

03 breakthrough

GARVAN NEWSLETTER DECEMBER 2006/ISSUE 03

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Garvan's explorations into the basis of disease and the role of genetic factors underpins many of our discoveries

In this third and final issue of the year we have made a few small changes to the layout. You can now see at a glance what is inside the issue. Read about the June and October appeal results and the exciting progress we are making with type 1 diabetes. From all of us at the Garvan, thank you and Merry Christmas.

Branwen Morgan,
Editor

Making News

Our prostate cancer researchers, led by Associate Professor Sue Henshall, have found a new marker for identifying the men who are likely to develop life-threatening metastatic disease (where the cancer spreads) years after their prostate cancer has been removed. The next step is to explore the relationship between this marker, called AZGP1, and the development of metastatic cancer in other groups of men with prostate cancer. This will give more weight to the finding and hopefully lead

to the marker being used routinely in clinics where it could aid the treatment decision-making process.

PhD student Bennett Shum, working under the leadership of Dr Michael Rolph, has found that a protein, called aP2, that is linked to diabetes & obesity, has a new role in controlling airway inflammation in asthma. This suggests that blocking aP2 function could be a novel treatment approach for asthma and other inflammatory lung diseases.

A collaboration between Chinese, Korean, and Australian scientists at Garvan has revealed that the natural plant product berberine, found in some traditional Chinese medicines, has the ability to lower blood sugar levels. Although this suggests that berberine may be a helpful new treatment for type 2 diabetes, it will still have to be evaluated properly following the defined clinical trials process, and compared with existing medications. This finding was not lost on the BBC who reported the discovery online.

Opinion



Few recent issues in science have generated as much excitement and controversy as the potential use of stem cells to treat disease. The hope is that, one day, it will be possible

to grow some of your own skin or blood cells in culture, reprogram them to become new nerve or muscle cells, then re-implant them to replace cells lost through disease or injury. At present, this hope is still a dream, but one that is coming closer to reality as we learn more about how immature cells (stem cells) develop specialised functions and how this process can be manipulated.

Stem cell research at Garvan is focussed on adult stem cells, particularly neuronal stem cells to address neurodegenerative disorders such as hearing loss, Parkinson's and Alzheimer's. Adult stem cells are technically more difficult to work with than embryonic stem cells*, but they promise to provide cell replacement therapies that are not limited by transplant rejection or concerns around safety.

However, knowledge gained from research on embryonic stem cells is very important in progressing our work with adult stem cells. The recent decision by Federal Parliament to extend the legislation regulating stem cell research to allow somatic cell nuclear transfer, or so-called 'therapeutic cloning' (under strict regulation) is a recognition of the potential of the research. At the same time we need to acknowledge, respect and address the very real concerns that many people have about the rapid development of these new technologies and how they may shape our future.

Professor John Shine AO FAA
Executive Director

*Adult stem cells are present in very low numbers and are more restricted in their 'potential', being only able to produce new cells of a similar type, i.e. neuronal stem cells give rise to new nerve cells, not new muscle cells; whereas embryonic cells could, under the right conditions, become any other cell type.



Bequests are a critical contributor to our ability to keep finding solutions to disease

Gifts that last

Some of the most wonderful gifts that Garvan receives come as a complete surprise in the shape of bequests. In 2006 we have benefited from the generosity of a number of far-sighted people who wanted to enable Garvan's spirit of intelligent enquiry to keep going, well beyond their lifetime.

To take just a couple of examples, Dr James Francis Ryan and his wife, Dr Josephine Ryan, blessed Garvan with a very significant gift in their will. James passed away in 2004. He was a radiologist by training and the editor of the Australasian Radiology Journal for 25 years. He was awarded a Gold Medal by the Royal Australian and New Zealand College of Radiologists for his outstanding service to the development, teaching and practice of this discipline. The Drs Ryan did not have children and bequeathed their estate to Garvan to be used for the areas of greatest need.

Sometimes people who have attended our free public seminars can't donate much in their lifetime, but keep sharing in our progress toward cures through a gift made in their will. Tragically, Mr Lindsay Franks died of cancer not long ago. He wanted his gift of the residue of his estate to support our further discoveries in cancer. Mr Franks chose to make what is known as a 'residual bequest', because that way, his loved ones were catered for first and then he could contribute to eradicating cancer with the remainder of his assets.

Our gratitude goes to the Drs Ryan and Mr Franks, as well as others who have or may consider making Garvan a beneficiary in their will. Please contact Carole Renouf on (02) 9295 8114 if you would like information on how to do this.

Quiz

1. What is the name of the hormone produced by the brain that can affect bone strength?
2. How many Garvan research groups work on type 1 diabetes?
3. Around 2 in every 3 women and 1 in every 3 men will have an osteoporotic fracture during their lives. True or false?
4. Which ABC actress is the voice of Garvan's online virtual tour?

Answers:
1. NPY, also known as neuropeptide Y
2. 4
3. T
4. Lisa Hensley

did you know?

Garvan scientists developed the low-dose intravenous insulin infusion method to treat a major complication of diabetes called ketoacidosis. It has saved thousands of lives.

See our Type 1 Diabetes feature on page 4

Appeal results

Thank you to all our loyal and new donors who contributed to our June and October Appeals – we raised more than \$242 000 and are still counting!

You can read more about our prostate cancer and type 1 (juvenile) diabetes research, which were discussed in our recent appeals, in this issue (see pp 1 and 4).

In June, we launched our campaign to attract much-needed new supporters.

Since then, 1212 people have made a first-time donation towards Garvan's

research into the prevention and cure of major diseases.

From the scientists and all of us at Garvan – a big thank you for your belief in our work.



Researcher Profile: Janet Watters

Janet Watters is a registered nurse based at the Garvan Institute clinic in Dubbo, the centre for the world's longest running osteoporosis epidemiology study: it began in 1989. She grew up in the town, trained there, and began her career at Dubbo Base Hospital, while also teaching nursing at the local TAFE & Charles Sturt University in Bathurst. But since 1992,

Janet has been looking after Garvan's osteoporosis study participants - over 3000 of them. Together with two other full time colleagues, Jodie (a research assistant) and Shaye (another registered nurse), Janet has been cataloguing participant data that scientists at the Garvan Institute in Sydney then analyse. The data include: a bone mineral density scan; weight and height measurements; eyesight, balance, sway, touch, and muscle strength tests; activity and medication questionnaires; and a blood test. Participants visit every two years for this battery of tests, which take about 1-1.5 hours to complete; some are now on their eighth visit. One of Janet's biggest challenges has been recruiting family members for the Garvan osteoporosis genetics study that began in 1997. But even that has been very rewarding. The best part, according to Janet, is the interaction with the local community. Since Garvan's Dubbo clinic moved to the central business district in 2002 its profile has become even larger. Janet and the team have just clocked up the 12 000th visit and are turning away residents from towns outside Dubbo who have heard about the study and want to be involved. Janet says that in the near future they hope to use the vast amount of data to look at the causes of other diseases like diabetes as the bone density scans, for example, simultaneously collect abdominal fat data. The lifestyle data could also yield clues about the interaction between genetics and 'environmental' factors such as diet and activity levels that together dictate disease susceptibility. However, this depends on whether funding can be found to keep this unique study alive. If you'd like to help, contact the Foundation on (02) 9295 8110.

Ask Garvan...

1. What is unique about Garvan?

Other medical research enterprises are often defined by their focus on very basic research without obvious clinical relevance; a single disease area; a major technology; or commercial potential. Garvan has a somewhat unique profile on the world stage, due to the integration of all of these aspects:

- A special partnership with a major teaching hospital (St Vincent's) that enables us to closely integrate basic and clinical research
- Established strengths in cancer, diabetes, autoimmune diseases, osteoporosis and brain diseases which allow us to bring a multi-disciplinary approach to these complex multifactorial disorders
- A willingness to combine traditional medical knowledge with the latest in genetic research
- Use of numerous state-of-the-art technologies, especially at the interface of biology and information technology. Garvan's size and diversity of research programs allow it to effectively maintain sophisticated technologies such as gene chip arrays, confocal microscopy, automated cell sorting, electrophysiology, and gene sequencing
- A commitment to attain practical outcomes from our research discoveries through innovative commercialisation approaches

2. How does Garvan avoid duplication and inefficiencies between its research and the research of others?

In 2005, Garvan published 135 articles in international scientific and medical journals that only accept new findings. Our researchers are part of a worldwide scientific community that competes for publishing discoveries and international funding. This competition is a key element in driving scientific success. Garvan scientists participate regularly in international scientific meetings where there is opportunity to share progress and pick up new ideas. They are also engaged in many active research collaborations all over the world (e.g. USA, UK, Europe, South Africa, South America, and China).

Type 1 Diabetes



Twins Thomas and Jordan Bennett both have type 1 diabetes

Photo: Courtesy of JDRF

In November, a group of Australian children with type 1 diabetes helped plant 15,000 needles on the lawns of Parliament House in Canberra. They represented how many times each child would need to inject themselves with insulin over a ten year period. It is a frighteningly large number.

For a parent with a child suffering from type 1 diabetes, the natural impulse to avoid causing a child pain must be offset with the knowledge that insulin injections are essential for them to stay alive.

Without insulin, the body cannot use most of the energy (in the form of glucose) that is obtained from food. Continuous high blood sugar levels can cause the body to go into a

life-threatening condition known as diabetic ketoacidosis, where organs start to fail and emergency treatment is needed.

Type 1 diabetes develops when the cells that make insulin (pancreatic beta islet cells) are destroyed by the body's own immune system; it is an autoimmune disease. We don't know why this happens, but there are a number of theories. And, by studying the patterns of inheritance of the condition within families, scientists have recently begun to identify gene mutations that increase the chances of the disease developing. Their next step will be to determine how these changes cause the body to turn on itself. This can be done using specially bred strains of mice that carry the same gene mutations.

Although we don't yet have a cure for type 1 diabetes, the outcome for

those with type 1 diabetes today is dramatically different from those who lived prior to 1922. Then, patients died within a few years of diagnosis; but in 1922 a young Canadian boy became the first person to receive purified insulin and his condition improved. For the next 60 years, insulin was purified from farm animals, namely cows and pigs. It was not until the advent of gene cloning that human insulin, produced by genetically engineered bacteria or yeast, became available. Our own Professor John Shine was one of the key scientists involved in cloning the insulin gene.

Yet, even today, having type 1 diabetes will shorten the average person's life by about 15 years and can produce debilitating health problems such as blindness, kidney damage, heart disease and amputations.

Every day five people are newly diagnosed with type 1 diabetes - also known as juvenile or insulin-dependent diabetes. It affects over 140 000 children and adults in Australia and over 16 million people worldwide.

Where to now?

One potential cure for type 1 diabetes that has become an important focus of global research investment is islet cell transplantation. Transplantation of pancreatic islet cells was first trialled as a therapy for type 1 diabetes in the 1980s, but was not successful until 2000, and last year the first living donor islet transplants took place in Japan.

In the future it may be possible to generate one's own new beta islet cells, but for that we must understand and be able to prevent the destruction of this 'self tissue'.

Despite the advances in islet transplantation, the procedure is not yet readily available and, as with other tissue transplants, patients must take anti-rejection drugs for the rest of their lifetime. However, earlier this year the Federal Government announced funding for an Islet Transplantation Program (ITP), to be managed by the Juvenile Diabetes Research Foundation, that will help take this from an experimental procedure to a viable clinical option for people with diabetes.

Garvan scientists, Dr Jenny Gunton, Dr Shane Grey and Professor Don Chisholm are heavily involved in this nationwide initiative. Don Chisholm, who has now retired from clinical duties, is an international diabetes expert and sits on the advisory panel.

Dr Shane Grey heads a group that focuses on understanding how and why the immune system starts to attack the beta islet cells in the pancreas. For the ITP, his team's role is to develop tests to monitor the recipient's immune system for signs of rejection as well genetic changes in the islet transplant. This is one of the four projects that falls under the ITP consortium's umbrella. Shane Grey is also working with Jenny Gunton to use microarrays to find the markers to predict, before transplantation, how the islets will function after transplant – that is, to identify a molecular signature for a successful graft.

Dr Jenny Gunton is the Australian Diabetes Society Council representative on the ITP oversight committee. At Garvan, her team are examining islet factors that regulate protein production (gene expression) in beta islet cells. They want to understand which genes are dysregulated in type 1 diabetes and the effect this has on disease onset and progression. Jenny is also involved in the clinical arm of the islet transplant program.

Dr Cecile King is another Garvan researcher whose work will help in understanding and treating type 1 diabetes. The main aim of Cecile's group is to identify specific molecules that could be targets for suppressing the T immune cells (also called

T lymphocytes) that have an essential role in causing type 1 diabetes. The group has found that the T cells that cause diabetes carry markers that allow us to track their movement to the gut. These T cells become activated and can infiltrate and damage beta islet cells in the closely-located pancreas.

Dr Pablo Silviera brings another line of expertise to Garvan's diabetes research. His group is working on the B immune cells (also called B lymphocytes) that produce antibodies against the beta islet cells. Their recent research has demonstrated that B lymphocytes' contribution to disease is mainly due to their unique ability to specifically take up beta islet cell proteins and present them to the T cells. After this interaction, T cells become armed to recognise and destroy the beta islet cells. They want to understand why the B cells that recognise the body's own tissue aren't eliminated, as they would be in healthy humans.

Type 1 diabetes is a serious disease that can be difficult to manage, but it is also an interesting condition that can shed light on how our immune system operates. This understanding will be of benefit to those suffering from other autoimmune disorders, such as multiple sclerosis, for which there is no treatment.

CRI raises \$1.13m for bioinformatics

On September 28, CRI Australia, the leading property development and services group founded by former Garvan Chairman Mr Peter Wills AC, hosted a dinner at the Shangri-La Hotel to celebrate its 25th anniversary and raise funds for Garvan.

Funds raised were directed towards our Bioinformatics Centre. This was established in 2002 to honour the achievements of Peter Wills' term as Chairman. Bioinformatics is becoming an increasingly essential part of our research. Born of the fusion of biology, computer science and mathematics, it allows our scientists to accurately model real biological events in disease and treatment down to the molecular level. It also allows us to model and predict events that could reveal the answers to disease.

The evening raised \$1.13 million after the Hon. Tony Abbott MP, Minister for Health and Ageing, announced that the Commonwealth Government would contribute \$1 million over three years to help take Bioinformatics



Peter Wills, Tony Abbott, John Shine, Bill Ferris (L to R)

into the next era. Donations from those attending the dinner totalled \$130 000.

The dinner was attended by almost 500 people from a wide cross section of business who gathered to honour Peter Wills and the way he chose to make this outstanding contribution to the community through the Garvan.

Staff Profile Warren Kaplan



Dr Warren Kaplan is not your typical Garvan scientist. His interest is in computers and harnessing their power to make sense of the multitude of processes that take place in the body; it is termed systems biology. Warren works with scientists from all of Garvan's research disciplines.

Q. How did you get to Garvan?

I grew up in South Africa and studied biochemistry and chemistry at university. Following my PhD in protein chemistry at Wits University in Johannesburg, I moved to Australia and worked at Sydney University and then for a small bioinformatics company. In early 2002, I was recruited by the Garvan Institute as a bioinformatics specialist for the newly-formed Peter Wills Bioinformatics Centre.

Q. How will systems biology help tackle health problems?

There's been an explosion in the amount of data that is being produced by medical researchers. This includes entire DNA sequences from numerous species, vast amounts of information about new molecular mechanisms, metabolites and signalling pathways in the body. But,

despite all this new information, it is still difficult to link the behaviour of the whole biological system with that of the individual molecular mechanisms. I think we need to use computational methods to form an understanding of the biology of a system - then we will be able to better understand the disease process and the role of environmental factors; as well as discover new drug targets and better diagnostics.

Q. What are some of the things you are working on?

One current project is designed to ensure that our stored data from microarray (gene chip) experiments, where the amounts of all the proteins in a particular tissue are calculated, is in line with that being produced internationally and conforms to international archiving standards. Since systems biology is an integrative science that is dependent on analysis of data from many sources, our systems must be able to withstand scrutiny. We are also designing software to mine this wealth of information to look for things like new biological markers for diagnosing cancers.

Science As Art 2006

It is often thought that science and art are two separate realms. Not so for those in the Garvan building. Since 2003, Garvan has been holding an annual 'Science As Art' competition, where staff are invited to produce an artistic scientific image. The aim is to encourage all staff to see and appreciate the beauty of nature, both in the laboratory and in the world around them. This year's 40-plus entries have certainly done that.

We were fortunate to have Maryke Steffens (TV presenter on ABC's Catalyst program), Dael Oates (Art Director for animations and visual effects company, Animal Logic) and Andrew Lee (Art Director, COSMOS magazine) as our judges. Their job was not easy. In the end it came down to the judges' understanding of how the artist observed beauty in their science or how they appreciated science in the world around them. The winning images were not necessarily the most obvious or 'prettiest' choices but, together with the submitted description, conveyed the artist's perception of science. According to Steffens, the winning image reflects parallels between the macroscopic and microscopic, cells and humans, multiplying and dividing. It is intriguing because it was found in an unexpected (and non science related) place; it is reflection of people in a sculpture.



Science As Art 2006 Winner: Mitosis of Man, Janet Watters

Congratulations to our winners:

Science As Art 2006 Winner

Mrs Janet Watters, Bone & Mineral Program, for 'Mitosis of Man' (see Janet's profile on pg 3).

Science As Art 2006 Runner Up

Mr Luke Anderson, Cancer Program, for 'An unpleasant reality'.

People's Choice Winner

Dr Nicholas Cole, Victor Chang Cardiac Research Institute, for 'Evolutionary Secrets' (see below).

People's Choice Runner Up

Dr Kharen Doyle, Neuroscience Program, for 'Love that nose no bounds'.

Thanks to the Park Hyatt Sydney and COSMOS magazine for donating competition prizes: a dinner for two at the HarbourKitchen&Bar valued at



Winner: Janet Watters (2nd from left) with competition judges



People's Choice Winner: Evolutionary Secrets, Nicholas Cole

\$250 and a COSMOS magazine subscription for 12 months. Winner Janet Watters also received an international travel award to attend a scientific meeting.

Garvan's 2007 Public Seminar Series

Garvan would like to invite you to our 2007 Public Seminar Series. 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. This year all seminars will be held at our building at **384 Victoria Street, Darlinghurst**. We have also added two evening seminars into our program so that those who are working during the day are able to attend.


Date	Topic	Time
Monday 12th March	Healthy Ageing – hearing loss, cancer, diabetes, osteoporosis, arthritis	10 am – 12 pm
Monday 30th April	Breast and Ovarian Cancer	10 am – 12 pm
Tuesday 12th July	Auto-immune Diseases - type 1 (juvenile) diabetes, lupus, Sjogren's disease	5 pm – 7 pm
Tuesday 7th August	Osteoporosis	10 am – 12 pm
Monday 17th September	The Ageing Brain: Parkinson's, Alzheimer's, adult stem cell research	10 am – 12 pm
Tuesday 10th October	Mental Health Disorders – depression, bipolar disorder, anorexia	6 pm – 8 pm

Free Tours of Garvan


Tours of the Garvan's state-of-the-art facility are held **every first and third Thursday** of the month at 10am. Tours start at 10am and run for approximately 90 minutes. Come along and see first-hand where we carry out our breakthrough medical research. Tours are free, however **bookings are essential**.

For more information or to book, please call **(02) 9295 8110** or email foundation@garvan.org.au

How to get to Garvan Institute

 Buses 389, 311, 300, 350 stop on Burton Street

Buses 378, 380, L82, 382 stop on Oxford Street

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

In memoriam Jan 06 - Nov 06

We gratefully acknowledge gifts received in memory of:

Mrs Buntly Mantel	Jan Keating
Mr Patrick Coyne	Lt.Col (ret) Neil Macarthur-Onslow
Mr Jock Bennett	Mr Richard McMillan
Mr John Bonser	Mr Bruce Muston
Margery Bonython	Mr Edward A Notter
Mr Andrew Bristow	Mrs Betty O'Neil
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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.

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