

Two-photon microscopy image of a lymph node showing the location of follicular memory T cells (represented by green spheres) in the B cell follicles (magenta) near the capsule (blue)

Making News

Memory immune cells that screen intruders as they enter lymph nodes

Scientists have discovered a new population of 'memory' immune cells, throwing light on what the body does when it sees a microbe for the second time. This insight, and others like it, will enable the development of more targeted and effective vaccines. Two of the key players in our immune systems are white blood cells known as 'T cells' and 'B cells'. B cells make antibodies, and T cells either help B cells make antibodies, or else kill invading microbes. B cells and killer T cells are known to leave behind 'memory' cells to patrol the body, after they have subdued an infection. The newly identified 'Follicular Memory T cells' are related to the T helper cells. However, unlike circulating memory B and T cells, they position themselves near the entrance of lymph nodes, particularly those that are potential sites of microbe re-entry.

The switch that might tame the most aggressive of breast cancers

Researchers have found that so-called 'triple-negative breast cancers' are two distinct diseases that likely originate from different cell types. The aggressive form of triple-negative breast cancer appears to arise from stem cells, while the more benign form appears to arise from specialised cells. This helps explain why survival prospects for women with the diagnosis tend to be either very good or very bad. The Garvan team has found a gene that drives the aggressive disease, and hopes to find a way to 'switch it off'.

An enzyme that enables the pathway to diabetes

Garvan scientists believe they have identified an enzyme, known as 'NIK kinase' that undermines the delicately balanced whole-body system that keeps blood sugar levels stable and low in healthy people. The disruption of this system can lead to diabetes. NIK kinase undermines this system by causing dysfunction in the three major diabetes players: the pancreas, the liver and muscle. NIK kinase activates a signaling pathway that affects many genes, switching some on and others off. The next step is to prove that NIK is a drug worthy target. Garvan is working with a California-based biotech company to do that, and hope to have results by the end of this year.

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From the CEO

You may recall that last year, the Garvan Institute was one of the first in the world to obtain technology that can sequence a whole human genome at a base cost of \$US 1,000. This acquisition has since accelerated Garvan's medical research. In the not-too-distant-future, it will provide widespread medical benefits, with significantly lower health costs, through early prevention and more targeted treatments – also known as 'personalised medicine'.

Today, Garvan researchers are using this genome-sequencing technology to find ways to improve early disease detection, improve treatments and, ideally prevent common, yet devastating diseases. These include cancer, diabetes and obesity, Alzheimer's and Parkinson's disease, hearing loss, osteoporosis, asthma, rheumatoid arthritis and multiple sclerosis.

Personalised medicine uses an individual's genetic information to help inform decisions about that person's risk of disease and approaches to treatment. In this way, the medical practitioners will be using this uniquely personal information to help guide health-related decisions.

This is a critical time for the development of personalised medicine. If we think specifically about cancer treatments, they have traditionally been very toxic and may have life-limiting consequences. There is no point using treatments that won't work and may, in fact, cause harm.

All too often cancers are detected too late to cure them. So, while it is important that doctors use the right drug in the right person, it is just as important that they understand who is at risk. This will mean that the medical community can direct its efforts at early detection in the most effective way.

For more information about Garvan's genome-based research, I encourage you to visit our website - www.garvan.org.au – or register for one of our free public tours.



Andrew Giles, Chief Executive Officer
Garvan Research Foundation

Garvan welcomes Professor Mark Febbraio

Garvan is very pleased to announce that Professor Mark Febbraio has joined us as Head of the Diabetes and Metabolism Division.

Previously, Professor Mark Febbraio ran a laboratory in Cellular and Molecular Metabolism at Melbourne's Baker IDI Heart and Diabetes Institute, and will continue his research at Garvan.

For the last decade, Professor Febbraio has been examining cellular and molecular mechanisms underlying obesity-induced insulin resistance, a precursor of diabetes. He has identified several promising target molecules and aims to develop new drugs to treat diabetes.

You can read more about Professor Febbraio, and his work on page 6.

Recipient of the inaugural Connie Johnson Fellowship in Breast Cancer announced

The recipient of the inaugural Connie Johnson Fellowship in Breast Cancer at the Garvan Institute was announced recently at Parliament House, Canberra.

The Fellowship, funded by the hugely successful *Love Your Sister* campaign, will support Dr Elgene Lim. Dr Lim is an outstanding breast cancer researcher who will take up the position as Principle Research Fellow in Garvan's Genomic Cancer Medicine Laboratory.

According to Connie, the development of the Connie Johnson Fellowship in Breast Cancer Research is an important step in achieving *Love Your Sister's* goal – ensuring no other young mum has to lose her life to breast cancer.

"We are incredibly proud of what we've achieved since Sam set out on his unicycle two years ago, and we are hugely grateful to the supporters who have helped us raise money for Garvan's cancer research," said Connie.

Dr Lim will take up his position at Garvan in the coming weeks.



Dr Elgene Lim and Connie Johnson

Professor Clark elected Fellow of the Australian Academy of Science

Congratulations to Professor Susan Clark, Head of the Genomics and Epigenetics Division, who was elected Fellow of the Australian Academy of Science in recognition of her outstanding contributions to science and scientific research.

Professor Clark is one of 21 new Fellows, 9 women and 12 men, to be elected in 2015 from around Australia and across all the natural sciences. The Academy now numbers a total of 503 Fellows.

Academy President Professor Andrew Holmes said, "Election to the Academy celebrates excellence and recognises contributions to science of the highest order."



Professor Sue Clark and Academy President
Professor Andrew Holmes
Mark Graham/Australian Academy of Science

To read more about Professor Clark and her work, visit www.garvan.org.au

Use your Smartphone to help fast track our cancer research

Vodafone Foundation has launched DreamLab, a world first Smartphone app that allows Australians to use the power of their phone to help speed up Garvan's cancer research.

When your Smartphone is fully charged, it will process a tiny research problem and send the result back to the cancer research team at Garvan. It's like working on a giant crossword with everyone solving a different clue.

Huge advances in DNA sequencing technology have enabled rapid and affordable sequencing of cancer genomes, creating a virtual tsunami of genetic information.

However, progress is limited by the huge computing power and associated expense required to analyse this information.

"There are many research questions that we want to ask, but some are just too computationally expensive, so we'd never dream of being able to ask them, or it would take us years and years. Vodafone's DreamLab gives us a free and dedicated virtual supercomputer to accelerate our cancer research" said Dr Warren Kaplan, Chief of Informatics at Garvan.

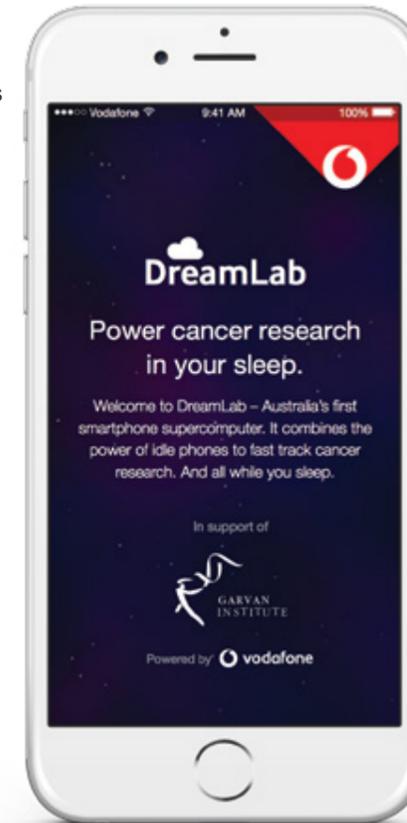
DreamLab will provide the computing power needed to run simulations to analyse and group cancers based on their genetic profile (rather than the cancer's tissue of origin). These new profiles will help researchers understand how different patients respond differently to various drugs, help predict which patients will benefit, and help find completely new strategies for treating cancer.

DreamLab is an online app so it needs data to work, but it's small and you can set your monthly contribution limit and choose whether to give on your mobile network, or on WIFI. If you're with Vodafone, the data you contribute on the Vodafone network will be free.

"Our three-year partnership with Garvan is part of our commitment to helping charities harness the power of mobile technology to improve the health of Australians", said Alyssa Jones, Head of Vodafone Foundation.

"We hope Garvan's already generous supporters will consider this a fun and easy way to provide additional support for medical research."

Download the DreamLab app now from the App Store or Google Play. For more information visit vodafone.com.au/dreamlab



Mrs and Mr Ann and Henry Roth

More than 20-years of invaluable support

Garvan is honoured to have the ongoing support of The Roth Charitable Foundation. Established in 1989 by Henry and Ann Roth, the Foundation honours the memory of Henry's father, sister and brother and the other six million Jews who were murdered in the Holocaust.

Garvan's relationship with the Roth Charitable Foundation began in 1994, when Henry's sons, John and Stanley, expanded the Foundation. At this time, they began supporting Garvan's breakthrough medical research, with a particular interest in dementia and Parkinson's disease.

In 2014, the Roth Charitable Foundation became a Garvan 'Life Governor' and renewed its support in 2015 with the establishment of the Roth Foundation Fellowship for Dr Bryce Vissel. Dr Bryce Vissel, head of Garvan's Neurodegenerative Diseases Laboratory is proud to be the Roth Foundation Fellow.

Dr Vissel and his team are focused on understanding disease mechanisms and discovering new potential therapies for the treatment of Alzheimer's disease, Parkinson's disease and spinal disorders. The Roth Charitable Foundation's long-standing support for Dr Vissel's work has been essential in enabling novel, robust research that would not otherwise have been possible.

"My brother and I are proud to honour the memory of our late parents by stepping up our level of support for the vital work of the Garvan Institute of Medical Research, and in particular that of Dr Vissel. We believe that Dr Vissel's neurological research has a huge potential to improve health outcomes and quality of life for the elderly, the numbers of whom are of course rapidly growing due to breakthroughs in the treatment of other illnesses and diseases," said Stanley Roth.

There are many millions of people affected by neurodegenerative diseases like Alzheimer's but there are currently no effective treatments that can slow or halt them. The generous, long-standing support of the Roth Charitable Foundation allows Dr Vissel's team to pursue alternative ideas through long-term research that could change the way we understand these diseases. Their ultimate goal, with this support, is to contribute to altered health outcomes for the many people worldwide who face the prospect of these devastating diseases.

The starving brain

In this article, Professor Herbert Herzog explains how specific neurons, as well as brain and gut hormones influence metabolic balance. More specifically, how, when deregulated, these hormones can contribute to the development of obesity or, the other extreme, anorexia nervosa.

For humans to maintain a constant and healthy weight, we need to correctly regulate our energy. This means regulating both our intake of energy – ie our food or calories, and our energy use. Maintaining a state of energy homeostasis (or balance), is a whole organism, multi-organ process. Whilst aspects we can control such as eating and our physical activity are involved; there are also cellular processes which are critical in overall energy balance and body composition. These include processes which control where and in which form energy is stored (called energy partitioning) and which energy stores will be used to retrieve energy. Energy can be stored and used from fat, muscle or bone.

Within the brain, a structure called the hypothalamus is the critical area for controlling appetite and the regulation of energy. Located in an area of the brain that has access to blood born factors and hormones, it receives vital information about the acute, as well as chronic energy status and energy requirements of the body. This information is then integrated into a complex neuronal network within the brain to adjust behaviours (such as feeding or eating), as well as to coordinate the adaptations to energy demand of different organs in the body, and that of the brain itself.

The two major populations of neuronal cells that are responsible for the communication of this vital information are the Neuropeptide Y (NPY) – the ‘feeding and energy conserving neurons’ and the opposing proopiomelanocortin neurons that mediate ‘satiety and the increase of energy expenditure’.

The work of our group over the last two decades has focused on the role of these NPY neurons. By using a variety of model systems we now have a clearer picture of what can go wrong,

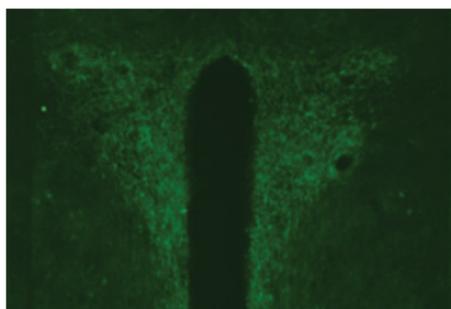
why obesity can occur, and why it is so hard to reduce weight. Importantly, we also discovered that the NPY system is not only critical for the feeding related aspects, but also plays a critical role in controlling energy demanding processes such as bone formation, reproduction and temperature control.

What happens when energy supply fluctuates

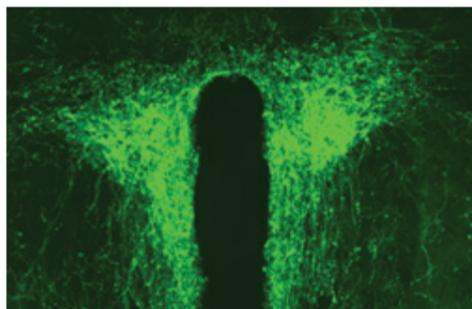
Under normal conditions NPY levels are strictly controlled. When one doesn’t eat, levels of NPY rise sharply. High levels of NPY signal to the body that it is in ‘starvation mode’ and it should try to replenish and conserve as much energy as possible. That leads to hunger and the drive to eat, as well as to reserve fat stores and use energy from other stores such as bone. When energy stores are replenished, NPY levels are reduced, as is the drive to eat.

Energy supply fluctuates on a daily basis. The short term fluctuations in food supply can be managed with relative ease by the body through this NPY pathway. However, when a period of energy oversupply continues over a longer period, such as with a long term increase in diet, somehow the normal regulatory processes that would reduce NPY levels are no longer fully functional.

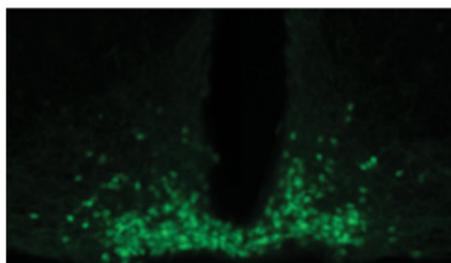
This can then result in a situation where NPY levels are chronically elevated and the brain wrongly believes it is in a starvation situation. This further drives the urge to eat and preserve energy stores in the form of fat, even when there is no need for it. Even worse, when obese people then try to diet, this starvation response is enhanced. It is like trying to put the brakes on, while some other mechanism simultaneously presses the accelerator.



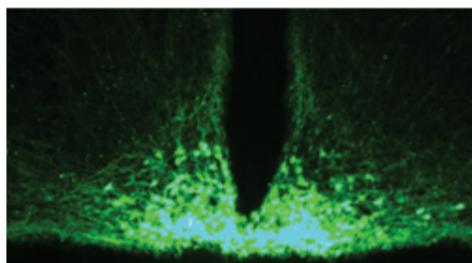
Brain NPY - Fed



Brain NPY - Starving



Brain NPY - Fed



Brain NPY - Starving

Starvation markedly increases NPY levels (indicated by the green signals in the images) in the brain.



Professor Herbert Herzog

“WHEN ENERGY OVERSUPPLY CONTINUES OVER A LONGER PERIOD...THE BRAIN WRONGLY BELIEVES IT IS IN A STARVATION SITUATION.”

Obesity is a modern epidemic

Evolution has provided us with these mechanisms to help us survive famine, and for most of human history, food oversupply was not an issue. So in evolutionary terms, it was unlikely that people were going to get very fat and mechanisms were only put in place to prevent us from losing weight.

Obesity is a modern epidemic, and the challenge will be to find ways of tricking the body into losing weight. That will mean somehow circumventing or manipulating this NPY circuit, probably with drugs.

Why do some people develop obesity, while others don't?

One interesting question is, why do some individuals on a particular diet develop obesity, while others on the same diet and lifestyle do not? By identifying genes that contribute to this, we hope to provide important new insights into the regulation of energy balance and help to identify potential new targets for obesity treatment.

To achieve this, we are currently performing a systematic dissection of the neural genes involved in the regulation of appetite and energy homeostasis using a technique that allows us to eliminate every gene in the fruit fly. Following this neuronal knockout, we monitor these flies for food intake and group them into low and high food intake categories.

Flies that show significant increase or decrease in food intake are then tested for neural regulation of whole body fat content, as well as alterations in energy expenditure.

We are particularly interested in the genes that lead to flies being fat, despite eating less; and flies that are lean, despite eating more. These candidate genes are then compared to human genetic studies, and the most promising genes will then be assessed in detail in other models.

Future research into eating disorders

The combination of molecular genetic and physiological techniques has allowed for great progress in identifying metabolic hormones and establishing their relationship to key neuronal systems controlling appetite, satiety and energy homeostasis. However, many questions regarding the regulation of food intake and energy homeostasis still remain unanswered.

It is important to understand the process of how the brain networks integrate peripheral signals that communicate energy levels to brain pathways, regulating energy balance.

The vast number of neuronal connections has made this a very difficult task. However, recent advances employing viral delivery systems in combination with sophisticated ‘Designer Receptors Exclusively Activated by Designer Drugs’ technology, has opened up new possibilities to get detailed insights into these complex networks and the identification of novel targets.

Garvan researchers hope to use this technology to identify targets that could be used as potential drug targets for conditions like obesity or anorexia.

Ask Garvan

Q: I have heard that Garvan has an online quiz. What is the purpose of the quiz, and where can I find it?

A: Yes, Garvan has produced a fun, online quiz that aims to engage and educate anyone who has an interest in medical science and research.



You can check how much you really know, learn about some of the work being carried out at Garvan, and why your support is vital.

Examples of some of the quiz questions include:

If you stretched out all the DNA from one human cell, how far would it go?

- A. 2 metres
- B. To the moon and back
- C. 12 metres
- D. No one knows

What percentage of fruit fly genes are similar to human genes?

- A. 35%
- B. 70%
- C. 10%
- D. 90%

How do you think you went? You can check your answers on the bottom of page 6. To have a go at some other fun questions, visit take.garvanquiz.org.au

In Celebration

Kevin Curby's Birthday

Frank Danieli and Aleksandra Masi's Wedding

Jared Dwyer and Rebecca Heys Wedding

Jess Hocking's Birthday (In memory of her sister Mia)

In Celebration of Dr Wendi Everton & Ms Norma Vivar





Staff Profile: Bronwyn Terrill

Can you give us a brief outline of your recent work history?

I've been a science communicator, writer and educator, specialising in genetics and molecular biology, for more than twenty years.

This is my first role back in Australia after 10 years working abroad in the UK and USA. In New York, I worked as a multimedia producer for Cold Spring Harbor Laboratory's Dolan DNA Learning Center, developing museum-style exhibitions and online educational resources about DNA and molecular biology of cancer. I then moved to Europe's largest genome centre – the Wellcome Trust Sanger Institute in Cambridge, UK – to set up and maintain its Public Engagement program. There, I led a team who ran onsite tours and education programs, developed genomics-focused online resources, and supported researchers in public-facing collaborations such as exhibitions, broadcast productions and alternate reality games.

When I arrived back in Australia, the Garvan Institute, with its investment and ambition in genomics, was really the only place for me to work.

What does your role at Garvan involve?

My role at Garvan is to plan and develop educational programs for communities and professionals about aspects of genomic medicine. If this research is going to transform medicine, there is a lot of work to do to ensure that it's used responsibly. This is a really varied role that builds on my previous experience across all types of media. I coordinate events, develop resources and generally talk with a lot of people about DNA, genomes and health.

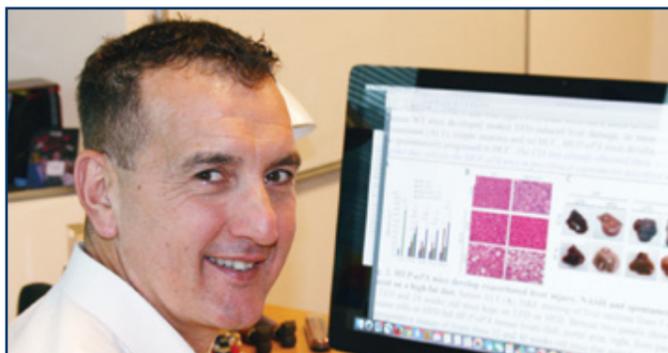
I am also involved in research collaborations that provide important insights for my practice, such as a NSW collaboration to understand clinicians' educational needs in genomic medicine, and an Australian Research Council-funded national consortium that is exploring Australians' expectations about personal genomics.

What inspires you about your work?

I'm particularly inspired by the close clinical relationships throughout Garvan. My previous roles have been one or more steps removed from the clinic. In Garvan, and particularly within the Kinghorn Centre for Clinical Genomics, I have the opportunity to work directly with clinicians who are using genomics to refine and extend their practice, while their clinical questions and data drive the next generation of research.

What do you enjoy doing in your spare time?

My spare time is spent exploring Sydney's beautiful parks and beaches with my husband and two girls, aged 4 and 6. After years in London and New York, we realise how lucky we are to be able to spend time outdoors all year round. I'm also completing my Master of Education thesis; so there's never really enough time to spare!



Staff Profile: Professor Mark Febbraio

What is the current focus of your work?

Our work aims to translate basic science discoveries into new therapeutics for disease. Even though I'm head of the Diabetes and Metabolism division, my work is not just about diabetes and metabolism. Rather, it is about pathways that regulate disease per se.

One of those pathways is the activation of a specific species of Heat Shock Protein (HSP) called HSP72. HSPs are a family of proteins produced by cells in response to exposure to stressful conditions. About 10 years ago we discovered that activating HSP72 can prevent insulin resistance which is the pre-cursor for diabetes.

That led to me forming a partnership with a bio-tech company called N-Gene Pharmaceuticals, of which I am a Honorary Chief Scientific Officer. Our lead molecule is called BGP-15 and is currently in a multicentre clinical trial for the treatment of Type 2 diabetes. We have shown that the drug and the activation of HSP72 may also have clinical efficacy for other diseases including Duchenne Muscular Dystrophy, Atrial Fibrillation and potentially, the drug could be used to improve fertility in obese women.

About 15 years ago, we discovered that skeletal muscle secretes Interleukin-6 (IL-6) and we coined the term 'myokine'.

Myokines are small proteins and peptides that are produced and released by muscle cells in response to muscular contractions. Once released, myokines travel through the circulatory system to other organs, altering the biology of those organs, and can play a role in protecting against metabolic disease, brain disorders and certain cancers. Now, many people work on myokines all around the world. We have synthesised a protein that we've called IC-7, and this is currently in non-human studies of Type 2 diabetes. We're hoping to take that into human work next year.

What is the biggest challenge in your area of research?

The biggest challenge for a researcher is finding the funds to do the work. The uncertainty – not knowing until October how many people I'm going to be able to hire next year – it's frustrating. Every other part of the job is an absolute joy. I honestly feel so privileged to do this work, and to have this position. I feel privileged to be a NHMRC-funded researcher. As such, I do see myself as a servant to tax payers, and that is why I always try and translate my research into clinical outcomes because I feel it is important to get cures and treatments for the diseases I work on.

What inspires you about Garvan's work?

Garvan has three things that really make it a great place to work. There is a good vibe – the people are generally just really nice to each other. They respect each other. In particular, it is a joy to work with the people in my division. They asked for me to come to Garvan, and that is a real honour for me. The collegiality among the senior scientists at Garvan is wonderful, and to a degree that I've not experienced before. A scientific organisation will work best if everybody parks their ego at the front door, and that is definitely the case at Garvan. Finally, and quite simply, Garvan's scientific excellence. This, combined with the leadership will keep Garvan at the forefront of medical research in Australia.

What do you enjoy doing away from Garvan?

By far, the most important thing to me is my two daughters. I am also an absolute exercise junkie. I used to be a professional triathlete, and I still exercise every day. I also have a passion for good food and wine. I love cooking and eating...at home, my kitchen is my lab!

Fashion Targets Breast Cancer is back

Garvan is thrilled to announce that it has obtained the Australian licence for Fashion Targets Breast Cancer. Since its inception in 1994, this highly successful international campaign, supported by some of the world's leading fashion brands and personalities, has run in 14 countries and raised more than US \$50 million for breast cancer research and health services globally.

The 2015 Australian campaign will raise funds for Garvan's breast cancer research. From 1 September, a limited edition fundraising t-shirt, designed by renowned New Zealand designer, Karen Walker, will go on sale through THE ICONIC, Australia's leading online fashion retailer.

Mr Andrew Giles, CEO of the Garvan Research Foundation says Fashion Targets Breast Cancer is an exciting opportunity. "At Garvan, we are always looking for ways to engage and inform people of all ages. Fashion Targets Breast Cancer is a unique and exciting opportunity for Garvan to broaden its reach in the community, while raising vital funds for the promising breast cancer research being carried out every day in Garvan's labs. We are thrilled to have this opportunity, and I encourage everyone to consider purchasing a limited edition, designer t-shirt in support of Garvan's important work."



To purchase your t-shirt, visit www.theiconic.com.au/ftbc from 1 September onwards. Hurry – stocks are limited!

Tee off at Tulip Time

Join us for a round of golf and raise vital funds for medical research on Friday 18 September at Mount Broughton Golf and Country Club, Sutton Forest (129km south-west of Sydney).

The Garvan Research Foundation and 2015 Tulip Time Festival are joining forces to raise funds and support the breakthrough medical research of the Garvan Institute of Medical Research.

By playing a round of golf, you'll help Garvan to pioneer research into major diseases affecting our community today.

For more information, or to register for the Golf Day, call Leigh Metham on (02) 9295 8115, or email l.metham@garvan.org.au

Join us for a tour

Throughout the Tulip Time Festival, Garvan is offering the opportunity to tour the Australian BioResources (ABR) facility in Moss Vale, an important mouse-based resource for medical research institutes and universities throughout Australia.

Tours will be held on Thursday 17, Friday 18, Thursday 24 and Friday 25 September at 10.30am. To book your place on one of the tours, visit www.giving.garvan.org.au/register-now or phone (02) 9295 8115. Spaces are limited, so book now to avoid disappointment.



Left to right: Mr Neil Perry AM, Mr Guillaume Brahimi and Ms Virginia Trioli

Black tie events support Garvan's research

Garvan supporters have had two chances to don their best dress or suit recently.

The annual Garvan Gala was a huge success, raising important funds for Garvan's Breakthrough Fund – helping Garvan to recruit some of the world's best scientists.

Held on Saturday, 2 May at the Sofitel Sydney Wentworth, guests enjoyed a menu designed by chefs Neil Perry AM and Guillaume Brahimi. The MC was ABC News Breakfast presenter, Ms Virginia Trioli who kept guests entertained, as did performer Anja Nissan (winner of The Voice 2014).

The Young Garvan All Ribbons Ball was also held at the Sofitel Sydney Wentworth on Saturday, 18 July. This annual five star, black tie fundraising ball featured live and silent auctions, a fantastic entertainment line-up including Casey Burgess and Jellybean Jam. The guest speaker was global entrepreneur and owner of O Bar and Dining, Michael Moore. During the evening, the 2015 Young Garvan Award was presented to Dr David Croucher, Group Leader in Garvan's Cancer division.

Thank you to all who attended these events, and all who donated the hotly-contested 'money-can't-buy' auction items. We are extremely grateful for your ongoing support, and for recognising the true value of medical research.

