



Why cancer research?

With cancer being a leading cause of death worldwide¹, it seems obvious that it would be an important research focus for any medical research institute.

However, this is only one part of the story of why the Malaghan Institute is involved with cancer research in particular.

The idea of a research institute was originally conceived in the early sixties by the Wellington Division of the Cancer Society of New Zealand and the Wellington Medical Research Foundation, as it was realised that if research were to be fostered in the Wellington region, steps would have to be taken to provide physical facilities for the work. At that time, relatively little research was being conducted in the area due to a lack of facilities, nor was it customary for Hospital Boards to support research in their hospitals.

When officially opened in 1979, the Institute was called The Wellington Cancer and Medical Research Institute (it was renamed the Malaghan Institute of Medical Research

in 1986 in recognition of the support of Len and Ann Malaghan), and the research aims were to be split equally between general medical research and cancer.

These days, while the Institute now focuses on a wide range of diseases, we are still committed to research into the causes and treatments of cancers, with just over half of all our scientists working on some aspect of cancer research. Our core cancer programmes are focused on exploiting the immune system to treat cancer through the development of vaccines and immunotherapies. Our scientists are also exploring several novel cancer treatment strategies that have the potential to enhance this research, which we highlight in this issue of Scope.

We are very proud of this work and of the fact that we have been able to translate some of our 'bench' research into early stage clinical trials, which we will update you on in Scope 48. Cancer affects many people in our communities and any steps we can take toward finding better treatments and cures will be profoundly felt for generations to come.

OUR RESEARCH
Vitamin C
and cancer

OUR RESEARCH
Pulling the plug
on cancer

AMI ROUND THE BAYS
Run for Research

¹ Accounting for 7.6 million deaths (around 13% of all deaths) in 2008 (World Health Organization; Globocan 2008, IARC, 2010)

From the Director



Cancer has been a plague on our society since the dawn of recorded history.

Since the first description of breast cancer and its treatment in ancient Egypt, scientists and clinicians have been working on a cure for this complex family of diseases – albeit with limited success.

Despite revolutionary advances in medicine and its practice over the past two centuries, cancer treatment has gone through a comparatively slow process of development. To some extent the belief that cancer cannot be cured persists even today.

Although the one-hit cancer cure remains elusive, over recent years several promising drugs have come to the market that extend the lives of cancer patients, such as Herceptin (breast cancer), Glivec (chronic myeloid leukaemia), and the prostate cancer vaccine Provenge.

Every great success story starts with a single idea and in this issue of *SCOPE* we describe three different strategies being developed at the Malaghan Institute for treating cancer. Only time will tell if they make it through the years of rigorous testing to become mainstream therapies used in the clinic, but that is the nature of basic research, and it is a journey we are all committed to seeing through to the end.

Prof Graham Le Gros

Using vitamin C to boost radiation therapy

Researchers have found evidence that high dose vitamin C could make brain tumours more susceptible to radiation therapy.

Glioblastoma multiforme (GBM) is a highly aggressive brain tumour that is ultimately fatal, because it is very resistant to treatments such as radiation therapy.

In radiation therapy a lethal dose of radiation is delivered to a tumour whilst sparing the surrounding healthy tissues as much as possible. Radiation kills both normal and cancerous cells by generating free radicals that destroy their DNA, however healthy cells have repair mechanisms that enable them to recover from the treatment more quickly.

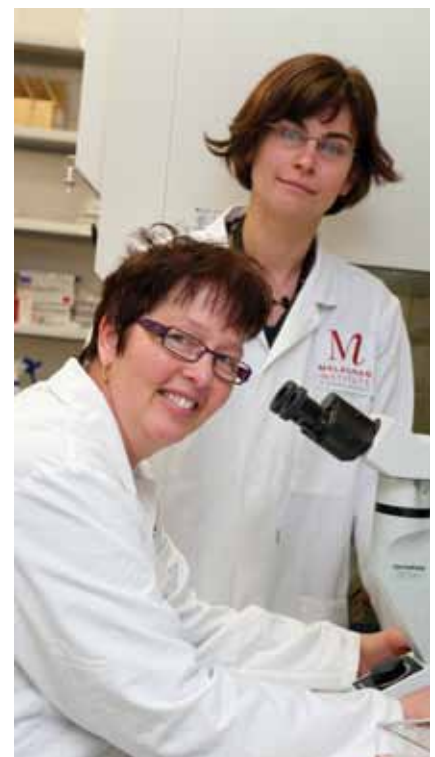
High dose vitamin C also generates free radicals in the acidic, metal-rich environment of a tumour, but not in normal tissues. Dr Patrix Herst, a senior lecturer in Radiation Therapy at the University of Otago, Wellington, therefore hypothesised that high dose vitamin C may work synergistically with radiation treatment to increase free radical damage to GBM tumours.

In collaboration with Dr Melanie McConnell, Dr Herst investigated the effect of combining high dose vitamin C with radiation on the survival of cancer cells isolated from GBM tumours. She found that pre-treating GBM cells with vitamin C did indeed make it easier to kill them with radiation.

The use of high dose vitamin C as an anti-cancer treatment is very controversial. Early studies using oral and intravenous vitamin C showed

a survival benefit for terminally ill patients but later studies using only oral vitamin C did not. Recent research has shown that vitamin C accumulates in the blood at concentrations high enough to kill cancer cells only when given intravenously.

If carefully designed clinical trials support Dr Herst's basic research findings that combining high dose vitamin C with radiation kills cancer cells more easily, there may be merit in combining both treatments for patients with radiation-resistant cancers such as GBM.



Dr Patrix Herst and Dr Melanie McConnell.

Pulling the plug on cancer

If you have ever experienced the frustration of a power outage you can appreciate how much we rely on energy to survive. The same is true for cancer cells - only in this case Prof Mike Berridge and his team are happy to be the ones pulling the plug.

It has long been known that cancer cells use nutrients differently than normal cells to produce energy. Elevated glucose uptake for example is a common property of metastatic tumours (cancers that spread). It is this increased need for glucose that makes cancer cells stand out from normal cells on positron emission tomography (PET) scans of tumours.

High glucose uptake is associated with glycolytic metabolism, a term used to describe cells that derive their energy from a pathway that does not involve burning oxygen via mitochondria - the more efficient aerobic energy powerhouses of the cell. Switching to a predominantly glycolytic metabolism has been suggested as a key survival strategy of cancer cells.

To investigate how energy metabolism affects the ability of cancer cells to form tumours and spread, Research

Fellow An Tan developed glycolytic models of melanoma and breast cancer cells. The mitochondria in these cells are not able to produce energy, so the cells rely entirely on glycolysis for their survival.

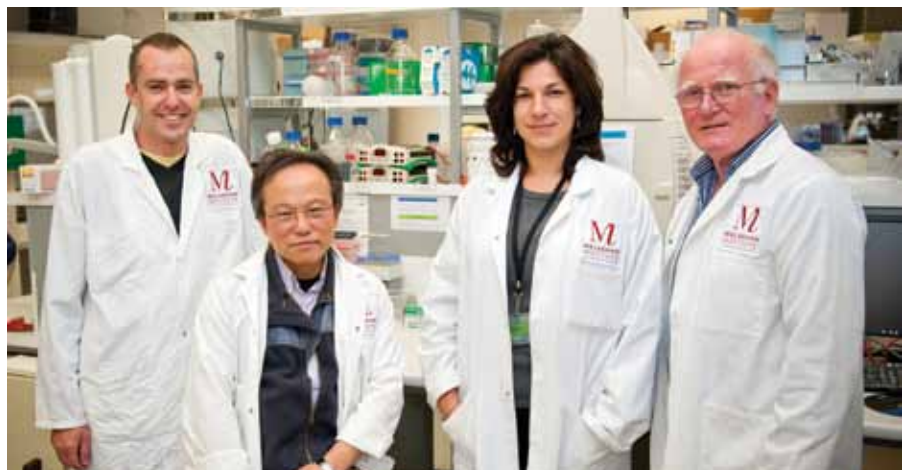
Based on previous findings it was anticipated that these glycolytic cells would be highly cancerous, however An instead found that the cells were unable to metastasise and form tumours in the lungs. Even more surprising, the tumours that did form appeared to have somehow acquired an ability to reactivate their energy-producing mitochondria.

Subsequent analysis of the cells by An and Dr James Baty has revealed a startling new phenomenon in tumour biology. The outcome has therapeutic implications for controlling the growth and metastasis of glycolytic tumours.

THE SCIENTISTS BEHIND THE RESEARCH

Professor Mike Berridge's history with the Malaghan Institute dates back to the late seventies, when he came to the Institute as the second Malaghan Fellow. Fast-forward to today and Prof Berridge is leading the Cancer Cell and Molecular Biology research team as they apply their knowledge of cell biology to the treatment of human diseases, with a particular emphasis on cancer and diseases involving altered energy metabolism.

The Cancer Cell and Molecular Biology research group emerged in 1980, just a couple of years after the Malaghan Institute opened. Prof Mike Berridge and founding group member An Tan have since worked together on a large number of projects. Along with the help of a steady flow of PhD students, their work has led to more than 90 international publications, one



Dr James Baty, An Tan, Carole Grasso and Prof Mike Berridge.

of which is amongst New Zealand's most highly cited original research papers - a direct measure of its scientific importance.

Currently working alongside Prof Berridge and An are Postdoctoral Research Fellow Dr James Baty,

Research Officer Carole Grasso and MSc student Alanna Cameron. Prof Berridge says of the group, "The spark of excitement and novelty that ignited the group more than 30 years ago remains alive today."

Can we treat cancer with bacteria?



Immunoglycomics PhD student Ashna Khan.

The potential of using bacteria to treat cancer has long been recognised, but can we do so without having to first make the patient sicker?

In the late 1800s American surgeon Dr William Coley made the remarkable observation that erysipelas (*Streptococcus pyogenes*) infection in cancer patients coincided with a shrinking of their tumours. Coley then used a crude mixture of killed bacteria called 'Coley's toxins', to activate the immune systems of his cancer patients. His theory being that the immune responses elicited by the bacteria were equally capable of destroying tumour tissue. Although Coley's results were encouraging, there were serious problems with this approach, mostly concerning how sick his patients became as a result of their treatment.

Fortunately science has progressed much since Coley's original

experiments and controlled injection of mycobacteria is now a standard first line therapy for bladder cancer, although not without complications.

In view of the varying, but promising, therapeutic activity of bacterial cell wall components in cancer therapy, efforts have been made to identify the molecules responsible for stimulating the anti-tumour immune responses.

Our Immunoglycomics team, led by Dr Bridget Stocker and Dr Mattie Timmer, were the first to determine how the length of a particular mycobacterial cell wall glycolipid influences the immune response. PhD student Ashna Khan was able to demonstrate this by synthesising a series of glycolipids of defined size and screening these against specific immune cells. Her work featured on the cover of the ChemBioChem journal at the end of last year due to its high scientific quality.

Ashna is now collaborating with Prof Franca Ronchese and Sabine Kuhn to develop safe versions of the immune-stimulating bacterial compounds for the treatment of cancer.

Three generations support the Run for Research

Taking part in the Malaghan Run for Research last month and raising over \$1,000 meant something very special to Wellingtonian Marie Gillies.

Ranging in age from nine to 68 years, Marie, along with her two daughters and two granddaughters, walked the 7km around the bays of Wellington together in memory of their beloved husband, father and grandfather, Bob, who died of cancer a year ago.

Bob was a fit and active 69 year old, still working and enjoying life, when he was diagnosed with lymphoma in November 2010. He sadly passed away, a mere four months later, on 27 March 2011.

"For us as a family, this was a difficult and shocking time and it is only through continuing research into cancer, that treatments can improve, and who knows, maybe a cure will be found," says Marie.

"It was our pleasure to take this small opportunity to help support the important research work the Institute does. I guess for us, cancer research will always remain an important priority."



Marie Gillies.

Run for Research success!

What a sight it was to see over 12,000 people line Jervois Quay in Wellington on Sunday 26 February for the sell-out 2012 AMI Round the Bays!

This year our involvement in this event was taken to a whole new level after being announced as the event's new Official Charity Partner. Around 130 people took part in the Malaghan Institute Run for Research and another 150 people participated as Malaghan Charity Runners, helping to raise over \$35,000 to support our research.

Melissa Moon, the two-time World Mountain Running Champion, World Stair Racing Champion and Malaghan Institute Run for Research Ambassador, gave a motivating speech to the crowd, kicking the event off to a great start on what was a stunning Wellington day.

The Run for Research brought together people of all ages, from all walks of life and fitness levels, however a uniting feature was their motivation to get behind a great cause and support the work of the



Pre-event Run for Research team photo.

Malaghan Institute. For some it was the loss of a loved one that drove them to take part and fundraise, for others, simply the knowledge that they were making a difference.

The event provided an excellent opportunity to reach the wider community and raise awareness of the Malaghan Institute in addition to raising important funds. To capitalise on this opportunity, the Institute was also supported by Lexus of Wellington who loaned a Lexus RX SUV that was branded with decals for the period leading up to the event.

This year marked the beginning of a great partnership between the Malaghan Institute, AMI Insurance and Sport Wellington and it is fantastic to have the opportunity to get the

Malaghan name out there and associated with such a well known and loved community focused event.

We have been humbled by the enthusiasm and dedication of the individuals and teams who took part in the Run for Research and the support of those in the community who donated. Thank you to everyone involved for making the 2012 Run for Research such a great success!



Dyhrberg Drayton Employment Law ladies enjoying the day.

Thank you to the following organisations for their amazing support of the 2012 Run for Research:

principal supporter



News under the microscope

Learning from the Best

Earlier this year we were fortunate to have two highly respected international immunologists, Prof Manfred Kopf (from Switzerland) and Prof Dan Eilat (from Israel), visit the Malaghan Institute to work with our scientists. This was a great opportunity for both our staff and students to exchange information and ideas with world leaders in the fields of cellular immunology and autoimmunity. Both visiting scientists stated that they were impressed by the facilities at the Malaghan Institute and by the calibre of the research being undertaken here.



Prof Manfred Kopf.

An evening at Pah Homestead 2012/2013



Prof Graham Le Gros, Sir David Levene and Chairman Graham Malaghan.

The Trust Board and Director of the Malaghan Institute hosted an evening of conversation and music at Pah Homestead in Auckland, on Sunday 1 April. The Auckland Youth Orchestra entertained 70 guests as they took the opportunity to view the current exhibition in the Wallace Arts Centre. The formalities for the evening included speeches from Sir David Levene and Prof Graham Le Gros, who focused on Positive Philanthropy. It was an enjoyable evening surrounded by great art and good company.

2012/2013 Entertainment Books

The new 2012/2013 Entertainment Books are now available! Did you know that you can purchase a book online and a portion of each book sold comes to the Malaghan Institute to support our research programmes?

Books for all regions are available - visit www.malaghan.org.nz/entertainmentbooks to find out more.

Kapiti Bookfair

Thank you very much to the Parawai Lions Club, who nominated the Malaghan Institute as one of the recipients of the proceeds of the Combined Lions Clubs of Kapiti Monster Bookfair held in October 2011.

Recent Grants (Oct 2011 – Mar 2012)

Our sincere thanks to the following Trusts and Foundations for their recent support:

- Margaret Neave Charitable Trust
- Southern Trust
- Springhill Charitable Trust & Frimley Foundation
- The Trusts Community Foundation

Remembering Sir Paul Callaghan

The passing of renowned physicist and 2011 New Zealander of the Year, Professor Sir Paul Callaghan, on 24 March 2012, saw New Zealanders from all walks of life come together to jointly mourn the loss of an exceptional

individual. Malaghan Institute Director, Prof Graham Le Gros says that it was a privilege to have known Sir Paul and that his contribution to science in this country will never be forgotten.

Five ways to support our research:

As New Zealand's leading independent medical research institute, the Malaghan Institute is reliant on grants and public support for its valuable work. We are registered with the Charities Commission and all donations over NZ\$5 are tax deductible. There are several ways for you to get more involved.

To find out more, contact Victoria Hale on 04 499 6914 x 821 or email vhale@malaghan.org.nz alternatively, visit our website www.malaghan.org.nz

1. MAKE A DONATION
2. SET UP AN AUTOMATIC PAYMENT
3. LEAVE A BEQUEST IN YOUR WILL
4. BE A SPONSOR (corporate or individual)
5. JOIN A VOLUNTEER FRIENDS GROUP



Research is our journey. Cure is our destination.