

What's Inside

Opinion	2
Donor profile: Annabel Catt	2
Appeal update	3
Researcher profile: Dr Vanessa Hayes	3
Feature: Type 2 diabetes, insulin resistance, Chinese medicine and fluorescing green jellyfish	4
Supporting research into lung cancer	6
Staff profile: Rachael Stewart	6
Events: 2007 Chairman's Dinner, Park Hyatt tapas	7
Garvan's 2008 Free Public Seminar Series	8
In memoriam	8



Marcia Hines with Garvan's Professor Don Chisholm at the 2007 Garvan Chairman's Dinner, dedicated to raising funds to establish the Don Chisholm Chair in diabetes research (see story page 7)

Impressive advances have been made over the last few months in all Garvan's research programs, with many scientists attracting deserved media attention. In particular, our Type 2 diabetes program was thrown into the spotlight, when scientists published findings offering hope for improved treatment in the future. Our feature story looks at this widely misunderstood disease, and where our future research efforts should lie.

Alison Heather, Editor

Making News

■ Findings published by Professor Fabienne Mackay, Director of our Autoimmunity Research Unit, may offer new hope to people suffering from a previously unsuspected form of lupus. Her research may explain why some lupus patients do not respond well to current treatments.

■ Researchers in our Eating Disorders Research Group have shown for the first time that dynorphins, the body's natural version of morphine, play a significant role in regulating weight gain and weight loss.

■ Dr Jenny Gunton was one of four inspirational early career scientists to be awarded an inaugural L'Oréal For Women In Science Fellowship. The award will help Jenny pursue her interest in the link between Type 2 (adult onset) diabetes and Vitamin D.

■ Dr Vanessa Hayes has received a prestigious New South Wales Young Tall Poppy Science Award in recognition of her research in prostate cancer.

■ Associate Professor Susan Clark will play a leading role in a \$5 million national research program, funded by

the National Breast Cancer Foundation. The program brings together experts in the fields of nanotechnology, surgical oncology, epigenetics, cancer genetics, pathology and bioinformatics.

■ Dr Shane Grey has been awarded a \$3 million Program Grant by the National Health and Medical Research Council and the Juvenile Diabetes Research Foundation. He will collaborate with specialists across Australia to improve the success rate of 'islet transplantation', a potential cure for Type 1 (juvenile) diabetes.



Opinion



In modern medical research, where our knowledge base is growing exponentially, collaboration between researchers, in different areas and with different skills,

is a critical ingredient for success. This has been clearly demonstrated in the exciting recent discovery by Garvan and St Vincent's researchers that a particular molecule, MIC-1, appears to play a major role in controlling appetite.

The team has found that most common cancers produce large amounts of MIC-1, which in turn targets receptors in the brain that switch off appetite. This leads to the extreme weight loss, common in late stage cancer, that often speeds death.

Antibodies against MIC-1, already developed by St Vincent's, make it possible to switch appetite back on. Hopefully, this will help give people the strength to survive treatment and improve their chances of recovery.

Conversely, when normal and obese animals are treated with MIC-1, they eat less and lose a lot of weight, suggesting that MIC-1 may also form the basis of a treatment for severe obesity.

Garvan's part of the project was undertaken by Professor Herbert Herzog, Director of our Neuroscience program. His work has given us all a better understanding of the part of the brain that regulates appetite. Our bodies send complex chemical signals to our brains, which interpret them and send back responses, in this case 'eat' or 'don't eat'. There are many such pathways that affect our bodies' responses to eating and satiety, and each new piece of knowledge is useful in generating a clearer overall picture.

Professor John Shine AO FAA
Executive Director

Donor Profile: In memory of Annabel Catt

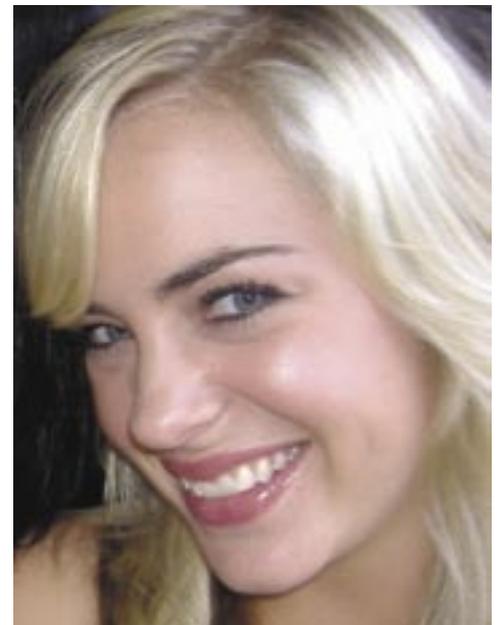
Annabel Catt tragically passed away in February 2007, following an overdose of PMA, a highly toxic amphetamine commonly sold as Ecstasy. As they planned her funeral, her family resolved that Annabel's death should celebrate the sanctity of life. To express this in a meaningful and positive way, they decided to request donations to their chosen charity, and Garvan was selected.

A vibrant and vital twenty year old, Annabel brightened people's lives wherever she went, although according to her family, she remained largely unaware of her impact. They remember her wonderful sense of humour, her megawatt smile and infectious laughter. She saw the good in everybody. Hugely popular amongst her friends and colleagues, Annabel worked as an optical dispenser, but dance was her first love. She was an accomplished classical, contemporary and jazz dancer and she also taught dance.

As well as having some prior contact with Garvan, Annabel's parents and brothers told us that they were reassured by the Foundation's compassionate, courteous and understanding approach. We are pleased to

remember Annabel with an in memoriam plaque which remains in perpetuity in our NAB Auditorium.

For more information on making an *in memoriam* donation, please contact Rachael Stewart, Supporter Services Manager, on 1300 73 66 77.



did you know?

Genetic predisposition plays a very large part in whether or not someone will develop Type 2 (adult onset) diabetes, contrary to the community myth that poor exercise and dietary habits are solely to blame. While it is true that 80% of people who develop Type 2 diabetes are overweight or obese, only 10% of obese people will develop the disease.

Quiz

1. Which part of the body makes insulin?
2. There are different kinds of prostate cancer, some less aggressive than others. True or False?
3. Which vitamin helps the bones absorb calcium?

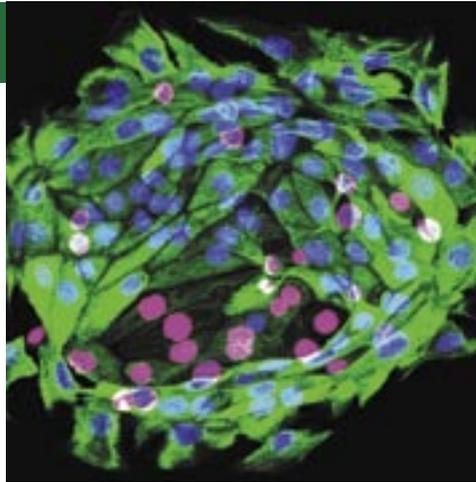
Answers:
1. The pancreas
2. True - with different treatment options
3. Vitamin D

Appeal Update

Garvan's October 2007 appeal focused on our research into diseases that affect the elderly, including osteoporosis, hearing loss, Alzheimer's disease and Parkinson's disease. Since sending the letter in October, we have had a tremendous response with more than 500 donors generously giving again to our work.

In his letter, Professor John Shine mentioned how Garvan's work on adult stem cells holds great promise for treating neurodegenerative diseases and hearing loss.

Adult stem cell work is particularly exciting as it opens up the possibility of auto-transplantation; that is the transplanting of a person's own cells into a different part of their body. Auto-transplantation means there would be no immune rejection



Mouse adult olfactory stem cells (J. Sullivan)

and therefore no need for long-term immunosuppressive drug treatments.

Thank you so much for your continuing support of our breakthrough medical research.



Researcher Profile: Dr Vanessa Hayes

Vanessa Hayes, head of Garvan's Cancer Genetics Group, was born and raised in South Africa. She completed her BSc and Masters degrees in human genetics at the University of Stellenbosch, and her PhD in the Netherlands, studying cancer genetics at the University of Groningen. After returning to South Africa to head a genetics laboratory, she was recruited to Garvan in 2003.

Cancer genetics, Vanessa's area of specialisation, is the study of the genetic changes in human DNA that occurs prior to, or during, cancer development. These changes can predispose someone to developing cancer, initiate the disease, cause its progression, or influence

disease outcome and/or response to treatments. Genetic variations may be inherited or they may be acquired in response to external carcinogens or a molecular event.

Vanessa's group is particularly focused on understanding prostate cancer. Vanessa works closely with epidemiologists from Melbourne who have collected DNA samples from over 4,000 men, with and without prostate cancer. Her team uses these samples to find genetic variations that influence a man's risk of developing prostate cancer.

"I regard this area as exciting because we know so little about what predisposes men to prostate cancer," she said. "We know the disease runs in families. We also know it's associated with certain ethnic backgrounds. Both of these things tell us there has to be a genetic element involved. While we have identified a region of a chromosome that appears to be linked to prostate cancer, we have not yet isolated a single prostate cancer gene. In that sense, we are working in uncharted territory."

Vanessa has just received the prestigious New South Wales Young Tall Poppy Science Award. Earlier this year, she was presented with The Premier's Award for Outstanding Cancer Research 2007.

BNP Paribas is a sponsor of Vanessa's work.

Ask Garvan...

1. What is the typical profile of a Garvan scientist?

Our scientists form a very diverse and interesting group of people, with as broad a spectrum of interests as you could imagine. Their innate intelligence and creativity means that many are also talented writers, musicians, artists and photographers.

About three quarters of our 420 staff are scientists. Typically, the core of a research team will be made up of a senior scientist, a postdoctoral researcher, and a PhD student researcher. We currently have about 60 researchers completing their PhDs at Garvan.

Our scientific community is dynamic and relatively young. The average age of our researchers is 33, and two thirds of our scientists are women. We also have a multicultural community, with representation from 30 different countries.

2. What are some of the most essential pieces of equipment used by Garvan scientists?

One of the most essential pieces of equipment used is the humble pipette. Pipettes are very important tools in science, as they can measure out very small amounts of liquid (such as one thousandth of a mL) and this sort of precision is key to rigorous experimentation. Pipettes can cost between \$400 and \$1000 each and each scientist has their own set which they are responsible for maintaining.

Of course, our scientists also rely on some very sophisticated and commensurately expensive equipment, such as 'smart' freezers, which contain cell and blood samples. A single freezer costs around \$12,000 and can contain up to five years' worth of work. Its contents need to be maintained at around minus 80 degrees Celcius. So you can imagine it would be disastrous if someone left the freezer door ajar. Should the temperature drop, our 'smart' freezers generate an email, SMS, phonecall and page to alert staff to take remedial action.



Type 2 diabetes, insulin resistance, Chinese medicine and fluorescing green jellyfish

In a discussion about Type 2 diabetes, Professor David James, Director of Garvan's Diabetes and Obesity Research Program, described the thinking, the methodologies and the new technologies he believes will help us solve the molecular events behind the initiation and progression of this destructive and ultimately life-threatening disease, which affects around 7% of the Australian population.

"What causes Type 2 diabetes? We don't know. We know that 80% of people who have diabetes are overweight or obese. We also know that only 10% of people who are obese will develop the disease. That's because it has a genetic underpinning."

Genes or lifestyle

"Many people who have Type 2 diabetes suffer from a sense of shame that they have brought it on themselves by eating too much or not doing enough exercise. These people need to be reassured that, unfortunately, their genes are responsible for the disease as much as their eating or lifestyle habits."

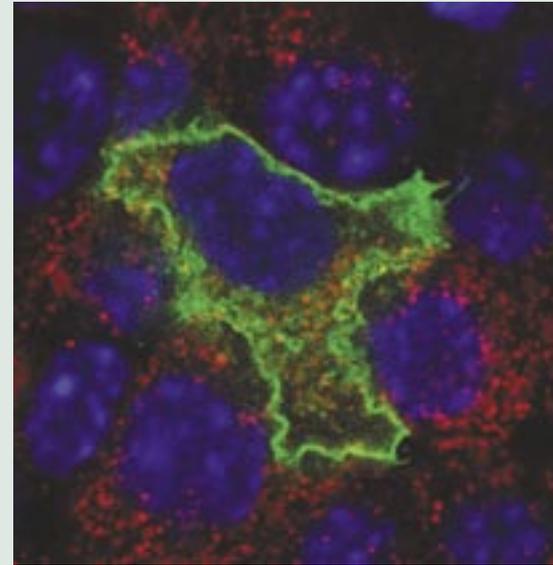
"Diabetes is a very complicated disease, because it involves so

many factors and impacts on all the major systems of the body. One of the reasons we do not yet understand the disease is that we do not fully understand the chemistry of the brain, and the brain communicates with all the other organs that give rise to the disease. It controls the liver, the pancreas and the amount of energy we consume."

"There is a lot of evidence to support the theory that each of us has a somewhat nebulous component in our make-up that sets a 'threshold' for our body weight, a set point that our bodies somehow defend by sending messages to the brain that we're hungry if we fall below the 'threshold'. It's obvious that some people have thresholds that tell them to eat much more than they need to maintain a desirable body weight."

The role of fat

"We can show that our fat cells release hormones that travel to the brain and give the brain information about how much fat we are storing. When the fat cells get big, they change the pattern of hormones they secrete. When they shrink, the opposite happens. We are very interested in the soluble hormonal factors secreted by fat cells, and



researchers in my program are actively pursuing different theories about them."

"We are also interested in fat itself. We have evidence, as do others, that if you eat too much, you accumulate certain kinds of fat in your cells. The accumulation of these fats somehow wreaks havoc in the cell. It's very complicated, but we think that they cause the production of oxygen free radicals, molecules that act in very destructive ways."

"All the thinking about hormones and fats is helpful, but the critical question remains: 'how do you get the disease?' What's the actual molecular series of events that happens when you get diabetes?"

Insulin resistance

"People with Type 2 diabetes do not produce enough insulin, a hormone made in the pancreas that helps convert the sugar in their blood

Insulin is manufactured in beta cells (nuclei stained blue) located in the pancreas and is stored in membrane bound granules or vesicles (stained red), scattered throughout the cell. On the appropriate stimulus, such as after a meal, insulin granules move to the edge of the cell, fuse with the membrane (stained green) and insulin is released

into energy in their muscles. At the same time, their muscle cells lose their ability to respond to insulin, a phenomenon known as 'insulin resistance'. It's one of the earliest defects observed in diabetes, and in my opinion, understanding what causes insulin resistance will tell us what causes Type 2 diabetes."

"Biology is very dynamic. When we eat, our glucose levels go up, and then they come down. As the glucose goes up, the insulin also starts to go up, but it doesn't go up immediately, it trails a little bit, and then it comes down. At the cellular level, there are multiple processes happening, simultaneously or sequentially, and we need to understand them all. That's why we need to look at these things in a dynamic way and in a living cell."

Jellyfish and molecular imaging

"One of the most exciting recent breakthroughs in biology has been the discovery of a protein, known as 'green fluorescent protein', found in a jellyfish. You can take this protein, paste it onto a protein

you want to research, inject that protein into a cell, then shine a light down a microscope and follow the movements of your fluorescing green protein, in a living cell, in real time."

"At Garvan, we have decided that we want to develop this molecular imaging technology in a big way and we want to use it as rigorously and creatively as possible. We have been fortunate that some supporters have generously donated the money to buy a couple of state-of-the-art microscopes. But it's not just about looking down the microscope and taking movies. Encoded within these movies is a boundless data set that can only be realised by detailed analysis and automated computation. To help us go to this next level, we have recently teamed up with the CSIRO Biotech Imaging division and have appointed a full time mathematician with expertise in imaging technology to help us extract the crucial data from these movies. This will enable us to measure the rate at which proteins move from one place to another in the cell and how such movements

are modified by hormones and other external influences.

"We are using this technology to understand how individual molecules work in the cell and in the organism. To do this, we're taking cells from embryos of animals that have had genes deleted. We can grow those cells in our tissue culture laboratory, and then coerce them to grow into, for example, a fat cell. Then we introduce our green fluorescently-tagged protein in a cell that's missing one gene and we can study the consequences of this with a very analytical eye."

Chinese medicine

"In addition to the approaches now made possible by these molecular imaging techniques, we are also pursuing our interest in unravelling the mysteries behind Chinese medicine. We have a formal collaboration with the Shanghai Institutes of Biological Science, which is helping us identify the chemistry of the active components in those Chinese herbs effective against diabetes."

"In my opinion, we must explore all realms open to us. I believe it will take a merger between the worlds of drug discovery, organic chemistry, biochemistry, cell biology and animal physiology to find out what causes diabetes. Then, and only then, can we begin to design really safe strategies to stymie its progression."



Staff Profile: Rachael Stewart



As Garvan's Supporter Services Manager, Rachael Stewart is the person who will take your call if you phone to donate money or volunteer your time. In addition to receiving and receipting donations, Rachael does all the data entry, keeping our all-important database up-to-date.

"The job suits both sides of my personality," she said. "The sociable part of me loves talking to people and finding out about their interests, while the meticulous part enjoys the data entry work. I like to know that everyone is getting exactly what they ask for, including information about diseases of interest."

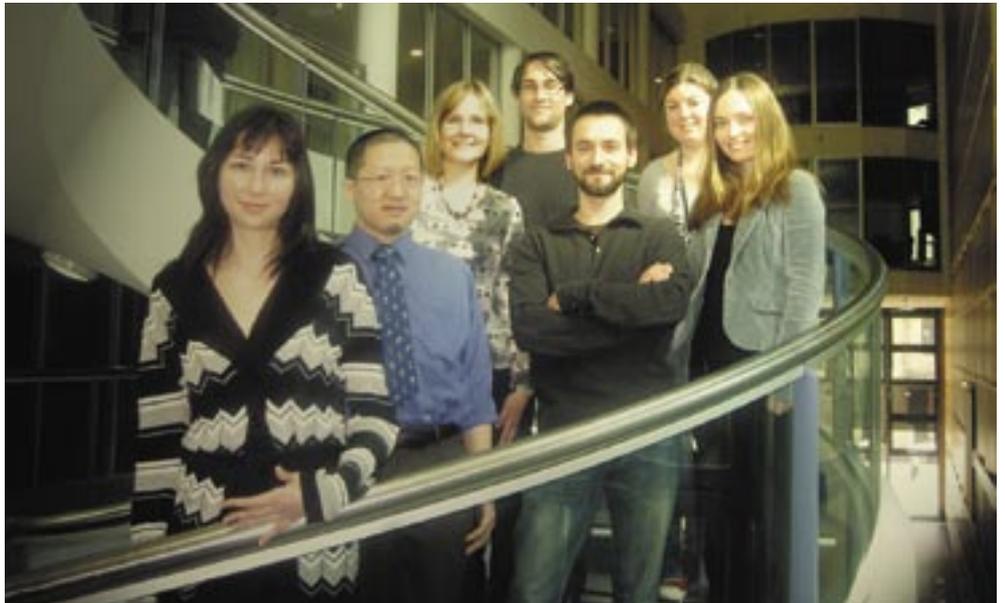
"A large part of my job is managing the In Memoriam program – where people donate in lieu of flowers at funerals. While dealing with grieving people is never an easy thing to do, it can be fulfilling when I feel I'm being of help."

Prior to Garvan, Rachael worked for a strata management company and the commercial department of a high profile Eastern Suburbs real estate agency. Before that, she was an apprentice jockey with every intention of turning professional. Why didn't she? "Even though I love horses, horseracing is a dangerous sport and the travel was difficult at a young age", she said. Horseracing's loss and Garvan's gain.

Supporting research into lung cancer

Lung cancer is an aggressive disease which, compared to other higher profile cancers, receives relatively little attention. In Australia, only 11% of men and 14% of women survive for five years beyond diagnosis, compared with breast cancer survival rates, for example, of 88%.

Garvan is very fortunate to have the support of a generous benefactor, Mrs Virginia Kahlbetzer, to undertake research into lung cancer. As a result, Dr Maija Kohonen-Corish and her team, together with Dr Wendy Cooper and Professor Soon Lee at Royal Prince Alfred Hospital, have achieved some exciting breakthroughs. Studying gene changes in cancerous lung tissue, they aim to isolate key alterations useful for determining patient prognosis and, in the longer term, improving treatment outcomes for lung cancer patients.



The lung cancer research team, from L to R: Dessislava Mladenova, Dr Jason Tseung, Dr Maija Kohonen-Corish, Nicholas Siggelow, Dr Laurent Pangon, Nicola Currey, Dr Tina Selinger

Their work has focused on the role of DNA methylation in the early stages of lung cancer. Methylation is a normal biological process that regulates gene function. During tumor growth, however, methylation is abnormally accelerated, preventing protective genes which would otherwise slow or halt the disease from activating.

In 2006, Dr Kohonen-Corish's team identified genes affected by aberrant DNA methylation on chromosome 3p, an area of the genome particularly important in lung cancer development. Focusing on a gene called DLEC1 ('deleted in lung and esophageal cancer'), they successfully showed how methylation causes its inactivation in lung cancer, a new finding. Additionally, they were able to show that methylation may be synchronized in two genes, DLEC1 and MLH1, during lung cancer development. The first paper from this research, jointly co-authored with Dr Cooper and Professor Lee, will be published in *Histopathology* this year. In the meantime, Dr Kohonen-Corish's team continues to study chromosome 3p alterations in lung cancer and examine the significance of synchronous methylation.

2007 Chairman's Dinner (Continued from page 1)

The 2007 Garvan Chairman's Dinner, held on 18 September in Garvan's Galleria, was dedicated to raising funds to establish the Don Chisholm Chair in diabetes research. Contributions to the Chair totalling over \$1,000,000 were made by the Federal Government; Diabetes Australia Research Trust; GlaxoSmithKline; and private individuals.

In addition, GlaxoSmithKline has established the GSK Don Chisholm Fellowship, a one-year fellowship which they have committed to fund for an initial two-year period.

Professor Don Chisholm is one of Garvan's most distinguished scientists and clinicians, as well as being a world-renowned expert on both Type 1 and Type 2 diabetes. At the Dinner, he was asked to comment on some of the 'eureka' moments along the way. In the



Professor Don Chisholm (at lectern) with Garvan Executive Director Professor John Shine

considered and modest manner for which he is renowned, he demurred.

"As a scientist, it's not so much about 'eureka' moments but more about a time when all the pieces of the jigsaw puzzle finally fit together,"

he said. "Discovering the role of gut hormones in releasing insulin was one such milestone for me. Another was our breakthrough in understanding the role of abdominal fat, as opposed to 'butt fat', in the development of diabetes."

Celebrate Park Hyatt partnership with tapas and cocktails



For over fifteen years Park Hyatt Sydney has been a Garvan Institute corporate partner, generously supporting Garvan's activities. The hotel has sponsored lunch meetings and dinners annually in their premier venue, and has always exhibited generosity in donating accommodation and special offer prizes for Young Garvan, and other public events.

To celebrate this successful partnership, Park Hyatt Sydney is offering Garvan supporters three complimentary tapas items with every two cocktails ordered, in their stylish newly designed waterfront lounge, Harbourbar. The new tapas menu can also be enjoyed from three new tapas bars and the chefs table, and is created by executive chef Alessandro Pavoni. The offer is current until December 23 (perfect for pre Christmas drinks) from 12pm daily and bookings are recommended (9256 1661 or hkbar@hyatt.com.au). Don't forget to show Harbourbar staff your latest copy of *breakthrough* on arrival.

Garvan's 2008 Free Public Seminar Series

Garvan would like to invite you to our 2008 Free Public Seminar Series generously sponsored by the Alcoa Foundation. These seminars provide a unique opportunity to interact with leading scientists and clinicians as well as hear personal insights from people affected by common disorders. All seminars will be held at **384 Victoria Street, Darlinghurst**. Bookings essential. Please call **(02) 9295 8110** or register online at www.garvan.org.au

Date	Topic	Time
Wednesday 13th February	The Ageing Brain – Parkinson's, Alzheimer's and Adult Stem Cell research	10am – 12pm (doors open 9am)
Wednesday 9th April	Healthy Ageing	10am – 12.30pm (doors open 9am)
Tuesday 6th May	Bowel and Prostate Cancer	10am – 12pm (doors open 9am)
Thursday 7th August	Osteoporosis	10am – 12.30pm (doors open 9am)
Wednesday 3rd September	Asthma and Allergies	6pm – 8pm (doors open 5.30pm)
Friday 14th November	Diabetes and Obesity	10am – 12pm (doors open 9am)

Free Tours of Garvan

Tours of Garvan's state-of-the-art facility are held on the first and third Thursday of each month – subject to availability. Tours start at 10am and run for approximately 90 minutes. See our building, hear about our latest research, meet some of our scientists and join us for morning tea. Individuals and groups are welcome, but bookings are essential.

To find out more or register, please call **(02) 9295 8108** or email foundation@garvan.org.au

How to get to Garvan Institute

 Buses 389, 311
stop on Burton Street

Buses 378, 380, 333
stop on Oxford Street

 Train to Kings Cross station,
turn right onto Victoria Street
and walk straight down toward
St Vincent's Hospital.

In memoriam July 07 - October 07

We gratefully acknowledge gifts received in memory of:

Ted Barton
Herbert Blundy
Peter Boersma
Allan Cameron
Jack Egan
John Fletcher

Norman Garvan
Max Gore
Helen Humphrey-Reeve
Roger Imber
David Officer QC
Neil MacArthur Onslow

Greg Park
Ross Schibner
Joan Struck
Joyce Tavares

Be part of progress

Please use this coupon if you would like to make a donation to Garvan's breakthrough medical research, or if you would like further information. We would love to hear from you.

My Contact Details

Title _____ First name _____

Surname _____

Address _____

Suburb _____ State _____ Postcode _____

Daytime Phone _____

Email _____

Garvan Supporter Number (if known) _____

Please Send Me Further Information About:

- Giving to Garvan in my will (strictly confidential)
- Volunteering with Garvan
- Giving regularly to Garvan through my bank account

Please Change My Contact Details:

- I no longer wish to receive *breakthrough*
- I only wish to receive *breakthrough* by email
- I only wish to receive appeal mailings in May/June
- I do not wish to receive any appeal mailings

My Gift Details

Yes! I want to help Garvan make progress with a gift of:

Gift of choice \$ _____ \$50 \$100 \$250 \$500 \$1000

My cheque/money order made payable to **Garvan Research Foundation** is enclosed

OR Please deduct the above amount once monthly annually from my Visa Mastercard Diners Amex

Card Number

Expiry Date 2007BT03

Cardholder's Name _____

Signature _____

Please complete this coupon and mail it to:

 **Garvan Research Foundation,**
Reply Paid 68593, Darlinghurst NSW 2010

 **Call: 1300 73 66 77** (9am to 5pm)

 **Fax: (02) 9295 8151**
(you can use this coupon)

 **Online: www.garvan.org.au**



**GARVAN
INSTITUTE**