



Making *NEWS*

Rapid reversal of diabetes after gastric banding surgery

Gastric banding brings about reversal of diabetes in some patients, and dramatic improvement of glucose tolerance in others, within 12 weeks. Professor Katherine Samaras, along with clinical researchers from Garvan and St Vincent's Hospital, followed 15 morbidly obese patients (body mass index over 40) after gastric banding surgery. All had Type 2 diabetes for at least five years, and most patients required anti-diabetic medications. Patients also showed significantly reduced inflammation – the numbers of circulating pro-inflammatory immune cells were much reduced, mirroring the degree by which glucose levels fell.

A smart way of using testosterone to prevent muscle wasting

Dr Vita Birzniece and Professor Ken Ho have developed a safe and effective treatment that could prevent the muscle wasting associated with many chronic diseases and with ageing. In healthy postmenopausal women, they demonstrated that a small dose of the male hormone testosterone prevented protein wasting. The pure crystalline testosterone, taken orally, went straight to the liver, and the dose (40mg/day) was small enough to ensure it was contained there, with no spill-over to the bloodstream and other organs. The next step will be to recruit healthy men with lower testosterone levels, as well as frail people, such as patients with kidney failure.

New hope for hormone resistant breast cancer

A new finding provides fresh hope for the millions worldwide with oestrogen receptor positive breast cancer. Dr Andrew Stone, Professor Susan Clark and Professor Liz Musgrove have shown that a specific change, which occurs when tumours become resistant to anti-oestrogen therapy, might make the cancers susceptible to treatment with chemotherapy drugs. In collaboration with scientists from Cardiff University, the researchers demonstrated that the BCL-2 gene becomes epigenetically 'silenced' in resistant tumours. This process is potentially detectable in the blood, providing a diagnostic marker. The researchers propose that, if the BCL-2 gene is silenced, patients with oestrogen receptor positive breast cancer would benefit from combination therapy. In other words, tamoxifen could be used in combination with a chemotherapy drug, to kill off vulnerable tumour cells.

▲ Samuel Johnson and his sister Connie, the inspiration behind the epic Love Your Sister unicycle trek raising funds for Garvan.



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From the CEO

As our Anniversary year comes to an end, it is wonderful to look back at the many celebrations we have held to mark Garvan's 50 years of breakthrough medical research. From the cutting of our official birthday cake by her Excellency Professor Marie Bashir AV CVO, the Governor of NSW; to the memorable service to acknowledge and honour the pioneering work of the Sisters of Charity through whose vision the Garvan Institute was established; to the recent public celebrations in Dubbo, it has been a wonderful year of celebration and re-engagement with many of our current and past supporters, researchers and students. To everyone who has been involved in making this such a successful year – a very warm thank you.

Acknowledgment must also be made to many people who have supported Garvan with generous gifts in recent months. Margaret Rose, the Chairman and Patron of Garvan's Ovarian Cancer Working Party donated a luxury two bedroom apartment in picturesque Breakfast Point, Sydney that raised more than \$760,000 to support Garvan's vital work in ovarian cancer research. She was joined in the venture by her dear friend Lee MacCormick Edwards who donated all the profits from her recent photographic exhibition at Maunsell Wickes Gallery in Paddington, Sydney.

As you read this, Australian actor, Samuel Johnson is continuing his twelve month odyssey to ride a unicycle around Australia; break a world record (by riding more than 15,000 kilometres on a unicycle); as well as raising more than one million dollars for breast cancer research at Garvan, all for the love of his sister Connie who, tragically, is terminally ill. The level of support that Samuel has been able to secure as he has ridden through towns, large and small, all over Australia has been heart-warming. We are all looking forward to cheering him across the finish line in Melbourne in mid-February.

To everyone who has supported Garvan this year – and indeed, over our long and proud history – very sincere thanks for your ongoing commitment. On behalf of everyone here at the Garvan Institute of Medical Research, please accept my very best wishes for the festive season and a very happy 2014.



Yours sincerely,

Andrew Giles
Garvan Research Foundation



The Sisters of Charity with Professor Les Lazarus (back row) and Professor John Mattick (right)

Acknowledging the invaluable work of the Sisters of Charity

The vision of the Sisters of Charity has been integral to the foundation of the Garvan Institute and its ongoing mission. Our brave start back in 1963 was made possible by the foresight and vision of the Sisters of Charity who recognised that their mission to heal the sick could not be fulfilled without research to not only treat disease, but to try to beat it.

Thanks to the Sisters' great foresight, along with the generosity of the James Patrick Garvan family with a £100,000 donation to support a new research unit within St Vincent's Hospital, Garvan has grown from humble beginnings to be recognised as a world leader in the fight against the major diseases of our time.

To honour the Sisters and recognise their invaluable role in Garvan's history during our 50th Anniversary, a morning tea was held, hosted by Professor John Mattick. Special acknowledgement was given to the many Sisters who have previously, and continue to provide support and guidance, not only to Garvan, but the St Vincent's Darlinghurst precinct and wider community.

Speaking at the event, Sisters of Charity Congregational Leader Sister Annette Cunliffe said, "Our vision and hope is to always have a special focus on the access of those in greatest need to the highest quality of treatment. Research will seek to prevent suffering as well as to alleviate it when it does occur, leaving a legacy of better health into the future."

A much-loved GP's legacy of good health lives on



Sandra Constantine is in no doubt that her decision to leave her estate to the Garvan Institute is the right one, and is certain that her late husband, Dr George Constantine, would agree.

Married for 38 years, George and Sandra's first meeting was something you might expect to see in the movies. Greek-born George and Sandra met on the island of Tahiti. They had both been on board an ocean liner bound for Europe – George as the ship's doctor, and Sandra as a passenger travelling overseas for the first time with her mother.

They fell in love, married and moved to Sandra's hometown of Melbourne, before finally settling in Sydney. Throughout their years of marriage, they filled their lives with the things they enjoyed the most – dear friends, a comfortable and happy home, fine dining, travel and visits to the theatre to enjoy opera, ballet and plays.

George established himself as a much-loved family GP who Sandra describes as, "A highly ethical and extremely dignified gentleman whose integrity and respectability was beyond reproach." To his patients, particularly those of Greek origin, Dr Constantine possessed all the inherent qualities of a loved physician: kindness, patience and caring empathy.

In 2001, Dr Constantine was diagnosed with Parkinson's Disease, and he sadly passed away from complications associated with the disease in 2005.

Since her husband's passing, Sandra has needed to re-address her own Will. "We have no children," Sandra says, "and as we had been each other's beneficiary, I was suddenly faced with a serious question – where to leave my estate?"

"As my husband had been a GP, I knew I wanted it to be put to use in the medical field, so I began doing some research and short-listed some organisations. Needless to say, the Garvan Institute stood out clearly and brightly, and after most welcoming, extensive and informative tours from Bequest Officer, Carol O'Carroll, I was overwhelmed by the research being carried out in the major areas of human disease.

"Apart from being humbled, more importantly, I felt that I was in the right place and that my estate would be left with the best, and most qualified minds and hands. Together, we have put in place the 'Dr George Constantine Fellowship', which will be allocated to the areas of Garvan's research where there is the most need. While I am now truly content and pleased, I know that my husband would be delighted."

Young Garvan All Ribbons Ball – supporting early career scientists

The 2013 Young Garvan All Ribbons Ball was a glittering affair. The exclusive black-tie dinner, held at the Hilton Hotel Grand Ballroom, Sydney raised much-needed funds for the Young Garvan Fellowship. MC for the evening was Michael "Wippa" Wipfli, and JellyBean Jam kept guests dancing all night!

The Young Garvan Fellowship is the main fundraising aim of the group, and provides \$50,000 each year towards supporting an early career scientist. Dr Tim Mercer was announced as the winner of the 2013 Young Garvan Fellowship, while Dr Phillippa Taberlay and Dr Daniel Hesselson were also awarded a special initiative grant of \$10,000 each.

Congratulations to the Young Garvan committee for another very successful All Ribbons Ball, and for its ongoing support of early career scientists.

Feature story: *Genomics in Pancreatic Cancer*

In recent years, scientific advances have made it possible to sequence the entire genome of many cancers, providing significant new and detailed information about how these cancers develop. Here, we look at how Garvan's Pancreatic Cancer research team is using genomics in the pursuit of new treatment options for this devastating disease.

Pancreatic cancer has the highest mortality rate of all the major cancers and is one of the few for which survival has not improved substantially over the past 40 years. It is the fourth-leading cause of cancer death.

Using high-throughput, state-of-the-art genomics technology, an Australian venture, The Australian Pancreatic Cancer Genome Initiative (APGI) led by Professor Andrew Biankin, from The Kinghorn Cancer Centre at the Garvan Institute of Medical Research / St Vincent's Hospital and Professor Sean Grimmond from the Institute for Molecular Bioscience at The University of Queensland, is improving the scientific understanding of the molecular underpinning of pancreatic cancer daily. The APGI is a member of the International Cancer Genome Consortium (ICGC), a worldwide collaborative effort to comprehensively catalogue the genomic and epigenomic abnormalities in over fifty major human cancers. The APGI brings together the expertise of pancreatic cancer scientists and healthcare professionals across Australia, and is dedicated to improving outcomes for pancreatic cancer patients and their families.

In October 2012, a landmark study published by the above team in the world leading scientific journal *Nature*, sequenced the genomes of 100 pancreatic tumours and compared them to normal cells to determine the genetic changes that may lead to this cancer. They found more than 2,000 cancer causing changes (known as mutations) in total, confirming the importance of some known mutations, such as in the KRAS gene, which was mutated in about 90 per cent of samples, but also revealed valuable new information about pancreatic cancer development and the extreme complexity of the disease. So while tumours may look very similar under the microscope, genomic analysis

reveals as many variations in each tumour as there are patients. This demonstrates that so-called 'pancreatic cancer' is not one disease, but many, and suggests that people who seemingly have the same cancer might need to be treated quite differently.

Furthermore, in August this year, the APGI contributed to an international study analysing the mutation patterns buried within cancer cells. 21 distinct mutational signatures were identified across several different cancer types, including pancreatic cancer, and it was revealed that the mechanism by which the damage occurs is similar across some cancer types. For example, it was found that some pancreatic cancers share a distinct genetic signature with breast and ovarian cancer.

Another potentially treatable sub-type of pancreatic cancer was also reported recently, through the work of the APGI. Cancer cells sometimes produce multiple copies of particular genes in response to signals from other cells or their environment, a process known as gene amplification. The APGI identified that just over 2% of pancreatic cancer patients have high-level amplification of the HER2 gene. This gene amplification is also found in breast and gastric cancers. HER2 amplified breast and gastric cancers are currently treated with the targeted therapy drug Herceptin, and gives hope that a small subset of pancreatic cancers may also be suited to this type of treatment.

All of the information gained to date has led researchers into the era of individual genomic diagnoses leading to custom-designed treatments or 'personalised medicine'. The first step has been acquiring a better understanding of the underlying genetic causes of cancer development, which is proceeding at a rapid rate, followed by working to implement this into health care systems to translate the knowledge effectively. We must also

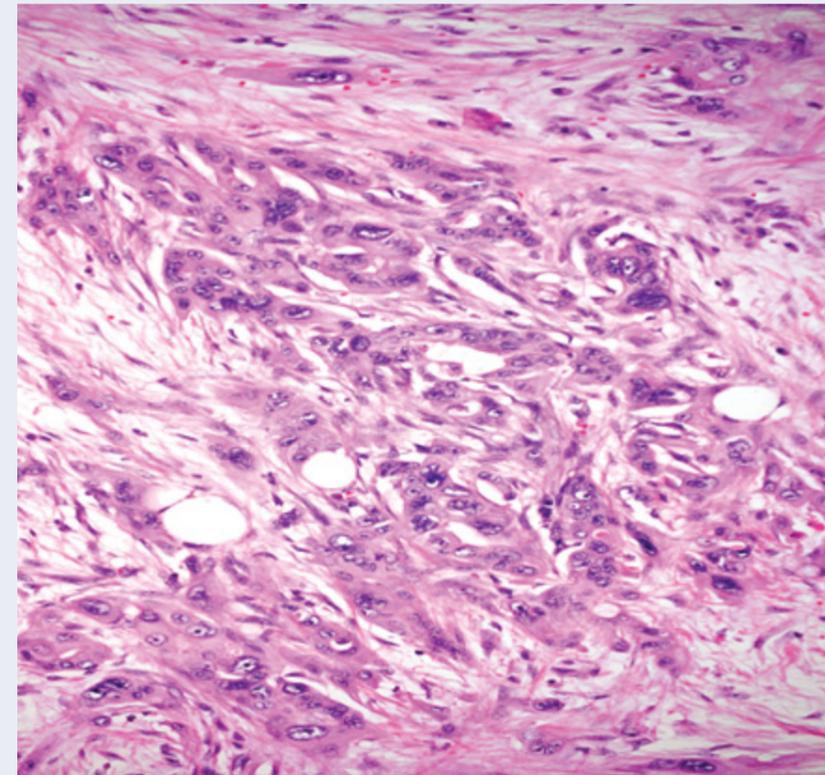
ensure that this new way of treating cancer patients is more effective in real people in real time.

Garvan aims to do this through the recently opened Individualised Molecular Pancreatic Cancer Therapy (IMPACT) study led by Dr Lorraine Chantrill, a medical oncologist and researcher in the pancreatic cancer group at the The Kinghorn Cancer Centre. This is a unique collaboration between the Australian Pancreatic Cancer Genome Initiative, Sydney Catalyst and the Australasian Gastro-Intestinal Trials Group.

IMPACT is a clinical trial assessing standard chemotherapy treatment versus personalised treatment based on specific tumour characteristics in patients with recurrent or metastatic pancreatic cancer. Potential patients will be screened for specific genetic characteristics using genomic technology, based on their biological material collected as part of the APGI study. If they happen to have one of three important molecular subtypes, they may be eligible for the study. For the moment, the study is confined to three therapies because they are known to be safe, and Australian oncologists use them for other cancers.

These three molecular subtypes are:

1. Pancreatic cancer with increased expression of the HER2 protein (occurs at a rate of 2%) - these patients may receive trastuzumab (Herceptin) in combination with chemotherapy.
2. Pancreatic cancer that does not have a mutation in the KRAS gene (known as "KRAS wildtype" occurs at a rate of 7%) - these patients may receive erlotinib in combination with chemotherapy.
3. Pancreatic cancer that has mutations in the DNA damage repair pathways (occurs at a rate of about 10%) - these patients may receive chemotherapy with mitomycin C.



Pancreatic cancer

The trial is currently open in three NSW centres: Bankstown, Royal Prince Alfred and Royal North Shore hospitals, and we hope to open soon in Perth.

This is an exciting initiative that is using information gained through genomic research to move closer to proving that personalising treatment for pancreatic cancer patients may be beneficial. While the team is currently working through all the challenges that such a complex and innovative study engenders, they are seeking additional funding to build the complex infrastructure required for such cutting-edge cancer trials.

We would like to acknowledge the generosity and bravery of Australian pancreatic cancer patients and their families who have donated their tumour tissue for the research that has enabled this trial to become a reality, and giving hope to people facing this disease in the future.

You can read more about the APGI's work, including the IMPACT study at www.pancreaticcancer.net.au

Ask Garvan

What happens during the different phases of a Clinical Trial?

Typically, clinical trials progress through four phases.

Exploratory, Phase 0 Trials or Pilot Studies are sometimes conducted among very small groups to test the body's response to a drug delivered once and in small doses.

Phase I Clinical Trials test a new concept (this could be a drug or a procedure) among small groups (often less than 100) to assess safety issues including dosage and potential side effects.

Phase II Clinical Trials study larger groups of people (sometimes hundreds) to discover if the concept works as intended, and to further assess its safety.

Phase III Clinical Trials study effectiveness in large groups (sometimes thousands) by comparing the concept to other standard or experimental interventions, as well as to collect information to help ensure safety.

Phase IV Clinical Trials are often carried out after the concept has been marketed. These record the concept's performance in clinical application, and collect data about side effects associated with long-term use.

Investigator-initiated studies are also conducted at Garvan, but do not follow the same phases as required for drug trials. These studies research the cause of disease and disease processes.

How do I become involved in a Clinical Trial?

Information about clinical trials carried out at Garvan can be found on the back page of this newsletter or visit the Garvan website - www.garvan.org.au/research/clinical-trials.

Team Phil and the Philip Hemstritch Fellowship in pancreatic cancer

Team Phil was established by Jane Hemstritch after losing her husband Phil to pancreatic cancer in March 2010, with the objective to raise much needed funds for pancreatic cancer research.

In October, Team Phil participated in the Melbourne Marathon for the third and final time with a whopping 52 participants. The effort is set to raise more than \$120,000, bringing Team Phil's total contribution to almost \$300,000 since its inception in 2011.

This remarkable effort is funding a three year fellowship for one of Garvan's most promising early-career scientists, Dr Marina Pajic, who proudly holds the Philip Hemstritch Fellowship in Pancreatic Cancer.

Congratulations Jane and congratulations Team Phil!



Jane Hemstritch

Garvan's longest serving scientists

During Garvan's 50th Anniversary year, we again take the opportunity to profile two of Garvan's longest serving scientists.

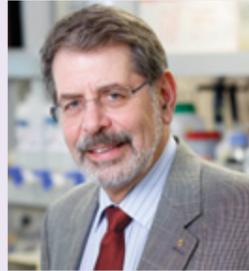
(29 years) PROFESSOR JOHN EISMAN AO

When Professor John Eisman began researching osteoporosis almost 40 years ago, the condition was mainly associated with older women who had broken hips or dowager's humps. Nobody understood how common or serious osteoporosis truly was. Sydney-raised, Professor Eisman began his career with research positions in Melbourne, the US and Switzerland, before returning to Australia in 1978 to practise as an endocrinologist, first in Melbourne, then back in Sydney at St Vincent's Hospital in 1984. He was appointed Director of Garvan's Osteoporosis and Bone Biology division at the same time – a position he held until 2011.

In 1989, Professor Eisman initiated the Dubbo Osteoporosis Epidemiology Study – the world's longest-running, large-scale study of fractures, examining men and women aged 60 and older in the regional centre of Dubbo, NSW. The study identified that osteoporosis is also common among men, who suffer about a third of all fractures. It has also helped to reveal that each fracture increases the likelihood of another, and that every fracture is associated with an increased risk of premature death.

As well as conducting twin studies to reveal the large part played by genetics in osteoporosis, Eisman and his Garvan colleagues have participated in each of the major multinational genome-wide association studies. Eisman was also instrumental in identifying the first gene associated with osteoporosis, and is using next-generation sequencing techniques with patients in Dubbo to uncover the genes responsible for bone density.

In 1997, Professor Eisman was awarded the Order of Australia for his contribution to medical research.



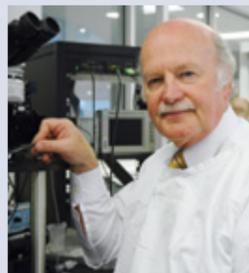
(26 years) PROFESSOR JOHN SHINE AO FAA

To many biology students today, Professor John Shine is best known for a discovery he made as a PhD student in Canberra. The 'Shine-Dalgarno Sequence' (a gene sequence responsible for 'switching on' protein synthesis) was first published in *Nature* in 1975, and was instrumental in the foundations of the biotechnology industry. Moving to the US in 1975, Shine and his colleagues were the first to clone both the human insulin gene – a momentous feat for millions of diabetes sufferers worldwide – and the human growth hormone gene.

In 1978, Shine returned to Canberra and set up a research lab at the Australian National University, but returned to the US in 1983 where he co-founded and directed a small start-up called California Biotechnology. In 1987, he decided the company had grown sufficiently and returned to Australia to take up the post of Deputy Director of the Garvan Institute. Shine then went on to become Executive Director, a role held for 21 years, retiring from the position in 2011.

Professor Shine remains at the forefront of research. His current focus is on stem cells in the nasal cavity, where nerve cells are replenished every 60 days. He says, "We take a biopsy of the nose and grow these stem cells in culture. We are trying to figure out ways to get them to multiply in culture, and to differentiate or convert them into mature nerve cells. These could potentially replace nerve cells affected by disorders such as Alzheimer's and Parkinson's disease."

In 1996, Professor Shine was awarded the Order of Australia for services to medical research, and in 2010 he won the prestigious Prime Minister's Prize for Science.



Tour de Cure – grants announced

In 2013 Tour de Cure is contributing to Garvan's Dr Goli Samimi and the Ovarian Cancer Research Program which aims to develop an early-detection test for ovarian cancer. Tour de Cure recently announced its fundraising results for 2013 and we are proud to report that Garvan's research has secured a grant of \$100,000. This investment will make a significant impact on the research capabilities of the Ovarian Cancer team in 2014.

Research into ovarian cancer is of particular importance as, of the more than 1,200 Australian women diagnosed with ovarian cancer each year, tragically, 800 will die. This is because ovarian cancer is mostly diagnosed at late stage when the cancer has spread beyond the ovaries and metastasised. Identifying women with ovarian cancer at an early stage will allow oncologists to more effectively treat these women and prevent the development of advanced disease.

Thank you to Tour de Cure and the Tour de Cure team!

Proudly supported by ...



Dr Goli Samimi (left)

Metromix Charity Golf Day

Metromix, a Sydney-based company providing high-quality concrete and quarry products, and delivery services to the construction industry in Sydney and surrounding regions, hosted its annual charity golf day in October, raising much-needed funds for the Garvan Institute. While numbers were down due to the bush fires that ravaged parts of NSW, Metromix, with the support of its generous customers and suppliers, still managed to raise a phenomenal \$10,000 for the Garvan Institute of Medical Research.

This was the second year that Metromix's golf day benefited the work of the Garvan Institute. Participants enjoyed a morning's golfing at Riverside Oaks Golf Course, including the chance to contribute to the cause at the charity hole, the 'Beat the Pro' hole and the guessing competition. They were then treated to a sumptuous lunch, and entertainment by the hilarious Paul Martell, who joked about returning to the Metromix Golf Day 20 years after his first appearance.

Some of the fabulous prizes throughout the day included a Stay and Play Package for four people thanks to Riverside Oaks and four Riverside Oaks polo shirts; a dinner cruise for two on Sydney Harbour thanks to Captain Cook Cruises; Family Day Pass to Taronga Zoo; and two \$50 gift vouchers thanks to Drummond Golf. Metromix also sponsored prizes including a SnowGoose Hamper valued at \$200; two Golf Pro Putting Practice Mats; a putter valued at \$200; six bottles of Chivas Regal Whiskey; six bottles of top shelf red wine; and six bottles of top shelf white wine.

Andrew Giles, CEO of the Garvan Research Foundation said, "It is terrific to see companies like Metromix who, not only recognise the importance of medical research, but also support it so effectively. I would like to extend my sincere thanks to Metromix, and hope other companies are inspired to follow its lead in getting behind Australia's gifted medical researchers."

For more information on how you can help raise funds for Garvan's world-class research, visit www.giving.garvan.org.au



Metromix staff at the charity hole for the Metromix Charity Golf Day



Dr Darren Saunders with the Ridley AgriProducts' Tamworth team

Taking Garvan research to rural and remote communities

Garvan recently worked alongside Ridley AgriProducts and the Cancer Council to take its free Cancer in the Community program to rural and regional areas in Victoria, NSW and Queensland.

The 'Healthy Families, Healthy Communities' presentation focussed on demystifying cancer and providing information on the latest in cancer research. Importantly, it also suggested practical ways to reduce individual cancer risk and the best ways to access local resources and cancer support.

According to Ridley AgriProducts' Townsville site manager Jeff Drayton, the company's partnership with the Garvan Research Foundation and sponsorship of Cancer in the Community is one way Ridley AgriProducts is helping, not only the Townsville community, but all rural and remote communities across Australia.

"Unfortunately regional communities like Townsville are hit pretty hard by cancer. I think everyone knows someone who has been touched by the disease at some point. For Ridley, it is important that the community has a better understanding of the disease, treatments and progress in cancer research. The community forum is for everyone and gives locals access to experts and information that they normally would not have, and allows them to learn about these important health messages and research," Mr Drayton said.

Garvan will continue the Cancer in the Community program in 2014. To find out more about our next locations, email: healthinitiative@garvan.org.au

