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Australian singer/songwriter Delta Goodrem was the star attraction at the special Gala Dinner jointly held by Garvan and St Vincent's Hospital at the Four Seasons in October. The event publicly launched the fundraising campaign to build the new \$100 million Garvan St Vincent's Campus Cancer Centre. Following her performance for more than 500 guests, Delta was announced as the Patron of the new Centre. A former cancer patient at St Vincent's, Delta said she was thrilled to be able to give back to the Campus and contribute to a Centre that will enable research findings to move quickly into patient care.

Dianne Lavender, Editor

Making News

■ Prof Jonathan Sprent's collaboration with California's Scripps Research Institute has led to the development of a novel complex designed to stimulate the immune system to fight cancer.

■ Garvan scientists identified a molecular process that may account for the extreme allergic reactions some people experience. By intervening in this process it may be possible to treat allergies.

■ A team of Garvan researchers, led by Prof Roger Daly, have identified a way to 'switch off' a key player in the molecular processes that trigger breast cancer and certain forms

of leukaemia. The molecule, known as Gab2, operates downstream of a major breast cancer oncogene, HER2, the target of the drug Herceptin. The team has found a novel way of blocking signals to and from Gab2, preventing it from fulfilling its role in cell proliferation.

■ Garvan and the CSIRO have signed a three-year collaboration agreement to investigate important cellular processes, including those impaired by diseases such as diabetes. The CSIRO and Garvan team have developed software that locates within minutes the main molecular process that fails in diabetes.

■ Freddy Yip, a PhD student in Garvan's Diabetes and Obesity Program, has uncovered an important piece in the puzzle of how insulin works, a problem that has plagued researchers for more than 50 years. This finding brings us one step closer to explaining exactly how insulin prompts fat and muscle cells to absorb glucose.

■ Garvan's Autoimmunity Unit, together with an international team of scientists, has identified processes that are heavily implicated in human multiple myeloma and other B cell cancers, moving us closer to developing quick tests and readouts that could help in the tailored treatment of patients.



Opinion



In the highly competitive world of medical research, it is essential to be at the cutting edge of international activities. Only by continually benchmarking our research output can we be sure that the

very limited resources available to support our work are being most effectively allocated. Although this is constantly monitored through our success in competitive grant applications and publication statistics, every major institute regularly carries out an independent review (about every 5 years) of its research programs. In Garvan's view it is important this review is carried out by a panel of international experts – leaders in their respective fields. We thus commissioned such a Review during 2008 to help us chart the course of our research for the next decade.

The Review Panel found Garvan's research performance to be "excellent" and recommended an increasing focus in several areas in the context of changing external environments. These included further increasing the close relationship between the Garvan and St Vincent's Hospital to develop leadership in translational research. In this context, the Panel enthusiastically endorsed our plans for a joint Cancer Centre where the research discoveries from the laboratories can be quickly translated into real improvements in patient care. Similarly the Panel also praised the Institute's focus in several major health care areas such as cancer, diabetes and obesity, neuroscience, osteoporosis and immunology / inflammation. With critical mass in each of these diverse areas, reviewers pointed out the many research "breakthroughs" that continue to emerge from the intersection of different disciplines – such as our finding of the mechanism by which the brain controls the density of our bones or the link between the nervous and immune systems with important implications for many stress related diseases.

The Garvan will now implement the recommendations of the Review as we look forward to the next decade of research discoveries and their even more effective translation into prevention and treatment of disease.

Professor John Shine AO FAA
Executive Director

Donor Profile: Rosemary Pryor

Fledgling research projects in Garvan's Neuroscience Program have received a very significant infusion of life this year, thanks to the generosity and far-sightedness of Rosemary Pryor. Novel projects can often struggle to get off the ground and reach the point where their leaders can successfully apply for competitive grant funding, but Rosemary's support has put some wind beneath their wings.

Feeling blessed to receive a surprise inheritance from a close relative, Rosemary – for many years a High School Biology Teacher and Head of Science – decided it would mean a great deal to her to make a real difference to scientific research at the Garvan: "I have always been fascinated by the miracle of life, how it is created and the intricate, mysterious processes through

which cells decide to grow, multiply and then differentiate into certain types. The area of genetics also has always been very appealing to me, and I would very much like to help people who suffer from inherited diseases". Rosemary has committed future support over a number of years from the Rosemary Pryor Foundation.

Initially, Rosemary's benefaction will go towards Garvan's research into the potential use of adult stem cells as neuroreplacement therapies. As a first step, this will allow Dr Kharen Doyle to gratefully recruit a postdoctoral scientist to join her currently very small team of two and accelerate her work. Rosemary believes that "in doing this, I feel I am helping to promote solid scientific research in areas which can be of enormous benefit to many in our society".



L to R: Yvonne Hort, Dr Kharen Doyle, Rosemary Pryor and Prof Herbert Herzog, Director of the Neuroscience Program

Did you know?

40% of children with asthma live with people who smoke.

Quiz

1. Can ovarian cancer be detected through the pap smear test?
2. There is a significant global push to understand changes that occur in the function of genes without a change in the DNA sequence. What is the name of this branch of research?
3. What part of the brain is responsible for regulating appetite and weight (as well as many other bodily functions)?

Answers:
1. No. There is currently no screening test for ovarian cancer
2. Epigenetics
3. Hypothalamus

Researcher Profile: Dr Alex Viardot

What is the current focus of your research?

Australia is facing an obesity epidemic leading to a drastic increase in type 2 diabetes. However, the mechanism by which obesity is triggering the disease is not entirely clear. Our Clinical Diabetes Group is interested in the earliest metabolic defects which occur many years before diabetes, with the aim of unravelling the primary defects and underlying disease mechanism. A special focus of my research is to investigate early changes in the immune system and its role in the development of type 2 diabetes. We are also studying subjects with Prader-Willi Syndrome, a known genetic cause of obesity, which is associated with impaired appetite regulation and partial protection from type 2 diabetes. We hope that this will lead to new ways of addressing the development of obesity and type 2 diabetes.

What are some of the recent findings from your work?

We have demonstrated that the hormone insulin has a strong anti-inflammatory effect on immune cells. We can show that with developing obesity (and the often

associated impaired action of insulin in most tissues) the immune system gets increasingly activated, resulting in a low grade inflammation process. This inflammation is thought to be responsible for many complications of type 2 diabetes, such as atherosclerosis and coronary heart disease.

What is the biggest challenge in your area of research?

Our group is mainly focussed on clinical studies to answer specific questions in human diseases. Finding volunteers who meet all specific study criteria is our daily challenge. To explore the very early phase of type 2 diabetes we are looking for healthy people with at least two close relatives with type 2 diabetes in their family, but with normal blood sugars. (More information about this study is available on page 8.)

What do you enjoy doing away from the research lab?

There is no better way to experience Sydney's beautiful atmosphere than to explore the harbour by sail or kayak, or Sydney's forests by mountain bike.



Ask Garvan...

How do funds raised by Garvan Research Foundation support the Institute?

The Foundation team undertakes a range of integrated fundraising activities to raise funds for the Institute's research. These include our three appeals per year and customised proposals for individuals of high net worth, companies and trusts.

Every year, we must raise sufficient general (non specific) funds to cover our annual grant commitment to the Institute (~\$1m). This is essential infrastructure funding, expended on maintenance and upgrading of core scientific facilities, purchase of equipment/technology and support staff salaries (such as IT and engineering, as distinct from administration). One of the directives issuing from the recent Scientific Review of Garvan is that the Foundation must enhance its ability to generate such infrastructure funding.

In addition to our annual grant, we raise specific funds designated by our supporters to support a chosen research project or program. The bulk of the funds currently raised by the Foundation are of this nature.

What is the importance of PhD students at Garvan?

Unbeknown to most people, the Institute plays a major role in education with around 70 students currently studying for their PhD at the Garvan. Our affiliation agreement with the University of New South Wales generates these. International students are also keen to study and research at Garvan.

Along with research assistants, PhD students form the core of any Garvan research team. It is important that in return, the Institute provide students with top-up funds to supplement their relatively meagre Scholarships; top-notch supervision; and the opportunity to attend and ideally present at key conferences nationally and internationally for their own development.

Currently, Garvan is fortunate to have a number of supporters who are keen to further the learning of young scientists and make funds available for this purpose. For example, Paul and Judy Hennessy have established the Stuart Furler Travel Fund (in memory of Stuart, who worked at the Garvan for over 20 years in the diabetes program) to help PhD students attend international scientific gatherings.



Antibody Therapies: A Revolution in the Making

Antibody therapies are revolutionising the treatment of cancers and inflammatory diseases. This new class of drugs, billed as “magic bullets” due to their ability to home in on a specific target, accounts for 50% of all new drugs in clinical trials in the US in an industry estimated to be worth USD24 billion.

This is despite very humble beginnings in the early 1980s when it seemed the therapeutic antibody would not deliver on its huge promise. Although early mouse-derived molecules introduced to the clinic in 1986 could block rejection of transplanted organs, it was not until scientists developed ‘humanised’ antibodies that this form of therapy emerged as a powerful treatment option for many diseases. The reason for this is two fold: firstly, unlike the earlier mouse molecules, these antibodies closely resemble human antibodies making them safer to use; secondly, scientists have gained greater understanding of how antibodies interact with cellular targets and the immune system. This growth of knowledge is now leading to more effective therapies and Garvan scientists are at the forefront of this new technology.

Engineering natural born killers

Antibodies are proteins naturally made by our immune system to attach to invaders such as bacteria, viruses and cancer cells to neutralise them. Our immune system can make millions of different antibodies and calls on the most suitable one to bind to a target like a piece of a jigsaw puzzle. For example, a flu virus will prompt the immune system to produce antibodies that will fit that particular type of flu virus, and only it. This unique property of “specificity” gives antibodies a distinct advantage over traditional chemical drugs. While chemical drugs have a higher failure rate in clinical trials and increased side effects, antibodies are cheaper to develop, bind to their target very tightly and are often associated with fewer side effects.

For example, rituximab (the first antibody approved to treat cancer) binds to the CD20 molecule on B cells and is now in routine use for the treatment of lymphomas arising from these particular white blood cells. Herceptin (used to treat some breast cancers) binds to HER2, a receptor for epidermal growth factor (EGF) found on some tumour cells in breast cancer and lymphomas.



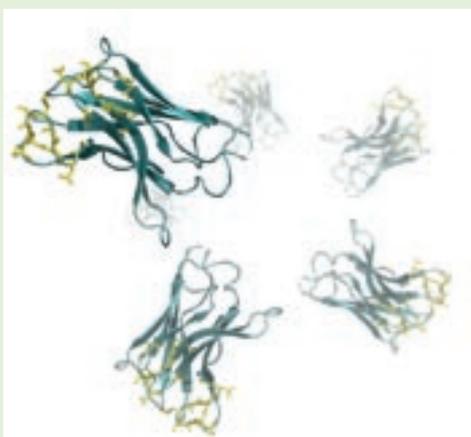
Antibody molecule (with variable regions shown in red)

There are 20 other antibody-based drugs on the market and hundreds awaiting Food and Drug Administration (FDA) approval in the US: engineering antibodies are emerging as a major commercial and therapeutic force. The industry was born out of basic research undertaken at the Laboratory of Molecular Biology in Cambridge, UK. Starting in the 1970s, with the discovery of mouse monoclonal antibodies by Cesar Milstein and Georg Kohler (which earned them the Nobel Prize for Medicine and Physiology), the technology rapidly transformed medical research. Following in Milstein’s footsteps, Sir Gregory Winter from the Laboratory (and Garvan’s 2008 International Fellow) later developed the first ‘humanised’ and eventually fully human antibodies. The majority of therapeutic antibodies approved by the US FDA to date were developed using the methods he invented. His work has transformed the lives of tens of thousands living with debilitating diseases such as rheumatoid arthritis, Crohn’s disease, multiple sclerosis and cancers.

Domain Antibodies

Dr Daniel Christ, head of Garvan's Antibody Engineering team, worked with Sir Gregory in Cambridge for a decade before bringing his highly specialised knowledge to Garvan. His team is working to harness the unique properties of antibodies and optimise their use in therapeutic applications. Despite success to date, many challenges remain if antibodies are to realise their full potential for treating human diseases. For example, mass production at a reasonable cost remains a problem; as does delivery to sites like the brain, intestine and solid tumours, which often lack effective blood supply. In addition, antibody-based drugs can only be administered by intravenous injection, which is time-consuming and inconvenient for the patient.

To tackle these obstacles, Dr Christ has stripped down the human antibody molecule, effectively shedding the weaker parts not necessary for its action. The resulting antibody fragments are known as domain antibodies. Using



Domain antibody molecules (with antigen binding sites shown in yellow)

this protein engineering approach, Dr Christ captures the most effective parts of the molecule, thereby making it smaller, easier to produce and more cost effective. Domain antibodies do not rely on mammalian (human or mouse) cells for production; instead they can be made using yeast or bacteria, significantly reducing costs. Currently his team is the only one in Australia working on fully human domain antibodies and this research holds huge promise for those suffering from inflammatory diseases and cancers.

There are other important benefits to the smaller, stripped-back antibody molecules. Firstly, they are much tougher than the larger full-length antibody constructs and can be rendered temperature and acid resistant, unlike many other proteins. As a result they may be suitable for oral administration in tablet form rather than as an injection. Secondly, the smaller size of the domain antibodies means they have the ability to access disease affected tissues and tumours which otherwise might be inaccessible to antibody molecules.

Dr Christ looks for the best antibody for a specific target by exposing millions of engineered antibodies to possible targets to see which will bind, a process not unlike a speed dating session for antibodies. He describes the process of identifying the right antibody molecule for an antigen target as "looking for a needle in a haystack: find the needles and then make more of them".

Australian scientist Dr Geoffrey Grigg Travelling Fellowship

Dr Christ will be reunited with his mentor Sir Gregory when the latter comes to Sydney in December for a symposium on antibody therapeutics hosted by the Garvan. At the same time, Sir Gregory and Garvan will pay tribute to a great Australian scientist Dr Geoffrey Grigg, who sadly passed away earlier this year. Dr Grigg was head of Molecular Biology at CSIRO and had strong links with Sir Gregory, spending time at Cambridge in the 1960s and 70s. Together they played a major role in setting up two highly successful UK antibody companies: Cambridge Antibody Technology and, more recently, Domantis. He was also the founder of Sydney-based antibody company Peptech Ltd (now Arana). In honour of his achievements, Garvan and the MRC Laboratory of Molecular Biology in Cambridge have jointly established the Geoffrey Grigg Travelling Fellowship, which will support the exchange of scientists between both organisations for up to three months, offering unique training and collaborative opportunities.

Gifts to support the Fellowship are welcome.



Staff Profile: Rob Lane



How long have you been working at Garvan and what were you doing before then?

I have been working at the Garvan for seven months as Engineering Manager and I'm pleased to say that time does fly when you are enjoying yourself !!! Before the Garvan I worked in a Business Development role for a company that supplies energy efficient technology for large buildings.

What do you enjoy about working at Garvan?

Knowing that I am a small part of an Institute that is trying to do good in the world.

Describe a typical day.

I get to work at 6.30 am and make sure that all is well within the building through an inspection tour and meeting with the rest of the engineering team. The rest of my day is made up of supporting the operations team, ensuring the engineering work is prioritised and completed in a timely manner and working with contractors on the various projects currently occurring throughout the Garvan. Most days I am out of the door by 5:00 pm.

What challenges are there working at Garvan?

The biggest challenge is keeping the building running smoothly and seamlessly while improving and maintaining the infrastructure, so that the real work can be done with a minimum of downtime and inconvenience. If we (engineering) are doing our job people should not have to do anything but enjoy their work and working environment.

What do you enjoy doing away from Garvan?

Spending as much time on the weekends with my family and, when I get an opportunity, cycling.

graysonline.com.au chooses to back Garvan

Group Managing Director, Cameron Poolman, is excited about the synergies between his business – graysonline.com.au – and the Garvan. He got to know Garvan Chief Operating Officer, John Dakin, and realised that there were many similarities between the two organisations: "John's passion was what first connected me with the Garvan. The culture at graysonline.com.au is also passionate. We have similar numbers of staff (400+); we're both innovative, Australian, non-bureaucratic and in growth phases; and we both continually benchmark our performance internationally and aim to improve. We're both aspirational companies."

graysonline.com.au is a phenomenal success story. The company was the largest traditional auctioneer in Australia, but changed its business model to online in 2000. Today grays delivers over 100,000 items per month nationally, sells over \$250 million annually and has grown its business fivefold. The company auctions everything from mining equipment to wine, IT products and even jewellery (particularly for the Garvan, where they auctioned choice pieces bequeathed by the Drs Ryan).

Poolman says: "How we act as a corporate citizen is extremely important to us. We wanted to build a philanthropic allegiance with one organisation and Garvan suited us: it stands for a lot of things that are important to grays". The company opted to support the purchase of a major high-tech piece of equipment in the flow cytometry facility.

To know exactly what company funds were supporting was important to Poolman: "We were reassured to know that the gift went directly to Garvan and made a tangible difference to not just one, but a number of research groups". Garvan looks forward to mutual growth with graysonline.com.au.



Chris Brownlee (L), who manages the Flow Cytometry Facility, thanks Cameron Poolman (R) for the valuable gift from graysonline.com.au

Young PhDs Spread their Wings

Three outstanding young Garvan researchers have received Merck Sharp and Dohme's 2008 Educational Scholarships, a sum of money awarded to a medical graduate undertaking a PhD at Garvan in bone or diabetes research. The Scholarships ensured Dr Alex Viardot, Dr Kerry-Lee Milner and Dr Sue Mei Lau were able to attend and present research findings at major international conferences.

Each of their research projects has considerable significance for the prevention or better therapy of insulin resistance and type 2 diabetes. Garvan is very grateful to Merck Sharp & Dohme for supporting this important travelling scholarship.

Dr Alex Viardot was also the recipient of the GlaxoSmithKline Don Chisholm Research Fellowship. Alex was appointed to the position following a global search. The role is dedicated to vital research into the causes of type 2 diabetes.



L to R back row: Luke Crowe, Michael Bramble and Alan Watts (Merck Sharp and Dohme), Prof David James (Director Diabetes and Obesity Program), Dr Alex Viardot and Colin Dienhoff (Merck Sharp and Dohme). L to R front row: Dr Sue Mei Lau and Dr Kerry-Lee Milner.

Garvan Open Day a Great Success



Tours were a popular Open Day attraction

The overwhelming response to Garvan Open Day left many staff and volunteers wondering if the Boxing Day sales had arrived. Visitors lined Victoria St outside the Garvan in anticipation of the doors opening. By the end of the day nearly 1000 visitors had come through our doors.

Over 80 scientists, staff and volunteers not only from Garvan, but from National Australia Bank, MLC, ASIC and BNP Paribas happily gave their time creating a great spirit of enthusiasm and collaboration. We wish to thank donors and their friends and families who joined us to find out more about our research.

Garvan intends to have another Open Day in 2010. In the meantime, if you would like an opportunity to go on a tour of the Garvan, tours run from 10am on the 1st and 3rd Thursday of each month. Bookings are essential, for more information please call 9295 8108.



Visitors arriving for Garvan Open Day

Great Australian Eulogies

Some of the most inspiring and touching eulogies written in Australia have been released in a new book, *Great Australian Eulogies*, edited by Richard Walsh and published by Allen and Unwin. The collection includes deeply moving tributes from Bob Carr to the Bali victims, Geoffrey Atherden to Ruth Cracknell, Richie Benaud to Sir Donald Bradman and Robert Oxenbould to Len Evans.

The contributors have generously donated half the royalties from the book to Garvan. By purchasing a copy you will be assisting Garvan's breakthrough medical research.

Volunteers Needed for Clinical Research Studies

We are currently recruiting for research studies, so if you meet the various prerequisites and if you are interested in helping our research in this way, we would like to hear from you.

OBESITY RESEARCH AND PRADER-WILLI SYNDROME

We need healthy, overweight, male and female volunteers, aged 18 to 45 years, preferably <170cm in height, to take part in a study looking at appetite regulating hormones as compared to patients with Prader-Willi Syndrome (a genetic defect causing obesity).

The study involves a meal study including metabolic tests (measurement of amount of fat and muscle mass, energy expenditure, and satiety hormones) during one or two mornings at the Garvan Institute.

If you are interested and suit the study criteria, please phone Trish Humphreys on (02) 9295 8215.

TYPE 2 DIABETES AND IMMUNE SYSTEM

We need volunteers who have at least 2 close relatives with type 2 diabetes, but who do not have

diabetes themselves. The study involves five visits to the Garvan Institute, and will focus on the status of the immune system and function.

If you are interested and fit the study criteria, please phone Trish Humphreys on (02) 9295 8215.

OSTEOPOROSIS RESEARCH

We are looking for male volunteers, aged 65 years or older who are not already on treatment for osteoporosis (thin bones) and have any of the following risk factors:

- low bone mineral density
- low body weight
- family history of osteoporosis

The study is testing an investigational medication for the treatment of male osteoporosis. During the two year study period participants will attend the Garvan on seven occasions.

If you are interested and wish to know whether you might be eligible, please contact Ruth Toppler on (02) 9295 8269 or Maureen Gaynor on (02) 9295 8255.

Coming Up

Garvan will start its 2009 Public Seminar Series with "Brain Power: harnessing the brain to fight disease". The seminar will look at the ways the brain influences physiological systems, such as weight management, bone formation and strength, and the immune system. Garvan scientists are investigating how the brain can be harnessed to manage disease conditions. Book early as seats are limited. To register call 02 9295 8110 or go to www.garvan.org.au

**Thursday 19th February 2009
10am-12:00pm (doors open at 9am)
Garvan Institute 384 Victoria Street
Darlinghurst**

The 2009 Free Public Seminar Series is generously sponsored by the Alcoa Foundation. Further details of the Series will be distributed shortly.

In memoriam July 08 - November 08

We gratefully acknowledge gifts received in memory of:

Sam Amuso
Clare Beggs
Albert Frank Bencsik
Ivars Bruzgulis
John Farrugia
Geoff Hewitt

Liz Humphery
Alina Jarvin
Muriel Jones
Lynne Joshua
Nick Levay
Joy Malouf

Vasiliki Merkouras
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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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