SCOPE 56
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Dr Robert Weinkove

Promising results for combination therapy for acute leukaemia

Acute leukaemias are among the most aggressive cancers – the number of leukaemia cells can double as quickly as every 24 hours. Leukaemias usually respond well to chemotherapy initially, but the risk of relapse is high.

Thanks to your support, the Malaghan Institute's early research into a vaccine treatment for acute leukaemia is promising. PhD student John Gibbins, now based in the Netherlands, collaborated with Dr Robert Weinkove on a new approach.

Robert, who spends part of his time treating patients as a Haematologist at Wellington Hospital and part working with Professor Ian Hermans' Vaccine Therapy Programme explains, "The problem with many cancers, including leukaemia, is that the chemotherapy doesn't get rid of every single malignant cell. When you are in remission, even if we cannot detect any disease, there may still be a few leukaemia cells within the body that could grow again and cause the leukaemia to relapse and often it is more resistant to chemotherapy when it comes back."

"We often try to prevent higher-risk leukaemias from recurring by doing a bone marrow transplant, but that in itself presents huge challenges; it carries very high risks of infection and other complications, and sadly is not an option for all patients because they have other illnesses, or because a suitable donor cannot be found."

Bone marrow transplantation describes the process of taking bone marrow stem cells from a healthy donor and infusing them into a patient after chemotherapy. This way, the patient's entire blood and immune system (including red blood cells, white blood cells and platelets) is replaced with that from a healthy donor.

Working with a model of acute leukaemia, the group found that a vaccine, made up of dead leukaemia cells treated with an immune-stimulating compound, was able to prevent relapse. The group's research was recently published by 'Blood', the American Society of Hematology's journal and the most cited peer-reviewed publication in its field.

"It suggests that there is a window after chemotherapy when we could administer a vaccine to help the patient kill off remaining leukaemia cells. While it's early days, the results in our models are encouraging."

The Vaccine Therapy Programme is now working to refine their vaccine by developing and testing synthetic versions that would be simpler to produce and deliver to patients.

OUR RESEARCH
Vaccine therapy for cancer

OUR PEOPLE
World first discovery

YOUR SUPPORT
You help us make a difference

From the Director

Welcome to our first Scope for 2015. There have been many exciting developments since the journal *Science* announced, in 2013, Cancer Immunotherapy as breakthrough of the year.

A new generation of cancer drugs called the 'checkpoint inhibitors', which effectively take the brakes off the immune system, have gained approval. While they are very expensive, they have opened new doors, but because cancer can be so adaptable no one drug and no one immunotherapy approach will beat this elusive family of over 200 diseases and we need further research.

The Malaghan Institute's research programmes are nimble; we take advantage of international breakthroughs and incorporate their knowledge, but we have also had a few unique twists of our own.

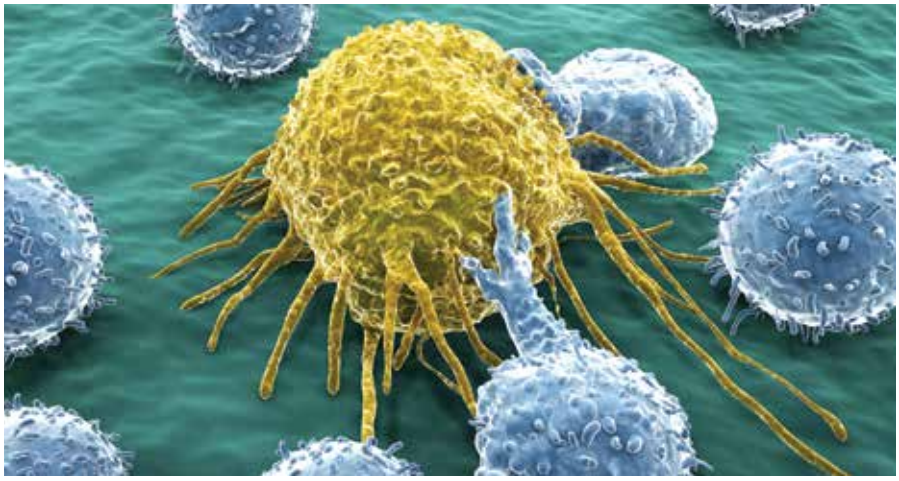
In this issue of Scope I would like to share updates from Professor Mike Berridge's recent breakthrough in cancer cell biology, to our current vaccine research, right through to how we are anticipating which future clinical trials will deliver the best results for New Zealanders facing a cancer diagnosis.

The Malaghan Institute is capable of producing the same breakthroughs as our peers internationally. We can, and will deliver treatments based on our research with your continuing support, for which we are always grateful.

Graham Le Gros

Professor Graham Le Gros

Vaccine therapy for Cancers



T cell attacking cancer

The components of the immune system have been identified step-by-step during the 20th century, which has enabled research into how we can employ it to battle cancer to expand in parallel.

Ralph Steinman's discovery of Dendritic Cells, DCs, in 1973 turned the spotlight on these rare white blood cells of the immune system. Making up less than 1% of our white blood cells, the DC's role is to interact and sample the cellular environment 'looking for trouble'. If they detect foreign bacteria or a virus the normally unexcitable cells become highly excited. They grow in size, enter the lymphatic system, travel to the lymph nodes and 'wake' up an immune response – the B and T cells. DCs are removed from blood transfusions because of this very quality. A DC from donated blood would automatically set off an unwanted response in the recipient, but in our own bodies they are less like to notice something amiss; cells going haywire, or cancer.

Researchers found they could 'educate' a DC in a test tube to notice a tumour cell and the path to an educative or therapeutic vaccine for cancer was born. There are several drawbacks to the first generation of cancer vaccines though. Firstly, the bespoke nature of the process means each vaccine is individually prepared and the relative rarity of the DCs means once the 'educated' DCs are returned to the patient the provoked immune response may not be strong enough alone to battle the cancer.

International investigations simultaneously turned to a complementary avenue; understanding why and what holds back a greater immune response. Turning off the molecules on the outside of T cells that keep our immune system in check, and prevent us attacking ourselves has led to 'checkpoint inhibitors' adding to the arsenal of cancer treatments.

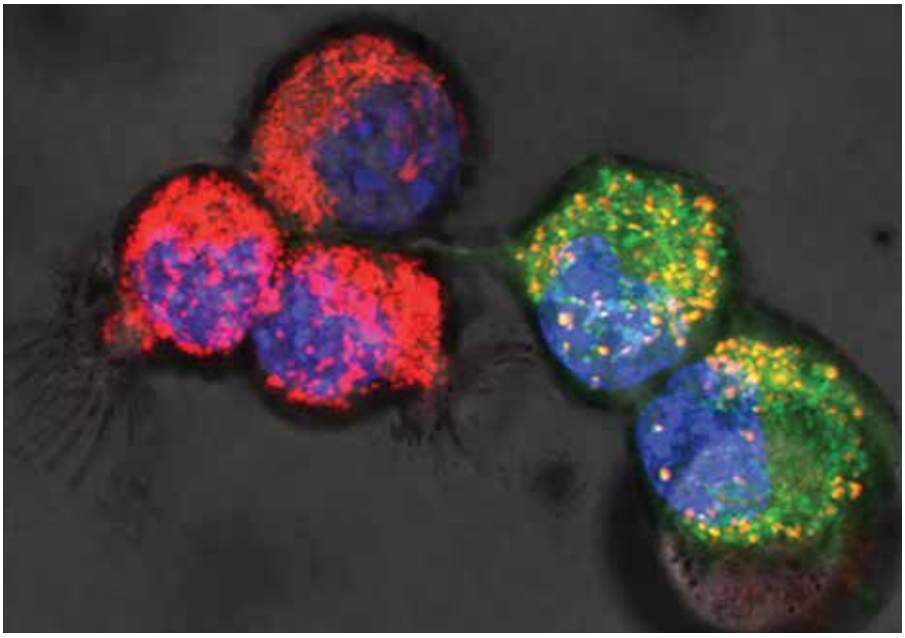
The Malaghan Institute employs these newer immunotherapy treatments in research programmes while investigating second generation vaccine possibilities; synthetic preparations which need not be made individually and can be given to anyone with a particular cancer. An adjuvant is sometimes administered with the vaccine. Our original adjuvant, alpha-galactosylceramide, derived from a marine sponge, is being trialled with a vaccine in patients with melanoma. This clinical trial began in July 2013 with forty-six melanoma patients, and while ethical guidelines prevent any discussion of progress, international and local discoveries will inform subsequent trials.

World first discovery

In the first week of January the Malaghan Institute's website attracted over 30,000 new visitors – mostly from overseas – as news of a cell biology breakthrough spread around the world. Cancer Cell Biology Group Leader Mike Berridge and his team, working on breast and melanoma cancer models, discovered that DNA moves from surrounding normal cells to tumour cells with defective mitochondrial DNA.

Senior Research Officer Carole Grasso's beautiful images highlighting the transfer of fluorescent mitochondria across nanotube membrane connections between cells have been reproduced internationally.

This research opens new possibilities for controlling tumour growth and spread throughout the body. The research could lead to new approaches to treat cancer; to encourage mitochondrial transfer to tumour cells with damaged mitochondrial DNA, and to encourage mitochondrial respiration which discourages tumour growth. Like many discoveries scientists make while investigating one disease, there are implications for another; it may be that this new understanding also offers future treatments for neuromuscular and neurodegenerative diseases involving the sensory organs, and even ageing.



Intercellular mitochondrial transfer

Mike has just visited his co-leader Professor Jiri Neuzil of Griffith University in Queensland and says their publication has opened several new opportunities for collaboration with scientists at the Pasteur Institute in Paris, Virginia Commonwealth University in the USA, the Garvan Institute in Sydney and with others closer to home.

THE BAD LUCK OF CANCER

During January and February an element of confusion crept into media reports; do we really have any say over whether we get cancer or is it just bad luck?

A paper in the journal Science, entitled 'Variation in cancer risk among tissues can be explained by the number of stem cell divisions' ran more frequently under the heading 'Bad Luck Cancer.' It created the impression that two-thirds of the incidence of various types of cancer could be blamed on random mutations and not 'unhealthy' living or heredity. Commentary in response to its publication ranged from the irresponsible; there's no point in looking after your health, to detailed questioning of the methodology and treatment of different cancers.

Professor Mike Berridge was one of the many international researchers in the latter group who clarified the research approach.

"They investigated only 31 of the 200 or more cancers that afflict humans; they divided some, like lung cancer into subgroups of smokers and non-smokers, whereas for melanoma they did not when there is a natural separation between the subgroups aligned to UV exposure. Additionally, for melanoma, the stem cell link itself is contentious, and not all cancers originate from the same stem cells. To complicate matters more they excluded the two highly prevalent cancers; cancer of the breast and prostate."

In short, Mike Berridge says correlations are not proof of causation, but the paper may provide useful information for further study. Meantime, early detection and keeping up your positive life choices remain vitally important in the fight against most diseases including cancer.

New approaches to breast cancer


Connie Gilfillan

Cancer research at the Malaghan Institute operates on several fronts with many intersecting approaches seeking breakthroughs and moving us closer to new treatments or cures thanks to the committed support we receive.

PhD student Connie Gilfillan is investigating Doxorubicin - a chemotherapy which has been used in the treatment of breast cancer for over 30 years - and investigating the role of dendritic cells in tumours.

"In 1984 Doxorubicin was approved, and while it's an effective treatment, it shares the fate of many cancer drugs; tumours become resistant to them. I wanted to find out whether the treatment leaves carcinoma cells more immune suppressive after 'chemo', or less able to respond to the immune system."

Immunotherapy hopes to unlock the body's own fight against cancer; but because cancer cells have incredible dexterity in eluding or hiding from the immune system, they are usually not detected and destroyed. If they are even less likely to be targeted after 'chemo' we need to find out additional ways to wake up the immune system.

"Dendritic cells, DCs, are the communicators of the immune system. They are a kind of first alert cell which notices something amiss and then travels back to the lymph nodes to get specialist cells to help. There are many ways that I am testing and probing their role. For example if I take them out of the system completely what happens? Or, if a tumour is immune suppressant does the presence of DCs make things better or worse?" says Connie. "While there is genuine excitement about what we are learning about the various immune cells, there are easily over a hundred to investigate and every small thing discovered adds to the big picture. I look at it like a family tree; the B cells, the T cells and DCs are at the head of the family but they have a whole family of cells under each, branching out in complexity. I am only looking at one cell and that may occupy me for three years! It is an amazing area of research and the Malaghan Institute is an incredibly stimulating place to be."

Connie is one and a half years into her PhD under supervisors Professor Franca Ronchese, Dr Melanie McConnell (VUW), and Professor Brett Delahunt (Otago).

Ride For Life

Louise Curtis has spent a great deal of her professional life inspiring people to keep fit and cherish their ability to enjoy physical recreation regardless of their age or abilities. She combines motherhood of two (teenage daughters) with part-time work as a Group Fitness Instructor at Kilbirnie pool, and a Green Prescription Support Person at Sport Wellington.

Her own diagnosis of an aggressive brain tumour has not stopped her professional inspiration for others; rather it has magnified it a thousand fold over the last two years as she says of her cancer, "I'm not having it," and sets off for another cycle ride.

She says the cycling helps with the stress and the pain but it is also a powerful symbol to her friends, her family, her supporters, and her participants and patients, that each day is a gift and she will use her own actions to raise the profile for cancer research and support.

"I read everything about cancer research from The Malaghan Institute and I feel I'm part of a larger team – of cancer fighters and cancer researchers. It's my greatest hope that fewer and fewer people will have direct experience of cancer, or that it will become easily treatable. And I know the staff at the Malaghan feel the same way."


Louise Curtis

Last year she rode thousands of miles to raise money for the Malaghan Institute and the Cancer Society, and 2015 is no different. She has just completed the Bike the Lake 43km around Lake Rotorua, on Feb 22nd, and has the 117km Bush Cycle Tour, and the 100km Taupo-Rotorua Flyer in her sights for March and April.

Run for Research 2015

Thank you to everyone who Ran for Research at the Wellington and Auckland Round the Bays in February and March.

The Malaghan Institute is very lucky to have amazing community support each year at events all around New Zealand. This year for the first time we not only had supporters Run for Research at the Wellington Round the Bays in February, but the Auckland equivalent in March. We also welcomed teams from Trade Me, MetService and One Post Office Square.

In another Run for Research first, to support our fundraising we auctioned off six unique prizes on Trade Me donated by the Hurricanes, Park Road Post Production, the New Zealand Symphony Orchestra, Jason Pine and the Wellington Phoenix, Lexus of Wellington and Ormlie Lodge.

People of all ages, from all walks of life, and all fitness levels took part, united by their motivation to join our scientists on the journey to find better treatments and cures for diseases that affect our friends, family and community. We thank everyone who was involved for all their training and fundraising efforts; through sharing their page and asking for donations, bidding on Trade Me prizes, hosting bake sales, quiz nights at work, and spreading the word about the vital work we do at the Malaghan Institute and why they choose to support us. And thank you to everyone that donated to their amazing friends, family and colleagues!

If you wish to fundraise for the Malaghan Institute, whether it is a running race, or any sporting event, please contact Niall Mackay: nmackay@malaghan.org.nz

Our Congratulations to Trustee Bryan Johnson (ONZM)

We are very proud to report that our Trustee and Deputy Chair, Bryan Johnson, was honoured in the New Year's Honours List becoming an Officer of the New Zealand Order of Merit (ONZM) for his services to business and philanthropy. As all who know Bryan will attest, his enthusiasm and energy have become an important part of the Malaghan Institute's makeup and purpose.

Malaghan Institute Charity Golf Tournaments

We are very pleased to announce the dates for the Annual Charity Golf Tournaments for 2015:

- Hawkes Bay – Friday 30th October at Hastings GC
- Auckland – Monday 2nd November at Remuera GC
- Wellington – Friday 13th November at Manor Park Golf Sanctuary

2015 signals the 18th year that our wonderful Friends of the Malaghan Institute have hosted these events and resulted in $1.6 million being raised to support our research. We would love to have you come on board for 2015 and become one of our Golf Partners.

For more information on how to swing in behind the Malaghan Institute please contact:

Jenny Sim jsim@malaghan.org.nz
or (04) 499 6914 ext 811

News under the microscope

Recent Grants (Jul 2014 – Feb 2015)

We would like to acknowledge the following Trusts and Foundations for their recent support: Arthur N Button Charitable Trust, Carol Tse (No.2) Family Trust, The Dr Marjorie Barclay Charitable Trust, EM Pharazyn Charitable Trust, FH Muter Charitable Trust, The Great NZ Trek Charitable Trust, The Herbert Teagle Masonic Perpetual Trust, Humphry Bayly Charitable Trust, Infinity Foundation, Jennifer Smith Family Trust, Leonard Monk Charitable Trust, Margaret Neave Charitable Trust, Margaret Russell Charitable Trust, The Nikau Foundation, The Nick Lingard Foundation, The Paddy Brow Charitable Trust, Pelorus Trust, The Southern Trust.

Nikau Foundation Scholarship

Malaghan Institute PhD Student Karmella Naidoo is the recent recipient of a Nikau Foundation Scholarship worth $20,000, supporting her research into the debilitating disease Eczema. The funds were made possible by the Nikau Foundation, on behalf of the Richard and Doreen Evans Charitable Trust.

Lab Partner Programme Launch for SME's

Small to medium enterprises looking to support the Malaghan Institute can now become a Lab Partner. Our new sponsorship programme launched in March this year with Dave Clark Design and Just Paterson Real Estate. A New Zealand Business Council for Sustainable Development report in 2010 found most NZ businesses feel social responsibility is 'the right thing to do'. Three years later a BNZ survey showed most businesses thought they should support their local communities, but most did little to publicise any community involvement.
At the same time as supporting ground-breaking research into cancer, asthma and allergies, Lab Partners will receive several benefits to help them promote their support to customers, clients, staff and the community.

MALAGHAN INSTITUTE OF MEDICAL RESEARCH LAB PARTNER 2015

If you have a business or know someone who would like to become a Lab Partner, contact Niall Mackay nmackay@malaghan.org.nz or (04) 499 6914, ext 821.

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Please return to PO Box 7060, Wellington, 6242

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Please call to inform us of your donation so we can send your tax receipt. Donations over $5 are eligible for a tax refund of up to 33%.

Or call **0800 MALAGHAN** (0800 625 244) to make a donation over the phone