

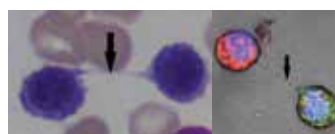
Professor Mike Berridge and Dr Rob Weinkove

Mitochondria discovery prompts bone marrow investigation

The world-first discovery earlier this year of mitochondrial transfer to tumour cells has created a wave of local and international follow-up. The phrase "research begets research" has never been more apt as a team at the Malaghan Institute begin investigations into mitochondrial movement between cells following bone marrow transplantation.

Professor Mike Berridge is naturally excited, "Our earlier work demonstrated transfer of genes from healthy cells to cancer cells without mitochondrial DNA. Cancer cells with damaged mitochondria acquire replacements from surrounding healthy cells, restoring respiration and tumour forming ability. In lay person's terms the tumour cells got back their energy generators. Using fluorescent probes and mitochondrial DNA sequencing we saw replacement mitochondria essential for respiration tracking between cells through membrane nanotubes. The possibilities for research are enormous. We are now trying to understand how to stop transfer of these "energy-producing engines" to cancer cells with mitochondrial DNA damage caused by radiation or drug treatment. We are

also interested in promoting mitochondrial movement to cells that are fatigued, damaged or dying. What Rob (Dr Robert Weinkove, part-time Malaghan researcher and haematologist at Wellington Hospital) and I will look at is the triggers that drive this process. We need to understand the basics as a foundation for future work." Mike explains further, "There is existing evidence of cytoplasmic bridges, resembling membrane nanotubes, joining cells that form red blood cells. These bridges look remarkably like the nanotubes we see with tumour cells. They may be involved in optimising haemoglobin production in red cells which carry oxygen for respiration. But there is so much to be learned. For example, we don't yet know whether damage resulting from radiation or chemotherapy in patients with leukaemia is a trigger for mitochondria movement, or if it occurs naturally."



Left: Cytoplasmic bridge
Right: Nanotube

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From the Director



To raise new questions, new possibilities, to regard old problems from a new angle, requires creative imagination and marks real advance in science," Albert Einstein once said.

I want to share our excitement regarding new possibilities in brain research, bone marrow transfer, and links between our gut microbiota and our response to vaccinations. They share a common theme of new angles and creativity.

In the last issue we focused on cancer immunotherapy and Professor Mike Berridge's world first discovery in cellular biology. Breakthroughs like this illustrate how real advances immediately open up potential for further discovery.

We also say goodbye to two French scientists who have both brought originality and inspiration to their research into parasitology and bioinformatics. Their departure is more au revoir rather than goodbye as collaboration continues. Time at the Malaghan Institute typically creates a bond of loyalty.

Loyal support continues to expand with close to half a million people watching Campbell Live on cancer immunotherapy, and a lecture by Dr Elizabeth Forbes-Blom being moved to a larger Auckland University lecture theatre, because demand outstripped the seating. I could not be more optimistic given the breadth and depth of our research, backed by your extraordinary support. I thank you all.

Professor Graham Le Gros

Mitochondria and the brain



Dr Melanie McConnell

Dr Melanie McConnell, long-time collaborator, now at Victoria University, will dedicate the next three years to study mitochondrial transfer in brain cells. She was recently awarded over a million dollars by the Health Research Council of New Zealand to fund her project.

Since the publication of the Malaghan Institute and Griffiths University's discovery in January, demonstrating mitochondrial DNA can shuttle between the cells in animals; the research community has become excited about potential implications for the treatment of disease.

Melanie explains two opposing concepts which have implications for neurodegenerative diseases and cancers, "In the case of cancers if we could find a way to stop the

transfer of material into a tumour cell; effectively starving them of the ability to generate energy, it would be a huge breakthrough. Alternatively, in the case of neurodegenerative diseases; conditions which affect the neurons in the brain such as Alzheimer's, Parkinson's and motor neurone disease, the prospect of finding out if we can revive injured cells would be similarly ground-breaking."

Mitochondria are often referred to as the powerhouses of the cells; they make energy. Mitochondria are responsible for creating more than 90 percent of the energy needed by the body to sustain life and support growth. When they fail, less and less energy is generated within the cell. Cell injury and even cell death follow.

Does your gut health influence how well you respond to the flu vaccine?

The role of our gut microbiome and our health is a relatively new frontier for immunology. How these trillions of gut bacteria develop, and their interaction with our immune system is the daily work of Dr Elizabeth (Liz) Forbes-Blom's team at the Malaghan institute. While the research spans several areas, a link between our gut microbiome and how well we respond to influenza vaccination is the latest subject of investigation.

Liz explains, "When we receive a flu vaccination, our bodies react to a dead or deactivated flu strain by creating protective antibodies. Ideally, we build up a memory of a disease we haven't experienced, so if or when we encounter it our bodies know exactly how to fight it. Recent cutting-edge investigations now link gut microbiota to the development of vaccine-induced protective immunity. People with a less diverse gut microbiome tend to not respond as well to vaccination, and ironically that can be the people most vulnerable to illness; the very young and the very old."

General health, nutrition, stress and the use of antibiotics are all known to play a role in the health of our gut microbiome, and in turn the health of our immune responses. Exactly what supports or limits vaccine efficacy and duration is unclear, but establishing cellular interactions in or between the microbiota in our gut and immune cells may form part of the puzzle.

Liz and the team hope to carry out a feasibility study with humans in the future.

The National Institute of Health Human Microbiome Project was established in 2008. The Human Microbiome, a group of non-human cells within our bodies, is referred to as the human microbiome. An ever-growing number of studies have demonstrated that changes in the composition of our microbiomes correlate with numerous disease states, raising the possibility that manipulation of these communities could be used to treat disease. Human Microbiome Project Consortium, *Nature*, 486 (2012), pp. 215-221

Latest research on peanuts reverses approach

Results from the LEAP study, Learning Early About Peanuts, published earlier this year have now been endorsed by several international immunology organisations, including the Australasian Society of Clinical Immunology and Allergy. Their consensus statement effectively reverses guidelines which, for the last 15 years, have advised parents away from introducing peanut products to infants, and in many cases delaying or avoiding introducing this protein source completely. Instead, the new research

provides evidence the early introduction of peanuts offers protection from the development of peanut allergies says Gut Immunology team leader Dr Elizabeth (Liz) Forbes-Blom.

"Research of this size, involving 600 children over a five year period, is a defining moment," she says, "At age five the children who had been given peanut-containing foods as infants were much less likely to have developed a peanut allergy than those who had been avoiding peanuts."

There may have been good intention in the original advice in 2000 from the American Academy of Pediatrics, Committee on Nutrition, but this evidence, if adopted into New Zealand guidelines, could slow the rate of hyper-allergic children we are seeing; the so-called Generation Allergy.

While the consensus statement is not a cure or new approach for those with an existing peanut allergy, prevention remains our best hope to reduce peanut allergy in children.

Over 600 children between 4 and 11 months of age at high risk for peanut allergy were randomly assigned to either regularly consume a food containing peanut protein, or avoid peanuts until age 5. The participants who consumed peanut protein were far less likely to be allergic to peanuts at the age of 5. Of the children in the nonallergic group, only 1.9 percent of those fed peanuts had developed an allergy by the end of the study, compared with 13.7 percent of the children in the group avoiding peanuts. The numbers represent an 86 percent relative reduction in the prevalence of peanut allergy. You can read more at: <http://www.leapstudy.com>



3-D printing

New possibilities for sourcing laboratory equipment and replacement parts are becoming possible due to the generosity of The Pelorus Trust whose generosity enabled the purchase of a 3-D printer.

Bioinformatician Dr David Eccles, who can usually be found analysing biological data or unravelling a DNA sequence, has added another string to his bow and is now printing laboratory disposables on a 3-D printer. This new innovation saves money and time as an incubator latch set can cost \$200, but can be printed for 70 cents.

International news reports illustrate

the power and application of this new technology; ranging from new limbs for victims of war, houses in remote villages in China, and even spare parts on orbiting space stations. While the Malaghan Institute is starting modestly our approach is careful and economically prudent.

David says, "Most labs in the Institute have incubators where



Dr David Eccles

scientists keep cultured material. Incubator latches are essential for temperature regulation, but they fatigue and break regularly. The cost of a \$200 latch set once or twice a year mounts up, but we can print our own custom design in an hour or so, for 70 cents. There is no paperwork or shipping delays; it serves the same purpose, but it's all onsite."

Au revoir to Tiffany and Alex

Many talented scientists come to work for a few years at the Malaghan Institute, and all are missed after they leave but we are doubly sorry to see Drs Tiffany Bouchery-Smith and Alexander Smith, a couple of post-doctoral research fellows from France, who have left after three years.

Tiffany will be joining the prestigious Ecole Polytechnique Federale de Lausanne where she will continue investigating how the immune system can cope with hookworm infection in the lungs, and Alex will start working as a bioinformatics research fellow at the Universite de Lausanne, where he will try and decode how DNA previously thought to be "junk" DNA actually supports a whole new layer of gene regulation.

Professor Graham Le Gros praises Tiffany's perseverance and determination to rid the world of

hookworm that, in April, led to the publication of their research in Nature Communications. Jointly, they hope to publish subsequent research which will bring the international community closer to breaking the lifecycle of the parasite. Hookworm causes misery to one billion of the world's poorest people and employing the immune system to fight it is the best prospect when whole populations are becoming resistant to oral drug therapies, and reinfection remains continual.

Professor Franca Ronchese acknowledges Alex's contribution



Dr Tiffany Bouchery-Smith and Dr Alexander Smith

to the Malaghan Institute, "Alex's understanding and capability in the field of bioinformatics and statistics has enabled us to make a solid start in our transcriptomics work. As we delve further and further into the workings of the immune system using increasingly high-throughput technologies, ever large amounts of data are generated, and using computers and statistical methodology to sift through it all becomes a necessity. Alex will be sorely missed."



ANZ Private Wellington research update

Our thanks to Peter Price, Regional Manager Central of ANZ Private, guests and supporters, who made this latest update of Malaghan Institute research such a success.

More businesses join our Lab Partners programme

The Lab Partner programme is a unique way for businesses to support ground-breaking research into diseases that affect us all.

Thermo Fisher Scientific, who supply us with lab equipment, Nichecom who have made donations to us since 2003, and CQ Hotels, who have a culture of community involvement since their inception in 1907, are the latest organisations demonstrating their support for us. We thank them and our other Lab Partners, Kinetics

Group, Just Paterson Real Estate and Dave Clark Design.

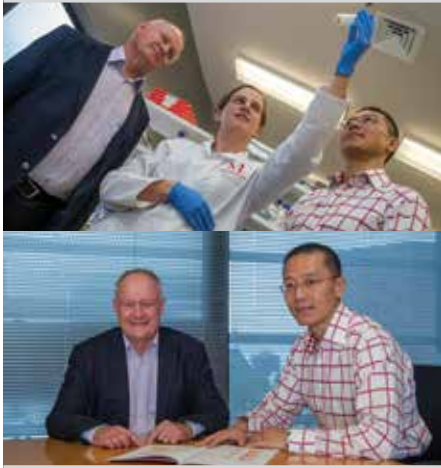
If you know of a business that would like to support our scientists, or if you want to know more about the partnership please contact:
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News under the microscope



Health Research Council Finance Manager visits

Grant Barrett recently visited with the Malaghan Institute Finance Manager David Lin. They spent time discussing finance but also took time to tour our facilities. In the top photo Senior Research Officer Evelyn Hyde demonstrates her work.

The Hawkes Bay Club

The Hawkes Bay Club recently held a Winter Game Dinner where Chairman of the Malaghan Institute, Graham Malaghan, was the guest speaker. The evening raised nearly \$15,000 to support our research. We are grateful for the enthusiasm and committed ongoing support by the Hawkes Bay Community.

Recent grants

Jennifer Smith Family Trust, Infinity Foundation, Brotherhood Bikers NZ, Independent Order of Oddfellows Inc.

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