

MALAGHAN INSTITUTE OF MEDICAL RESEARCH

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Stem cells are the "master" cells that give birth to each of the specialised cells within our bodies during organ and tissue development The specialised cells might be neurons, immune cells or in some situations, cancer. Embryonic stem Cancer Cells under attack cell research has



received a lot of media attention in recent years. It shows great promise for the treatment of spinal cord injuries or neurological disorders such as Parkinson's disease, however intense controversy surrounds the fact that the cells used in these studies are isolated from human embryos. Prof. Berridge's cancer stem cell research does not use embryonic tissue, but instead relies on models of the cancer stem cell that have properties almost identical to those of tumours.

Prof. Berridge's group has developed a novel technique for screening potential anticancer drugs that block a vital life support system used by cancer stem cells. The target is at the outer surface of the cell in contrast to the vast majority of anticancer drugs that act inside the cell to block cogs in the machinery of the cell division cycle. By taking advantage of the huge biodiversity of New Zealand's marine and terrestrial organisms, Prof. Berridge's group has identified several different groups of compounds that interfere with the cell surface life support mechanism and halt tumour growth in mice. Selected



compounds will now be modified to target them specifically to the outer surface of the cell to enhance their anticancer activity and minimise potential side effects

Collaborating with Prof. Berridge on this project is Dr Melanie McConnell, a recent arrival to the Malaghan Institute from the Mount Sinai School of Medicine, New York, USA. Supported by a Roy McKenzie Fellowship, Dr McConnell will examine the relationship between the life support system used by cancer stem cells and gene expression. Dr McConnell will also use her experience in clinical trial support to assist in the phase III melanoma vaccine trial being undertaken at the Malaghan Institute in conjunction with the Queensland Institute of Medical Research.



Dr. Melanie McConnell

Targeting the cells responsible for perpetuating the cancer, rather than simply focusing on reducing tumour mass, is a revolutionary concept that promises more effective cancer treatments and possible cancer cure.

Turning an obstacle into an opportunity

As often happens in science, a stumbling block in one area of research can present a solution for another. This is certainly the case for two of the Malaghan Institute's star researchers, Professor Franca Ronchese and Professor Graham Le Gros, whose combined insight and creative thinking has turned a potential bottleneck in cancer immunotherapy into a new way of looking at treatment opportunities for diseases such as allergy or asthma.

While attempting to improve the effectiveness of a dendritic cell cancer vaccine, Professor Ronchese discovered that under certain conditions specialised cells (called CD8+ cytotoxic T lymphocytes (CTL)) were killing off the dendritic cells before they could do their job. Although this presented somewhat of a problem to the longterm usefulness of the cancer vaccine, it raised the possibility that dendritic cell killing could be used to an advantage in other ways.

Dendritic cells guide the development and direction of an immune response and act as 'scouts' by identifying infection or disease. For reasons that are not completely understood, in some situations they instruct the immune system to stimulate inappropriate allergic or inflammatory

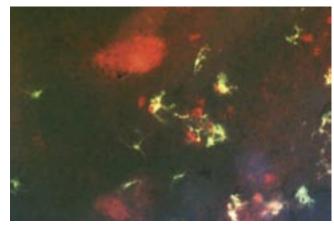
HRC funding success for Malaghan scientists

Three Malaghan Institute research projects received grants in this years round of Health Research Council of New Zealand (HRC) funding. The first of these is the Immunity and Immunemediated Diseases programme, which lies at the core of the Institute's research activities and focuses on the discovery of the basic immunological processes that operate during cancer, asthma and tuberculosis, with the goal of developing effective immunotherapies for the treatment of these diseases. Grants were also



responses, which can lead to diseases such as asthma or arthritis respectively.

In research that has recently received funding from the hotly contested Marsden Fund of New Zealand, Professor Ronchese and Professor Le Gros will investigate the basic biology of the regulatory mechanisms that control the immune response, and determine whether it is possible to change the "flavour" of immune responses by manipulating dendritic cell survival. If successful, this project will offer exciting new opportunities for the treatment of immune-mediated diseases.



(Red) CTL Cells killing Dendritic Cells (Green)

awarded to the Multiple Sclerosis and Vaccine Research groups to further their research into alternative treatments for autoimmune disorders and cancer respectively. "HRC funding recognises the value and contribution of the Malaghan Institute to the health research scene of New Zealand," Professor Le Gros, Director of the Malaghan Institute, said. "Only through innovative medical research can we deal effectively with the massive human health problems of today"

Young scientist recognised

In the last issue of Scope we overviewed the Infectious Diseases Group's research into identifying better ways to protect future generations of New Zealanders from Tuberculosis (Tb). It is with great pleasure that we now announce that one of the talented young PhD students within this group, Ms Kylie Quinn, was awarded joint runner-up in the Advancing Human Health category of this years MacDiarmid Young Scientist of the Year Awards. These awards are named after New Zealand-born Nobel laureate Professor Alan MacDiarmid. and are given in recognition of excellence in research, science and technology.

In her award-winning poster, entitled 'Tb's partner in crime: How Tuberculosis hijacks our cells to hide', Kylie describes how the bacteria that cause Tuberculosis may escape destruction by the immune system by hijacking the cells responsible for shutting down an immune response.

This award is a fantastic achievement and acknowledges the great progress

Kylie has made into unravelling the mechanisms used by Tuberculosis to evade the immune response. With a recent outbreak of Tuberculosis in the Central North Island, it is a comfort to know that scientists at the Malaghan Institute are part of a worldwide effort to develop a more effective vaccine against this debilitating disease.



Kylie is presented her award by the Minister of Research, Science & Technology, Hon Steve Maharey and Graeme Fraser, Chair of the Health Research Council of New Zealand.

The Ultimate Gift

The ultimate gift to show your support for the research of the Malaghan Institute, and our hopes for a disease free future, is a bequest in your will.

As a charity, the Malaghan Institute relies on the generosity of its supporters to continue our work, and a gift in your will is a way of ensuring our research into Cancer, Asthma, Arthritis, Multiple Sclerosis and Infectious Diseases will protect future generations from disease well beyond your lifetime.

To receive information about leaving a gift in your will and how these funds are managed, please tick the box below and enter your contact details on the reverse of this form.

> Yes, please send me information on how I can leave a gift in my will and invest in a disease-free future



From bench to bedside:

A behind the scenes look at the Melanoma Vaccine Trial

Have you ever wondered how a tumour biopsy is used to make a cancer vaccine? Or how the vaccine works? For many the concept of being able to teach a patient's own cells to seek out and destroy a tumour is more magic than medicine, so in this issue of scope we thought we would give you a behind the scenes look at this revolutionary approach to cancer treatment.

The Clinical Trials Project Manager responsible for vaccine preparation at the Malaghan Institute is Ms Julie Walton, under the supervision of Dr lan Hermans. On receiving a patient's tumour biopsy from the Wellington Cancer Centre, Julie's first task is to evaluate whether or not there are sufficient useable cells in the sample for preparing a vaccine. If there are, the tumour cells are killed so that they cannot cause further cancer when injected back into the patient. These killed tumour cells are then 'fed' to dendritic cells grown from the patient's own blood, which digest the tumour into tiny pieces that can be recognised by the immune system. The product of this is a vaccine which is then injected back into the patient, where the dendritic cells present the tumour pieces to the patient's T cells (which are released by the immune system to fight disease) and

instructs them to hunt out and destroy the tumour. Each patient receives 13 vaccinations in total to ensure that the immune system is fully informed about the task it has to perform.

The process of turning a patient's samples into a vaccine takes about 10 days, many of which involve working in the laboratory uninterrupted for 10-12 hours at a time. When Julie isn't in the laboratory she is kept very busy with the paperwork associated with running a Good Manufacturing Practice (GMP) facility, for which we received official accreditation from Medsafe in July this year. The Malaghan Institute would like to acknowledge Julie's unrelenting dedication and ongoing contribution to our successful involvement in this trial.



From Left: Julie Walton, Catherine Wood (Nurse) and Dr. Ian Hermans in the recently accredited GMP facility at the Institute

This newsletter was generously supported by:



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Friends of the Malaghan Institute

Once again, the Friends of the Malaghan Institute have put together some fantastic events in their local areas that have been enjoyed by many and contributed greatly to our fundraising efforts.

The Hawkes Bay Committee celebrated some of their best local produce in a Wine and Olive Oil Presentation in June. Held at the gorgeous Sileni Estates Winery, guests were treated to tastings of Sileni Estates and Ngatarawa Wines finest, which complimented the Olive Oils of The Village Press perfectly. The evening was capped off with a wonderfully prepared meal which showcased not only the quality of produce available in the Bay, but also the talent of the staff at Sileni.

Thank you to the Hawkes Bay Committee for a spectacular night and to the sponsors: Sileni Estates, Ngatarawa Wines and The Village Press.

Please look on our website for details on how you may purchase beautiful wines and olive oil from Sileni Estates and The Village Press. A portion of the profits from each bottle sold will help fund our research into Cancer Stem Cells.

www.malaghan.org.nz

It was all 'bobby socks' and 'stiff skirts' for Aucklanders attending the 'Rebel With a Cause' 50's Bash in July. The Auckland Friends Committee hosted a great night of fun and nostalgia, dancing the night away to music from the 50's. Thank you to the committee for their efforts and to all those who attended the 'dance to end all dances', there will be many already looking forward to the next one!

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Issue 33, 2006

Up-Coming Events

October 14th Doctors & Nurses Bash (Auckland) October 27th Hawkes Bay Malaghan Golf Tournament

November 3rd AMI Insurance Malaghan Golf Tournament (Auckland) November 13th ING Malaghan Golf Tournament (Wellington)

January 20th-22nd Waikanae Lions Garden Trail (Kapiti Coast)

February 19th-23rd Malaghan Institute Lollipop Appeal

For information about any of these events please look on our website: www.malaghan.org.nz or call 04 499 6914 ext 852

Grants received in 2006

We would like to thank the following supporters for their generosity which has enabled us to purchase vital equipment this year:

The Trusts Charitable Foundation

- The Meller Trust
- HB Williams Turanga Trust
- The Lion Foundation
- AMI Insurance
- Ryman Healthcare



Targeting cancer at its source

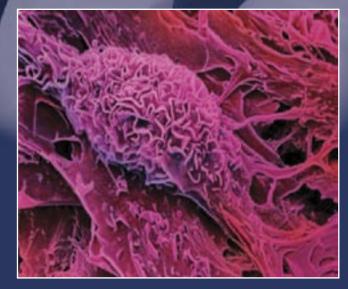
Cancer is a disease that has afflicted people throughout recorded history. It is responsible for nearly a third of the deaths in New Zealand and has had a devastating impact, both personally and financially, on individuals, families and nations worldwide.

Over the last 50 years the focus of most anticancer drug development has been on rapidly dividing cancer cells. However, remissions are often transient, drug resistance a major problem and drug withdrawal can result in an aggressive return of the cancer. This is because the cancer stem cell that gives rise to the disease is unaffected by treatments that kill rapidly dividing cells.

"The irony is that cancer can now be considered a disease of non-dividing cancer stem cells, rather than of rapidly-proliferating cells, which form the bulk of the tumour but cannot sustain tumour growth indefinitely", Professor. Mike Berridge said. "What is desperately needed is more knowledge about the basic cell biology of the tumour-perpetuating cancer stem cell".

continued inside

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Cancer Stem Cells



