Making NEWS

Losing six kilograms reduces artery stiffness by 20 per cent in obese people with Type 2 diabetes. Diabetes carries a six-fold greater risk of heart disease due to atherosclerosis, or hardening of the arteries. Garvan’s Associate Professor Katherine Samaras and Associate Professor Christopher Hayward from St. Vincent’s Hospital have shown that arterial stiffness is directly associated with inflammation – that is, activation of white blood cells and genes that regulate inflammation.

Garvan researchers Dr Lowenna Holt, Associate Professor Greg Cooney and Professor Roger Daly have identified a gene that regulates muscle size, a finding that could help unlock therapies for Type 2 diabetes and diseases such as muscular dystrophy, where muscles are weakened and damaged. While researching ways to improve the response of muscle to insulin, they observed that a particular strain of genetically modified mice – missing the Grb10 protein – had large muscles. Even newborn mice missing Grb10 had larger muscles, indicating that this protein regulates muscle development before birth.

A biological phenomenon known as ‘somatic reversion’ – when an abnormal gene spontaneously becomes normal again – explains why some patients with a rare immunodeficiency known as X-linked lymphoproliferative disease (XLP) live much longer than expected. Many XLP patients die before they reach 10 years of age, and the majority have a life expectancy of less than 40 years. However, Garvan researchers Dr Umaimainthan Palendira and Associate Professor Stuart Tangye discovered that a substantial percentage lived much longer than expected, even approaching the age of 50.

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From the CEO

The past few months have been an exciting period for Garvan. As well as important breakthroughs that you can read about in this issue, we have been fortunate to have some of the world’s very best scientists and researchers visit the campus to share insights.

Some of the major visitors were Professor John Stamatoyannopoulos from the University of Washington (Seattle) Genome Center and Professor Yehiel Zick and Professor Michael Walker from the Weizmann Institute of Science, Israel.

A particular highlight was a visit by Professor Elizabeth Blackburn, the first Australian woman to win a Nobel Prize, who gave a lecture particularly aimed at engaging with high school students considering a career in science. She gave her talk, ‘From Tasmanian Schoolgirl to Nobel Laureate’, to a packed Garvan Auditorium made up of school students from across NSW and Garvan researchers – all of whom left inspired.

Of course, a major ongoing highlight has been to see The Kinghorn Cancer Centre steady rise from the ground as it approaches completion, ready for occupation by both Garvan researchers and clinicians from St Vincent’s. As this issue goes to print, we will be rapidly approaching our opening date of 28 August 2012.

The Kinghorn Cancer Centre – like much of the work undertaken here at Garvan – takes place thanks to the generosity of the general public. Thank you for your ongoing support.

Yours sincerely,
Andrew Giles
Garvan Research Foundation

Professor Elizabeth Blackburn talks with students from Wenona School.

Opinion

Medical research institutes and medical scientists are motivated by the quest to cure or, preferably, prevent human disease. In Australia and other advanced countries, the defeat of most infectious diseases means that the major health burden has switched to the more complex diseases like cancer, osteoporosis and neurodegenerative diseases that, regrettably, increase with age.

This is true in cancer where, over the past 30 years, identifying the genes that are mutated in cancer was the prerequisite to the development of drugs to block them. The same is true of osteoporosis – a silent killer, as many people die within months to a few years of a major fracture, yet we don’t know who will die or why. However we do know that treatment reduces the risk of fractures and of premature death. We need to find out whom we need to target.

The trouble is, we do not yet understand the origins of osteoporosis or neurodegenerative diseases like Parkinson’s and Alzheimer’s disease. We also do not have a good understanding of how bone strength is regulated, nor how the brain functions.

Garvan has major research programs in these areas, and a team of extraordinarily gifted and dedicated individuals who spend most of their waking hours wrestling with these questions. We take a strategic approach that, on the one hand, investigates promising leads in the hope of making immediate improvements in diagnosis and treatment while, on the other, tries to understand the fundamentals of the processes involved, giving insights and clues for the future.

I hope that you will join us by supporting both targeted projects and our efforts in the underpinning science. Sometimes progress seems frustratingly slow, but we can take heart from the extraordinary pace of change. It is only just over 200 years since the first atomic table, and only 70 years – one lifetime – since the development of penicillin. All we can say about the future is that things will change faster than we think, but usually not in the way that we think.

Comedian Paul Martell did an outstanding job as MC, and kept the audience in stitches. Talented performers included The Sydney International Orchestra; The Australian Army Band; Sydney; VIX – The Sydney Philharmonia Youth Choir; Jane Scatt; Scott Redburn; Erin James, The Macquarie Singers; Adam Scicluna, and Jenny Liu. Young performers Harry Ward on violin, Brian Kim on flute and singer Fabian Andrés gave rousing performances.

The audience was also privileged to hear musical arrangements by the great Australian Maestro, Dr Tommy Tycho AM MBE, who attended the concert. From classical and contemporary music, to opera and comedy, through to the stirring patriotic finale that left the audience with goose bumps – the Garvan Australian Spectacular really did have something for everyone.

We would like to sincerely thank the organising committee – Dr Steve Watson, Ken Lang AM and especially Pauline Cash Cumming, as well as all performers, staff and volunteers who gave so generously to make this concert such a success. Funds raised at the Garvan Australian Spectacular were donated to the Garvan Institute of Medical Research.
breakthrough

Feature story: Understanding the most complex organ in the human body – the brain

Garvan's Neurological Diseases Division aims to increase our understanding of fundamental processes in the brain and the neuronal systems involved in disorders such as Parkinson's disease, Alzheimer's disease, schizophrenia, eating disorders and hearing loss.

Recently, the program has expanded its interest to another major organ of the body that interacts with other organs in the body and, for example, how it controls bone formation, as well as the brain's role in the regulation of pain. This research aims to identify new therapeutic approaches in these areas, with specific interest in regenerating the nervous system for therapeutic purposes. It also aims to achieve a better understanding of the brain's control of body functions including the regulation of energy balance (intake and expenditure), which can affect fertility, mood, weight gain and physical fitness.

In this article, we highlight Garvan's work in Parkinson's disease, Alzheimer's disease, eating disorders and pain research. We discuss some of Garvan's recent findings in these areas, and how these findings increase our understanding of the most complex organ in the human body – the brain.

Parkinson's disease

It is estimated that one in every 350 Australians is living with Parkinson's disease, and each day, 30 new cases are diagnosed.

The symptoms of Parkinson's disease result from the progressive degeneration of neurons in the midbrain. Neurons in this part of the brain control the release of a neurotransmitter called dopamine. Dopamine stimulates motor neurons – nerve cells that control the muscles. When dopamine production declines, the motor system nerves are unable to control movement and coordination. By the time of diagnosis, the movement and coordination of patients with Parkinson's disease are affected.

Although there are many theories about the cause of Parkinson's disease, so far none have been confirmed. A few cases have been shown to be inherited and have been traced to mutations in four different genes, including the alpha-synuclein gene that Garvan is investigating.

Garvan's researchers are taking a range of approaches to investigate Parkinson's disease, particularly focusing on researching the mechanisms behind this degeneration.

We know that certain pesticides, toxins and genes (such as the alpha-synuclein gene) cause Parkinson's disease, but why the cause of the disease is not fully understood. A gene called Parkin is a candidate for playing a role in Parkinson's disease.

Another aspect of Garvan's research is investigating the mechanisms behind the release and control of dopamine in the brain. Once the basic pathology of Parkinson's disease is understood, we can develop a therapeutic approach to treat the disease and restore movement control.

Advances in whole genome and exome (the genetic information present on the DNA or genomes) sequencing techniques now make it possible to identify disease-relevant genetic variants and sequencing RNA as associated with sporadic and familial Parkinson's disease.

This capability means Garvan researchers are in a position to use our expertise in areas like gene discovery; the cell biology and molecular biology of Parkinson's disease; our access to animal models of Parkinson's; and our expertise in drug discovery to advance the development of new therapeutic approaches for Parkinson's disease.

Another exciting research project involves seeing how we can harness the brain's own adult stem cells which normally function to repair the brain and form new nerve cell connections, to potentially help treat Parkinson's disease, as well as other neurodegenerative or neurological disorders. To do this, Garvan's Adult Stem Cell Group studies neural stem cells, isolated from the adult olfactory neuroepithelium (situated in the nose) and grown in the laboratory in the form of oligodendrocyte progenitors. The aim is to isolate, identify and test lines of these cells to determine whether they can be used to form new neurons in the central nervous system of patients who have Parkinson's disease.

At Garvan, we are taking a range of approaches to investigate Alzheimer's disease. Our scientists are researching the mechanisms at the synapses (where one neuron makes a connection to another) that are important in memory formation. We are trying to understand if these mechanisms are somehow involved in the neuron dying in Alzheimer's disease.

Recently, Garvan researchers demonstrated a significant biochemical change in a protein called CEMP2. This change appears to occur specifically in the brains of people with Alzheimer's disease, but not in other forms of dementia. It also appears to be present in the animal models of Parkinson's; and our expertise in drug discovery to advance the development of new therapeutic approaches for Alzheimer's disease.

Although the sporadic form of Alzheimer's disease has similar pathology to the familial forms – sporadic and familial. The sporadic form is the most common. Although the sporadic form of Alzheimer's disease is the most common, we are particularly interested in a new gene called Bin1 that is genetically associated with the predominant sporadic form of the disease. We have found that it is controlled by an important brain enzyme called GSK3. Importantly, we have shown that Bin1 is important for survival of neurons in flies, suggesting that defects in GSK3-Bin1 signalling could contribute to neuron death in Alzheimer's patients. We believe this provides a novel therapeutic strategy to help protect neurons from dying and slow the rate of neurodegeneration.

Alzheimer's disease

Alzheimer's disease is a degenerative condition of the brain, characterised by the loss of memory and cognitive function. Although there is no cure for Alzheimer's disease yet, it can be managed and the symptoms alleviated for a time. A person may live anywhere from three to 10 years with Alzheimer's disease, with the average length being seven years.

In 2012, it is estimated that more than 278,000 Australians are living with dementia. Alzheimer's disease is the most common type of dementia, and presents in two forms – sporadic and familial. The sporadic form of the disease is usually diagnosed after the age of 65 and is by far the most common. In the less common familial form, the disease runs in families and usually affects people aged in their 40s or 50s.

Pain research

It is thought that more than 50 per cent of the population will experience some form of chronic pain within their life, especially patients that suffer from arthritis, cancer, diabetes, migraine, or nerve injuries. Despite the astonishing prevalence, there are few effective therapeutic options for these patients.

One of the major goals of Garvan's Neuro-Pain Research Group is to identify and characterise new genes that participate in the severity of chronic pain, with the aim to develop a new generation of therapeutics for this debilitating condition.

To this end, Garvan researchers have developed a novel, systematic strategy for identifying new components of the pain pathway using the fruit fly - Drosophila melanogaster. 70 per cent of human disease genes have an equivalent

Neural stem cells growing in culture. Neural stem cells have the potential to be used as a therapeutic cell-based therapy to treat Neurodegenerative disorders. These neural stem cells have grown into neural cells supporting their survival.
Staff Profile: Romain Rouet

What is the current focus of your work?
I am a PhD student and member of the Antibody Engineering laboratory at the Garvan Institute (under the supervision of Dr Daniel Christ). Antibodies are effector molecules the immune system produces to fight bacteria and viruses. However, in recent years they have also been increasingly used as drugs by changing their specificity to kill cancer cells and to reduce their toxicity.

In the Antibody Engineering laboratory we have two major aims: to generate new anti-cancer antibody drugs and to identify strategies to increase their stability. I mainly work on the second aspect – stability. This is a major problem for the pharmaceutical industry, which is currently unable to take many promising drugs forward because of poor stability. The drugs simply “crash out” of solution and form insoluble aggregates.

What are some of the recent findings of your work?
I have been able to identify key residues within antibodies that control stability and tendency to aggregate. Moreover, together with my colleagues, I have been able to develop a general strategy to overcome this problem. This has created a lot of excitement and has recently been published in Proceedings of the National Academy of Sciences, which is the official journal of the US Academy of Sciences.

What is the biggest challenge in your area of research?
The biggest challenge is really to find a general approach to target aggregation – a strategy that suits most antibodies, independent of their specificity. Maintaining activity – the interaction with the antigen is the other major hurdle. We have been able to show that our method is so powerful, we can even improve existing drugs that are already on the market. With more than 50 per cent of all new drugs being antibodies, our work has the potential to dramatically improve how we develop targeted therapies.

What do you enjoy doing away from the lab?
I try to spend time exploring Sydney and the rest of Australia. It is really a beautiful country with many different landscapes. I have visited Queensland, Western Australia, Tasmania and now intend to go to the Northern Territory. I also enjoy running. I try to do a few races every year and this year, I hope to help the Garvan Chang Giants win the next CitySurf team competition.

Last year, you won the Castle Harlan Award. How has this benefited you and your work?
Thanks to the Castle Harlan Award, I was able to attend the PEGS Protein Engineering Summit 2012 in Boston (USA) in May. This is one of the key protein engineering conferences, with talks from leaders in the field. I was able to meet them, talk about their work and the challenges they faced.

In addition, I also started looking for potential post-doctoral positions. I will also visit industry collaborators in Cambridge (UK) in September. They have an extensive range of equipment that is not necessarily available in an academic environment. I plan on doing experiments there, to supplement our current work at Garvan.

Ask Garvan

Q: What is ‘translational research’?
A: Translation research sees scientific discoveries resulting from laboratory, clinical, or population studies, transformed into clinical applications that will reduce incidence, morbidity and mortality of disease.

The Kinghorn Cancer Centre, which is due to open in just a few weeks, will be an excellent example of this translational research (also known as ‘bedside to bench’) approach to cancer.

When it is fully operational, the 250-plus researchers and clinicians working in this purpose-built cancer centre will ensure that challenges faced in the clinic will drive laboratory research, and that laboratory research findings are applied quickly back into clinical care.

As well as state-of-the-art clinical and consulting rooms and laboratories, the centre will provide workspaces and meeting rooms so that researchers and clinicians can come together into multidisciplinary teams to exchange information and ideas about the diagnosis, treatment and care of cancers.

Life-saving diagnosis leads to 13-years of service

In 1997, Graham Curtis was diagnosed with acromegaly, a debilitating disease most commonly caused by a non-cancerous tumour on the pituitary gland.

It was under the care of Endocrinologist, Professor Ken Ho who, at the time was head of Garvan’s Pituitary Research Unit, that Graham first became aware of Garvan’s work.

“Professor Ho encouraged me to attend one of Garvan’s free public seminars. I was very impressed. At the end, I filled in a questionnaire and said I’d be interested in volunteering.” That interest resulted in 13-years of dedicated service.

“My motivation was simple. I felt that by volunteering at Garvan, I was in some way paying back Professor Ho and his team for saving my life. It was my way of returning the favour.”

It is this same motivation that has led Graham to also become a Garvan ‘Partner for the Future’ – one of a special group of people who have left a gift to Garvan in their will.

“There’s not a great deal of research being done into pituitary disorders, so I would particularly like my bequest to assist Garvan’s efforts in this area.”

To find out more about becoming a Garvan ‘Partner for the Future’, contact Carol O’Carroll on 02 9295 8117, or email c.ocarroll@garvan.org.au

Garvan’s Glittering Gala

On Saturday 12 May, Garvan hosted its second annual Garvan Gala, raising more than $400,000 for the John Shine Translational Research Fellowship Fund at Garvan.

Held at the Overseas Passenger Terminal, with a spectacular view of the harbour and the Sydney Opera House, VIP guests included The Hon. Tanya Plibersek MP – Federal Minister for Health and Ageing, and The Hon. Jillian Skinner MP – NSW Minister for Health and NSW Minister for Medical Research.

Guests were entertained throughout the evening by the MC, Walkley Award winning journalist Annabel Crabb, while they dined on an exquisite menu designed by Neil Perry. Award-winning soprano Greta Bradamon made her way through the room, thrilling guests with her outstanding performance.

Throughout the evening, guests had the chance to win a vast array of wonderful prizes. Many purchased a key to try and open a locked box containing a Paspaley South Sea Pearl Marquise Pendant with Tanzanite and Pavé Set Diamonds in Platinum on a Paspaley White Gold Chain, valued at $8,560. They also had the chance to guess the number of Lindt balls in a jar – the prize, of course, being the jar filled with 877 Lindt balls!

The exciting live auction featured fabulous prizes, including:

• The John Singleton Experience – helicopter flights, private tours, meals and a night’s accommodation at a number of Mr Singleton’s spectacular properties;

• Lunch with Michael Clarke aboard the luxury cruiser, Ghost II;

• Neil Perry cooking for a dinner party of ten in your home;

• A Leo Robba original artwork; and

• Two return business class QANTAS tickets to either London or New York, including five nights at a luxury Accor five star hotel.

The Silent Auction also generated excited bidding for prizes including:

• A luxury Thailand getaway;

• Opening night tickets to Madama Butterfly (Opera Australia);

• Opening night tickets to Signs of Life (Sydney Theatre Company);

• Tickets and Imusine transfers to the Bledisloe Cup at ANZ Stadium;

• Tickets and Imusine transfer to see Lady Gaga at Allphones Arena;

• An experience in a QANTAS flight simulator; and

• A framed, colour print of the winner’s DNA profile, to name a few.

Raffle prizes included trips to Hayman Island and Sheraton Mirage on the Gold Coast; lunch at Bathers Pavilion; RM Williams boots; Dinosaur Designs homewares; a box of Arras Tasmanian sparkling wine; a year’s supply of Movenpick ice-cream; a total Lindt experience, and a luxury hamper from Hampers Only.

Sincere thanks must go to all the generous sponsors and supporters who donated these wonderful prizes for the event.

Team Phil – Doing the hard yards for Pancreatic Cancer Research

In 2011, a group of runners calling themselves ‘Team Phil’ competed in the Melbourne Marathon Festival. They participated in memory of Philip Hemstritch, and many others who have lost their battle with pancreatic cancer. They raised an extraordinary $79,611.98 for Garvan’s pancreatic cancer research program, including its lead role in the Australian Pancreatic Cancer Genome Initiative.

Team Phil’s outstanding effort has led to the establishment of The Philip Hemstritch Fellowship in Pancreatic Cancer Research. This three-year Fellowship has recently been awarded to Garvan’s Dr Marina Pajic, a promising early career scientist.

Team Phil will again be competing in the Melbourne Marathon Festival on 14 October 2012. To join Team Phil or for more information, email jane.hemstritch@mac.com

L/R: Garvan Research Foundation CEO Mr Andrew Giles, Executive Director of the Garvan Institute Professor John Mattick AD FAA, Garvan Gala MC Ms Annabel Crabb, Garvan Research Foundation Chairman Mr Geoff Dixon, and Chairman of the Garvan Institute Mr Bill Ferris AC.
Clinical Studies

Study on Fat Metabolism
We are looking for healthy volunteers: men and postmenopausal women, aged 50-70 years for research into hormones and body fat. This study involves visits over a 14 week period to the Garvan to study the effects of three commonly used medications, oestrogen (women only), letrozole and tamoxifen on the burning of fat in the body. We will investigate how fat is utilised at whole body and liver level. For further information please contact Dr Vita Birzniece (02) 9295 8483, v.birzniece@garvan.org.au or Vanessa Travers (02) 9295 8232, v.travers@garvan.org.au (St Vincent’s Human Research Ethics Ref No 09/090).

Metabolism – Genetics of Obesity Study
Do you think you could be overweight? Volunteers are needed to screen for a gene that links to obesity at the Garvan Institute. It involves only one visit during which measurements and a blood test will be taken. If you are suitable, you may enter the second part of the study to receive a full metabolic assessment.
For further enquiries, please contact Dr Daniel Chen (02) 9295 8557 or d.chen@garvan.org.au, or Jen or Renee, (02) 9295 8215, j.evans@garvan.org.au (St Vincent’s Human Research Ethics Ref HREC/10/SVH/133).

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