



breakthrough

GARVAN NEWSLETTER JULY 2006/ISSUE 02



This is one of the feature photographs from the 2005 Annual Report that brings together researchers, donors and beneficiaries of the research. (L to R) A/Professor Greg Cooney, Bruce & Juliet Kirkpatrick, Professor Don Chisholm and Isaac Gorelik.

We really appreciate hearing from our readers and the comments we have had about our new newsletter are overwhelmingly positive. Thank you. Some of you were keen to ensure that a strong scientific focus remains our top priority. We hope that this and future issues will address that need.

Please keep giving us your feedback.

Branwen Morgan, Editor

News

A couple of highlights

Associate Professor Sue Clark and her team have published research in *Nature Genetics* which formulates a new concept for how cancer cells can escape normal growth controls. The team found that large regions of DNA, rather than single genes, are 'switched off' in colon cancer. "These large regions – referred to as suburbs – contain genes that normally function to prevent the development of tumours", says A/Professor Clark. This finding may have far-reaching implications for the new generation of cancer therapies some of which are based on 'switching on' these inactive regions.*

A short time ago, Dr Andrew Biankin, Head of the Pancreatic Cancer Research Group spoke with ABC radio evening presenter James O'Loughlin about being a medical researcher. Dr Biankin has also been heard on local radio stations discussing a new pancreatic cancer support network as well as his research that aims to find novel prognostic markers of outcome and response to therapy for pancreatic cancer, which may help clinicians decide whether a patient should be subjected to surgery.

*Garvan's epigenetics research is also covered in the current issue of *Cosmos* for which we are including a subscription invitation.





Opinion



The federal budget was obviously good news for medical research and for the Garvan. Overall there was an extra \$905m for medical research. There were three main areas important to us:

1. An increase of \$500m over the next four years for the National Health & Medical Research Council budget. Currently, the NHMRC budget for competitive grants is about \$450m pa. In 2010 it will be about \$700m pa.
2. An additional \$170m for new research fellowships over nine years. For the next five years, approximately ten new senior fellowships (each for five years) will be awarded each year. At present there are approximately 70 - 80 new and renewed fellowships awarded each year across Australia.
3. Specific one-off grants, totalling \$163 million, to 17 research institutes for development and expansion. The largest of these was to the Florey Institute (\$37m) in Melbourne and will go towards their new building plans. The rest ranged from \$2m to \$15m, including \$14m allocated to Garvan and Victor Chang.

The majority of the \$14m will be put towards the construction of a new building adjacent to the Garvan. When completed, the St Vincent's research & biotechnology precinct will accommodate over 750 scientists making it one of the largest research centres in the Southern hemisphere.

Whilst this is good news, the development of the new facility and the increase in researcher numbers will place greater strain on the day-to-day funding of our infrastructure needs. This 'riddle' of success means it is increasingly difficult to support the science as we grow.

We are also under more pressure to raise the necessary funds to translate our research discoveries into real advances in disease prevention. But we believe we can meet this challenge with the help of all our dedicated and highly-motivated supporters. Your continuing support is crucial to our success – we thank you for your generosity.

John Shine



Donor Profile: Park Hyatt Sydney

On May 8 Garvan took up a fabulous offer from our long-time sponsor, the Park Hyatt Hotel, of a dinner for 40. We opted to use this offer to acknowledge and thank some of our most loyal and long-term supporters.

A selection of Garvan volunteers, Partners for the Future (who have made Garvan a beneficiary in their will), and other donors enjoyed the beautiful view from the Opera Harbour Room, as well as chef Danny Drinkwater's cuisine. Dr Aaron Ciechanover from Israel (see page 3) was able to join us, as well as both the outgoing and incoming General Managers of the hotel and a range of Garvan scientists.

The Park Hyatt has another great offer running till 30 September, its 'Celebrate Package'. For \$565, this includes overnight accommodation; full breakfast for two; a chilled bottle of Domaine Chandon on arrival; valet parking for one car; \$100 credit for hotel food and beverage, and a luxury gift. If you would like to book, call 13 12 34 and quote the 'Celebrate Package'. Garvan guests will also be treated to a glass of champagne in the harbourkitchen&bar on the night of your arrival, when you present this publication. To add to the celebrations, every "Celebrate" package booking will go into the draw to win two tickets to one of the hotel's monthly Pret-a-Portea Fashionista Afternoon Teas.

Quiz

1. About 100 000 people in Australia are newly diagnosed with type 2 diabetes every year. True or false?
2. What percentage of Australians will suffer from some form of mind and brain disorder during their lives?
3. How many people currently work at the Garvan?
4. What vitamin is essential for bone formation?

Answers: 1. T - A new report released in May showed 275 people are diagnosed with type 2 diabetes each day. 2. 75% 3. 370 scientists, students and support staff 4. Vitamin D

did you know?

Compared with a child born in 1900, a newborn child today will live 24 years longer if they are male and 25 years longer if they are female. Public health initiatives are largely responsible for this dramatic increase in life expectancy.

Staff Profile: Liz Musgrove

Liz Musgrove has worked in the Biological Testing Facility for eight years, since she was eighteen. Originally an animal attendant looking after husbandry and general wellbeing of the animals, Liz is now in charge of the rederivation by embryo transfer of mouse lines (a procedure used to generate pathogen free mice). "The most rewarding part for me has been learning these new skills and having great success within this area. My ability to get positive results means that research staff can carry out their research with fewer complications – because the mice are pathogen free," says Liz.



Ask Garvan...

What is Garvan's International Research Fellow Scheme?

The scheme funds a visit by a leading international scientist to the Garvan. Dr James D Watson, co-discoverer of the DNA helix, was the first Garvan International Fellow in 1998. The aim of the scheme is to inspire students and staff, provide an opportunity for direct interaction, and enhance Garvan's international network. The visit is also the catalyst for a full day symposium on the relevant field of research. This year's international Fellow was the 2004 Nobel Prize Laureate in Chemistry, Dr Aaron Ciechanover, co-discoverer of the ubiquitin protein degradation pathway. He spoke with **breakthrough** about his passion and his prize.

What is the ubiquitin protein degradation pathway?

Inside cells, proteins are constantly being synthesized and destroyed. The addition of ubiquitin molecules onto a protein is the first step in the protein degradation pathway. We now know that conjugation of ubiquitin to relevant targets is precisely regulated both temporally and spatially, and that deficiencies and malfunctioning of this critical pathway have been implicated in immune system disorders and the pathogenesis of a number of diseases including cancer. Previously a neglected area of research, the field of intracellular proteolysis and the ubiquitin system has now exploded to such a degree that it is impossible to keep up with all the tens of thousands of publications on this topic.

Did you have a 'Eureka' moment?

No, our discovery came very slowly.

What would you be doing if you weren't in science?

I have hobbies: I am a keen collector of Judaica artifacts, an avid listener to music, and I like to walk, but I can't imagine not doing science.

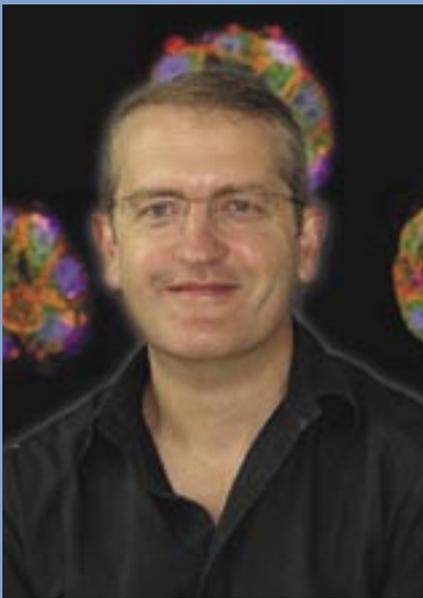
What's your take on the awarding of Nobel Prizes?

Nobel prizes recognise seminal discoveries that at the time may have seemed of limited significance. If I understand correctly the philosophy of the Prize awarding bodies, I think they recognise those who discover where the first drop of a broad river like the Amazon comes from, and not those who deepened and broadened its waterway. Hence scientific Nobel prizes are usually awarded many years after the original publication of the first discovery, after others have confirmed, by many studies, its basic importance.

Researcher Profile: Roger Daly

Professor Roger Daly heads the Signal Transduction Group in the Cancer Program.

Cancer is a group of diseases that arise because of abnormal cell growth and survival. Roger's team want to know how growth signals are transmitted within a cell. This knowledge will then enable them and others in the field to intercept the signals and potentially stop the development of cancer.



Q. What are you currently focusing on?

We are particularly interested in three proteins: Gab2, cortactin and Grb14, which are involved in either the transmission of signals within the cell or the regulation of these signalling events.

Q. Have you found anything interesting recently?

We are very excited about our studies on cortactin. Cortactin regulates the formation of the cytoskeleton, an internal cell scaffold that determines cell shape and regulates cell movement. We knew that high levels of cortactin are found in some breast and head and neck cancers, and that it helps promote the spread of cancer cells. But our research has identified a new function for this protein. We have shown that it prevents the degradation of a cell surface receptor involved in cancer development. This prolongs its action in the cell and may aid cancer development. We are now honing in on the mechanism by which this happens so that we can work out ways to block this effect.

Q. How will you do this?

We are currently working with Dr Will Hughes in the Molecular Imaging Facility to visualize how cortactin affects the movement of receptors from where they are activated at the cell surface to where they are normally degraded inside the cell. This should reveal the mechanism underlying cortactin's effects on receptor signalling.



Workplace Giving

The Garvan Institute works closely with a number of organisations that have implemented employee giving in their workplace. Employees are able to make donations to community organisations of their choice in an efficient and tax-effective manner, eliminating the need to collect receipts or wait until the end of the year to claim a tax refund. For employers, workplace giving provides a low cost, simple way to create partnerships between business and community organizations as well as build employee morale.

As part of the workplace giving partnership, Garvan's supporters are invited to visit the Institute and see how their contributions are helping our research efforts.

"The tour of the Garvan Institute was extremely interesting and personally rewarding. Not only did we see first hand the spectacular building that houses the Institute, but discovered how the building allows medical scientists working on different projects to openly interact with other groups and share the discoveries in a true team atmosphere. The tour also explained the funding and breakdown of the main research programs. I already knew it was a worthy charity and the tour certainly added to my knowledge and admiration of all those involved in ultimately saving lives."

Steve Clarke, AGL

Seminars

Garvan's well-known public seminars are on the road under the banner of the Garvan Good Living Seminar Series. With the support of Nestlé Australia, our scientists and clinicians are leaving the comfort of Garvan's Darlinghurst location and are joining forces with local counterparts to take Garvan research into the greater Sydney community and beyond.

Our March pilot seminar on nutrition and disease, held in Hornsby, attracted over 200 attendees. With our car trunks brimming with information packs, we then made our way to Gosford, where the Healthy Ageing seminar showcased the latest research in the areas of arthritis, osteoporosis, diabetes and dementia to over 200 local attendees.

This is what some of them had to say:

"Thoroughly enjoyed it, very interesting and informative. Easy to understand and listen to. Thank you and also thank you for making it free! – Excellent!!!"

Ruth Newton, Gosford

"I am a GP and wanted to hear a presentation to a mostly non-medical audience. Was reassured that I am able to share this information in detail with my patients. Excellent presentation."

Anna Stevenson, Gosford

The next seminar in the Garvan Good Living Series is on asthma, multiple sclerosis and juvenile diabetes. It will be held in the Castle Hill Hill's Function Centre on July 27 at 6:30pm. (www.garvangoodliving.info)



Volunteer Profile Graham Curtis

Q. Why did you become a Garvan volunteer?

I suffer from a very rare pituitary disorder called acromegaly. In 1997, I had an operation performed by Professor Ken Ho who is the Head of Garvan's Pituitary Research Unit and the Chairman of the Endocrinology Department at St Vincent's Hospital. Following the operation, I attended a public seminar at Garvan where I saw a leaflet about volunteering at Garvan. I felt that volunteering was my opportunity to repay the debt to Professor Ho and the Garvan scientists and to thank the people to whom I owe so much. I have been a Garvan volunteer ever since – that's eight years now.

Q. What do you enjoy most about volunteering for Garvan?

It keeps me out of trouble! But seriously, by volunteering at Garvan I'm contributing to the work of the Institute, which is saving the lives of many people, including myself. It's also a great place to meet some very interesting people. I would tell anyone thinking of volunteering to check out what's involved and just go for it!

A free half day public seminar on pituitary disorders will be held on August 5. For further information, or to register, please contact the Australian Pituitary Foundation on (02) 9594 5550 or by email: pituitary@bigpond.com



Select a Charity Mortgage Finance launch

(L to R) Professor Don Chisholm AO, John Montgomery, Ray Joseph Mancini, Ray Veleski, A/Professor Greg Cooney, and Michael Pollard at the Select-a-Charity Mortgage Finance launch on June 15.

Mortgage broker Michael Pollard recently approached the Garvan with a novel fundraising idea. Michael is no stranger to illness, having suffered from type 1 diabetes for many years and, more recently, a stroke. He wanted to donate 50% of his commission on loans to Garvan's diabetes research. However, Michael also set himself the ambitious goal of bringing his colleague mortgage brokers on board and establishing a proper mechanism for donation.

Select-a-Charity Mortgage Finance is the organisation Michael has founded to achieve just that, and it was launched on

15 June with an initial donation of \$10 000 to the Garvan's diabetes program.

Select's claim is that it can match any advantageous loan product or rate on the market, and facilitate effortless donation to charity at the same time. The Garvan is Select's initial beneficiary but, over time, Michael and his colleagues plan to extend this offer to a number of charities.

If you would like to know more about Select-a-Charity Mortgage Finance, please call 1300 MY GIFT (1300 694 438).

Young Garvan forums say "No" to drugs and stress

In the last few months Young Garvan have held two very successful forums. Sydney professionals gathered at the Institute on March 9 and June 1 respectively to hear about the health and ethics of drug use in sport and the effects of stress on our health and wellbeing.

The Doping in Sport forum was well-timed to coincide with the Commonwealth games in Melbourne. As Professor Ken Ho, who conducts research into the detection of growth hormone abuse, said: "The existence of high governance in sport simply reflects the value society places on it...Fairness is deeply rooted in civilised society and is valued by athletes and spectators: it's central to the spirit of sport. Winning is essential, but so is fair play".

To discuss whether stress is killing us, Young Garvan invited advertising guru and author Siimon Reynolds; clinical psychologist Dr Antony Kidman, St Vincent's ER Department Head Gordian Fulde and our own A/Professor Fabienne Mackay. Deal or No Deal's Andrew O'Keefe compered the event. All panellists answered "yes" stress is killing us, but it was said that simple steps can be taken to cope with stress such as: develop a love of humanity – support those who need help and take away the stigma of people coping with mental stress; be honest, recognise that you have stress and seek advice; make and take time in your day to reflect.

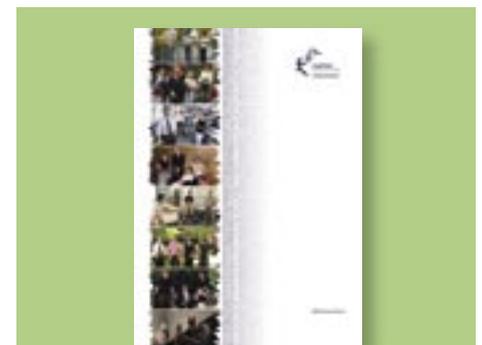


Singapore PM visits Garvan

The Singapore Prime Minister Mr Lee Hsieng Loong visited the Garvan on June 16 to hear about how our research and funding compares with that of Singapore. PM Lee (L) was taken on a tour of the immunology labs by A/Professor Fabienne Mackay (R).

Virtual tour launch

We have now launched our virtual tour, produced by Dakota Media. This ten minute online tour, at www.tourgarvan.org, aims to give viewers an insight into how Garvan scientists make discoveries. We hope viewers from around the world will be impressed by Garvan's research and facilities – at the same time attracting potential new staff.



Annual report published

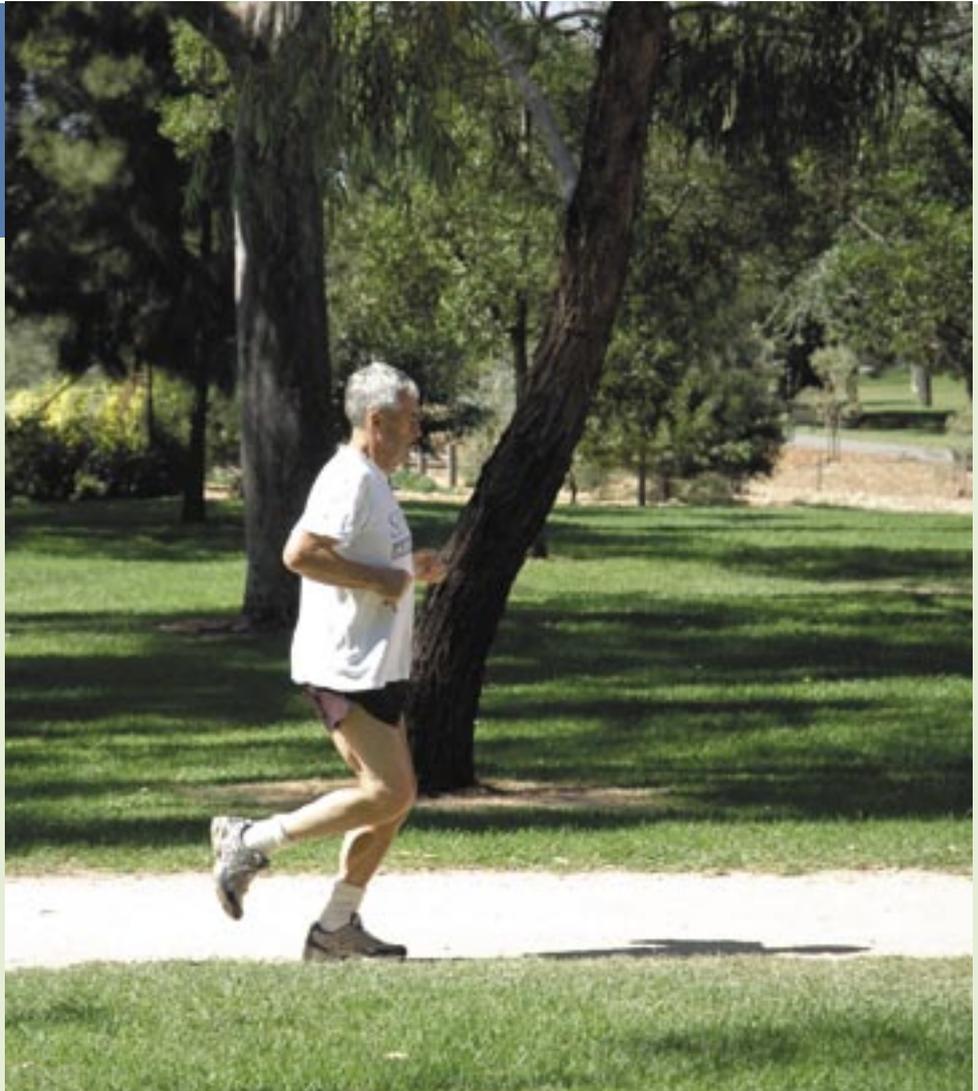
The aim of the 2005 annual report was to show the interdependence and connections between Garvan staff, supporters (both corporate and individual), clinicians and volunteers. Turnbull Ossher came up with the photographic concept of the Garvan logo chain linking the parties, which was implemented by Richard Weinstein photography. The report can be downloaded from the Garvan website (news & events section). A small number of hard copies are available.



Healthy Ageing

Some people say it happens overnight. It may be a particular birthday or a life-changing event, like becoming a grandparent or even a parent. All of a sudden you look in the mirror and realise you are getting older. There's not much we can do about it - perhaps buy more expensive face creams in the hope they will delay extra wrinkles or start visiting the hairdresser more often for a colour touch up. But what we all hope for as we age is that we will stay healthy and have quality of life. All of Garvan's research programs have relevance to healthy ageing: type 2 diabetes, cancer, arthritis, osteoporosis and dementia. Here is an overview of some of their recent findings.

Researchers in our **diabetes** program are continuing to make progress in understanding how our cells utilise glucose, what makes someone insulin resistant (unable to respond to the insulin signal to take up glucose into body cells), and how increased dietary fat can lead to type 2 diabetes. One of things they have discovered recently is that fat around the organs in the stomach (intra-abdominal fat), rather than fat under the skin (subcutaneous fat), is the main reason why people lose the ability to take up glucose. Microarray analyses (a tool for studying large numbers of genes simultaneously) are currently being carried out on fat samples obtained from patients undergoing abdominal surgery to find out which proteins have significantly



altered levels in patients who have developed insulin resistance. Another project is studying, in detail, the fats that have adverse effects on insulin signalling: saturated fats.

Although diet and exercise are major factors in fat accumulation, they do not fully explain the increased incidence of diabetes as people age. Recent evidence suggests that a component of a cell, called the mitochondria, that 'burns' fat may become less efficient as we age and contribute to inappropriate fat deposition and progression to diabetes. We are carrying out longitudinal studies in fat-fed animal models to determine the molecular

changes that could adversely affect mitochondrial function.

The chances of getting **cancer** increase as we get older because every time a cell divides it must copy all of its genetic material. Thus the likelihood that errors will creep into the 3 billion bits of DNA code gets greater with each cell division. Combine this with existing risk factors like smoking, or the presence of an inherited risk factor gene, and the chances increase even further.

Every cancer is different. A tumour that occurs in breast tissue will have different properties from one that occurs in the pancreas, which is why we have specialist cancer research

groups in addition to groups who study control of cell growth and division. A short time ago, we found a new way in which cancer cells maintain their control.

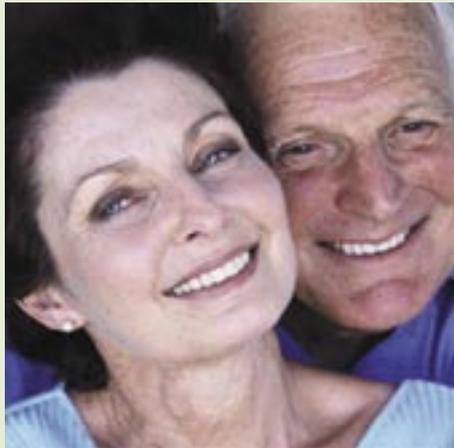
Our cells become cancerous when the normal controls over cell growth and death go awry. This deregulation has traditionally been linked to DNA or mutations of single genes or deletion of large sections of the chromosome. However, more recently, it has become clear that gene silencing in cancer can also occur in the absence of changes to the DNA sequence: a phenomenon known as 'epigenetics'. DNA methylation is one of the main epigenetic processes.

In cancer, the DNA methylation pattern of many genes changes. However, until now, it was believed that only individual single genes were silenced by methylation. Now it seems that non-methylated genes that reside in a particular 'suburb' near methylated genes are also silenced i.e. their physical proximity to the methylated genes affects their ability to function.

Our cancer researchers developed a new method to scan the entire complement of the 30 000 plus genes – the entire genome – in the cancer tissue samples, which allowed widespread changes to be identified in specific parts of the genome. They were amazed to find the extent of gene silencing and are now carrying out experiments to determine if these same regions are switched off in other types of cancers.

Osteoporosis has been described as a 'silent thief' because individuals

may not know they have it until their bones are so weak that a strain, bump or fall causes a fracture. Most of us know that calcium and sunlight, in order to manufacture vitamin D, are important for healthy bones. But we have shown that a hormone produced by the brain, called NPY, has an enormous effect on bone mass. When we block NPY signalling via one of its receptors (Y2) in the brain, we see a doubling of bone mass in adult mice in five weeks, which is extremely fast. It had been thought that NPY and



another brain hormone called leptin, had similar effects. However, our new studies show that whilst they have the same effect on the inner (cancellous) bone scaffolding, they both block its formation, they have opposing effects on the outer (cortical) bone; NPY blocks cortical bone formation, but leptin actually aids it.

Bone strength is related to the relative amounts of cortical and cancellous bone, the shape of the bone, and its material property. Garvan's interest in osteoporosis means we are primarily interested in bone strength, which is determined by the cortical bone. Therefore, we

will now be concentrating on how we could utilise the NPY-mediated pathway to increase bone strength.

For many of us the possibility of losing our mental faculties is most disconcerting. Evidence in the early 1990s thankfully revealed that we do generate new brain cells throughout life - overturning the old dogma. Moreover, more and more studies have verified the adage 'use it or lose it' - another reason to try your hand at Sudoku!

About two-thirds of adults aged 65 years and older with **dementia** have Alzheimer's disease. Yet Alzheimer's can only be accurately diagnosed by autopsy, as it is characterized by very specific molecular changes in the brain. There are a number of genetic changes that are associated with an increased risk of Alzheimer's, but less is known about genes involved in fronto-temporal dementia (FTD), which also makes an appearance in the over 60s. Because of the complex nature of brain and mind disorders, studies that involve large families with a history of disease continue. They are vital in tracking down potential gene culprits - of which there will be many. In the meantime, there are several medicines that may help in slowing memory loss.

So what can we do to stay healthy as we age? It seems obvious: eat a balanced diet that is low in saturated fats, exercise regularly, and avoid known risk factors. And when we can't help what our genes dictate... support medical research to find the answers.

Acknowledgement

Thanks to the generosity of a very special Garvan donor, our Imaging Unit now houses a world first: a Zeiss second generation total internal reflection fluorescence (TIRF for short) microscope.

TIRF is a relatively new technique allowing the accurate imaging of events at the surface of a single cell by shining a laser beam at an oblique angle.

This particular microscope is the demonstration model, which Zeiss personnel came out from Germany to configure with Garvan researchers. However, the time had come to return the microscope to Zeiss, had we not been fortunate enough to find the funds to purchase it.

Thanks to this most timely gift, we will now be able to image two to three different molecules in a single living cell simultaneously, at a superfast rate (about 50 images per second). We will also be able to pinpoint the events we need to see at the cell surface far more accurately, without extraneous data.

For example, we can now observe the effects insulin has in real time: from when it binds to a cell and triggers the events that lead to glucose entry and its subsequent metabolism. This is a process that may be defective in type 2 diabetes. The new microscope will help us 'see' where defects occur and test whether potential cures could work. The same capabilities will have wide application across our work in other areas such as arthritis and cancer.



Competition

What is A/Professor Greg Cooney (R) saying to Garvan's COO John Dakin (L)?

Our competition winner will receive a free year's subscription to Cosmos. Cosmos, a bi-monthly science magazine, is one of our newest corporate sponsors.



Congratulations to Mrs Maloney of Darlinghurst who won last issue's caption competition. Her caption was "Joh! The dryer is the wrong way around!"

Erratum

In the first issue, we incorrectly stated that the winner of the Science as Art people's choice award was Joseph Daniel; it was in fact James Burchfield. Sorry James.

In memoriam July 05 - June 06

We gratefully acknowledge gifts received in memory of:

Mr Jock Bennett	Mr Kerry Midson
Mrs Margery Bonython	Mr Bruce Muston
Ms Josephine Brown	Mrs Eva Nagler
Mr Bill Bruce	Mr Bill Neville
Mrs Yvonne Buwalda	Mr Bill Nicholson
Mr Fred Cardoza	Mrs Betty O'Neil
Mr Harry Caredes	Mrs Angelica Papadopoulos
Mr Rex Francis Carson	Mrs Nota Papanikolaov
Mr John Chilvers	Mr Lionel Poole
Mrs Pamela Crawford	Mr Keith Pracy
Miss Rita Curren	Dr Clare Annette Rae
Mrs Helen Dunnett	Mr Thomas M Roche
Mr Frank Egan	Mrs Rouloqalis
Mr Stanley Elias	Mrs Ena Schofield
Mr John Laurence Goldsmith	Mr Alex Shumsky
Mrs Olvie Gore	Mrs Luisa Tesoriero
Mrs Nola Hibberd	Mrs Judy Twigg
Mrs Katina 'Tina' Annette Hooke	Mrs Joyce Wall
Mr Roy Johnson	Mr Bill Ward
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Mr Harold Lambden	The Hon John Murray Wheeldon



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