stimulants such as pollen or house dust mites because as infants they were not exposed to the infections required to fully develop their immune systems.

Prof Le Gros' research group decided to test this hypothesis by looking to see if they could restore 'immune balance' in experimental asthma models with controlled bacterial infections. Strikingly their research showed that treatment with the bacteria used to make the TB vaccine, actually prevented the inflammatory immune responses normally associated with asthmatic lungs. This research revealed a new way of potentially treating asthma - by simply giving the immune system something else to focus on!

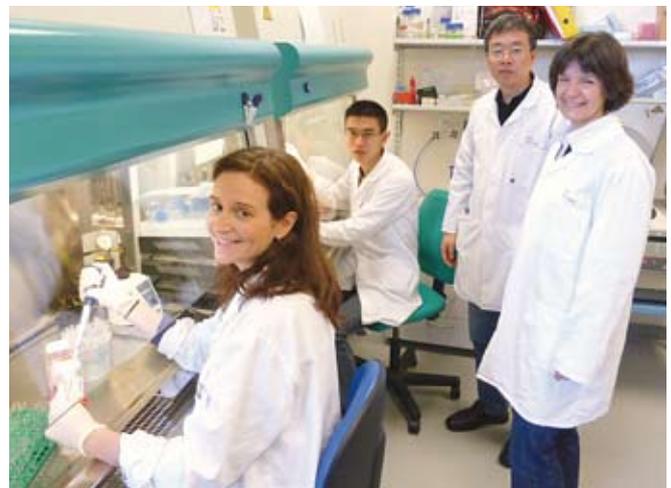
Prof Le Gros' published scientific paper describing this landmark discovery has been extensively cited and used by scientists, clinicians and drug companies to identify safer versions of the bacteria and their extracts for the development of a vaccine to treat asthma in humans. There are now several new compounds being developed in the USA that are in the late stages of clinical trial and the FDA approval process – a wonderful testament to the original pioneering research undertaken by Prof Le Gros' research group here at the Malaghan Institute.

Stumbling block for cancer vaccine - stepping stone for asthma vaccine

Prof Franca Ronchese and colleagues at the Malaghan Institute have spent over 15 years developing a cancer vaccine that works by stimulating the immune system to attack a patient's tumour. One of the biggest hurdles they have faced is maintaining the intensity of the immune response over time.

Part of the reason for this is that under certain conditions specialised cells called cytotoxic T lymphocytes (CTLs) attack and kill the dendritic cells before they can do their job. Although dendritic cell killing is a stumbling block for a cancer vaccine, Prof Ronchese made the pivotal connection that this same phenomenon could be used to tone down the immune response in diseases where the immune system is overactive, such as asthma. Her research group went on to make the striking discovery that stimulating CTLs to get rid of dendritic cells in the airway prevented the development of allergic airway inflammation in an experimental model of acute disease.

This exciting research received HRC funding earlier this year to further explore the potential of CTL immunotherapy as a treatment for allergic asthma. This is a fine example of how a problem presented in one area of research has the potential to provide a breakthrough in another. The key to undertaking science that redefines our understanding and treatment of disease is in recognising such opportunities when they appear.



From left, immune cell biology researchers Evelyn Hyde, Joel Ma, Dr Mark Yang and Prof Franca Ronchese.

Did you know?

- Asthma is a chronic respiratory disease of major concern in NZ
- It affects 1 in 4 children and 1 in 6 adults
- During an asthma attack the lining of the bronchial tubes swells, causing the airways to narrow - this makes it hard to breathe in and even harder to breathe out
- The final symptoms of allergic asthma are due to activation of the Th2 immune response (which normally serves to protect us from parasite infections) by harmless environmental triggers such as pollen or house dust mites
- The current treatment for asthma is the use of steroid based preventer inhalers, which work to decrease airway inflammation

Understanding cell death could lead to breakthrough in motor neurone disease

Senior Malaghan Institute scientist Dr Melanie McConnell has built an entire research programme around finding ways to identify and kill cancer stem cells – a rare population of cells found within tumours that are thought to be the main cause of relapse and metastasis. Ironically, this research has led to an innovative spin-off programme focused on keeping cells alive.

Cancer stem cells have the unique ability to renew themselves and use an extensive network of survival mechanisms to evade chemotherapy and radiotherapy treatments. As her understanding of these survival pathways grew, Dr McConnell

realised that cancer stem cells might just hold the secret to extending the life of cells that die prematurely, as in motor neurone disease.

Patients with motor neurone disease suffer increasing weakness of the muscles, due to the death of the neurons that feed into them and there is currently very little that can be done to stop this. Dr McConnell, with support from the estates of Ellen, Sinclair, Barbara and Alison Wallace, hopes to develop approaches that actually prolong the survival of neurons – a creative flip-side to her usual role of trying to kill cancer stem cells.

Searching for an effective therapy for rare lung disease

LAM or Lymphangioliomyomatosis is a devastating progressive lung disease that few have heard of. However, for the 21 New Zealand women who suffer from the disease, LAM is a big deal.

LAM causes shortness of breath, chest pains, coughing and lung collapse and there is no known cure. Because LAM is so rare it doesn't receive a lot of attention. Malaghan Institute scientists Prof Mike Berridge and Dr James Baty hope to change this by using their innovative cancer research to help LAM sufferers in a small but significant way.

Although LAM is not presently classified as a cancer, LAM cells have cancer-like properties such as loss of cell growth control, mutations and the ability to spread elsewhere in the body. With support from the NZ LAM Trust and the LAM Australasia Research Alliance, Dr Baty is taking a closer look at LAM cells to find out if there is a small population of cells with cancer stem cell-like properties. If these cells exist in LAM, they will need to be targeted for effective LAM therapy.

Dr Baty says the driving force behind his research is his desire to help people for whom there are very few treatment options currently available. He enjoys the challenge of deciphering the many signalling pathways involved with cell growth, proliferation and survival that are deregulated in LAM patients, and believes the most effective approach for treating these individuals might be with immunological therapies and/or drug treatments currently in use for cancer patients.

Both Dr Baty and LAM Trust Director Bronwyn Gray recently attended the 1st European LAM Conference held in Udine, Italy.



Dr James Baty pictured with NZ LAM Trust Director Bronwyn Gray, who has spent the past 11 years raising awareness and funds for research into LAM. For further information on the NZ LAM Trust, please visit www.lam.org.nz.

What's been happening...

Our scientists in the spotlight

"Ever Wondered?", a new science show on TVNZ 7, takes you behind the scenes to look at what is being achieved at the cutting edge of science in NZ. Kylie Price, the Institute's Flow Cytometry Manager, along with Neurosurgeon and Malaghan Clinical Research Fellow Mr Martin Hunn, recently featured in an episode that looked at how science and technology is aiding medical research. Another Malaghan Institute scientist who you may have caught a glimpse of on TV recently is Infectious Diseases Group Leader, Dr Joanna Kirman. Dr Kirman was filmed for the TV3 show 'What's really in our...' discussing bacteria and viruses in the episode on 'Soaps and Cleansers'.



Flow Cytometry Suite Manager, Kylie Price, being filmed for an episode of TVNZ 7's Ever Wondered?

Science Learning Hub website

Our scientists have also been sharing their knowledge and passion for science on the Science Learning Hub website. Managed by the University of Waikato, this website provides resources for teachers of school years 5-10 and is developed in collaboration with NZ scientists. Keep an eye out for our scientists in the upcoming section entitled 'Fighting Infection' on www.sciencelearn.org.nz.

AMI Insurance – supporting valuable research

AMI Insurance has again shown its wonderful support for the Malaghan Institute by confirming their principal sponsorship of the upcoming Auckland charity golf tournament. AMI's partnership with the Institute has spanned more than a decade and their generosity has included the sponsorship of our annual Lollipop Appeal, Asthma Laboratory and many Friends fundraising events. A huge thank you to John Balmforth (CEO) and his team at AMI Insurance and our congratulations on their recent 'Services to the Community' award from the 2010 Australia and New Zealand Insurance and Finance Industry Awards.

Launch into Inner Space

Long time supporter and leading NZ Fashion Designer, Petrena Miller, has created some unique fashion garments for a new range called "Inner Space". These tops are available for sale through retailers in NZ and Australia with a percentage of sales donated to the Malaghan Institute. First revealed on the catwalk during the Auckland Friends' fundraiser, these garments display an image of a dendritic cell that has been turned into something very funky and fashionable. They make great gifts for yourself or for others (there is even a T-Shirt for the guys!). Visit www.malaghan.org.nz/inner_space/ to find your nearest retailer.



'Inner Space' garments from Petrena Miller Designs – modelled at Malaghan fashion fundraiser.

Recent grants

We are thrilled with the response we have received between July and September 2010. Thanks to these organisations for their great support:

Infinity Foundation Ltd

Clyde Graham Charitable Trust

HB Williams Turanga Trust

The Southern Trust

Up-coming events

STOP PRESS! The Malaghan Institute will be involved with Wellington's Inaugural Cancer Symposium in February 2011, which will feature top cancer clinicians from the world-renowned Mayo Clinic in Rochester, Minnesota, USA. To find out more, visit www.malaghan.org.nz.

2010 MALAGHAN CHARITY GOLF TOURNAMENT REMINDER... Hawkes Bay (Friday 29th October), Wellington & Auckland (Friday 12th November). For further details, please contact Vicky Hale on 04 499 6914 x821 or vhale@malaghan.org.nz.