breakthrough December 2011 | Issue 18

Professor John Mattick AO FAA
Image courtesy of Paul Harris, seesaw photography

The Garvan Institute of Medical Research recently announced the appointment of Professor John Mattick AO FAA as the Institute's next Executive Director, following the retirement of Professor John Shine AO FAA.

Professor Mattick will begin his tenure at Garvan in January 2012, and is taking every opportunity in the lead-up to his arrival to meet Garvan staff, board members and supporters.

Read more about Professor Mattick, his impact on medical research, and his hopes for his time at the Garvan on page 5.

Making *NEWS*

'Brown fat' is believed to be a wondrous tissue that burns energy to generate heat, that could help us fight obesity. We are obese when we have too much 'white fat', which is basically an organ of energy storage. In contrast, brown fat is like a heat generator. Around 50g of white fat stores 300 kilocalories of energy. The same amount of brown fat burns 300 kilocalories a day. Garvan researchers have shown that brown fat can be grown in culture from stem cells biopsied from adults – giving hope that one day we might be able to either grow someone's brown fat outside the body and then transplant it, or else stimulate its growth using drugs.

Identical twins have identical genomes, but that is where it stops. There are subtle differences in their personalities, how they look, how they act and in their susceptibility to disease. How can this be? According to scientists from Garvan and Queensland Medical Research Institute, it all depends on how the "epigenome" is modified by the environment. More specifically, it depends on exactly how particular parts of the genome are affected by 'methylation', or the attachment of hydrocarbon molecules - 'methyl groups', that literally change the voice of the genome, silencing some genes and amplifying others. These findings are based on an eight-year study involving 512 adolescent twins (128 identical twin pairs, as well as 128 non-identical twin pairs), with an average age of 14.15 years.

Garvan scientists have discovered that a single gene controls a very complex process, apparently forming the crucial link between eating a high fat diet and developing diabetes. Compounds are already being developed for blocking the gene – known as Id1 – as it has known adverse effects in cancer. This drug development work would very much shorten the path from discovery to prospective treatment in the case of Type 2 diabetes.

GARVAN INSTITUTE

Inside this issue:

From the CEO

Welcome to the final issue of *breakthrough* for the year. As you will read, we have some very exciting news with the appointment of our new Executive Director, Professor John Mattick AO FAA who is joining us early in 2012. Professor Mattick has an outstanding reputation as one of Australia's leading scientists and will bring a wonderful range of skills to the Garvan.

I am sure that many of our supporters will be delighted to know that our current Executive Director, Professor John Shine will not be going very far way – in fact, he won't even be leaving the building! Professor Shine will return to the lab to further pursue his passion for medical research.

As the year draws to a close, it is wonderful to look back at some of the amazing breakthroughs that have been made here at Garvan in areas as diverse as pancreatic cancer, childhood deafness, asthma and Type 2 diabetes (to name a few!)

The year has also been great personally for some of our researchers who have won prestigious awards. Congratulations to Dr Alex Swarbrick who received the Cancer Institute of NSW's 2011 Premier's Fellow of the Year Award and Dr David Chang who received the CINSW 2011 Premier's Scholar of the Year Award, as well as a Pfizer Oncology International Studentship.

To all our wonderful supporters – thank you for helping Garvan continue its vital, world-class work in 2011, and we look forward to your ongoing support in 2012.

My best wishes to you and your loved ones for a safe and enjoyable festive season.

Yours sincerely,
Andrew Giles
Garvan Research Foundation

"Opinion"

As I retire as Executive Director at the end of the year, I take this opportunity to reflect on the past 20 years at this remarkable institution. I have been extremely privileged to be at the Garvan and to witness firsthand the many exciting research discoveries that have emanated from the institute. It clearly is an institute that should make all Australians very proud and I have been continually humbled by observing every day the generosity of our supporters and the dedication, intelligence, creativity and commitment of all the staff. While we all appreciate our good fortune working in research, we are all very aware of the responsibility that comes with it – to ensure that the critical trust and support of our community is honoured by a focus on producing the very best research and a focus on delivering improved health outcomes for all.

Although the past 20 years has seen amazing progress, the next decade promises even more. The Garvan has been most fortunate to attract Professor John Mattick as the next Executive Director. John is an outstanding Australian and an international leader in the analysis and understanding of the human genome – the area which is truly bringing us into the era of personalised medicine. Under John's leadership and with your ongoing support, the exciting growth planned for Garvan (the first example being the Kinghorn Cancer Centre), will rapidly come to fruition.

Professor John Shine AO FAA
Executive Director

Welcome: ***Professor John Mattick*** *AO FAA*

Garvan welcomes new Executive Director, Professor John Mattick AO FAA

Professor John Mattick, holder of a prestigious NHMRC Australia Fellowship at the University of Queensland and the inaugural Director of the University's Institute of Molecular Bioscience (IMB), has been appointed as Garvan's new Executive Director.

Professor Mattick is excited to be joining Garvan, which he considers to be an outstanding medical research institute. He also believes it to be best placed to lead Australia into the next generation of medical research.

Although currently residing in Brisbane, Professor Mattick is a born and bred Sydney-sider.

"I grew up here, mainly in the inner west. I lived for a while as a student at the bohemian (Woolloomooloo) end of Victoria Street," (the same street on which Garvan is located).

In 1988, Professor Mattick was lured to Queensland by an invitation from the University of Queensland to apply for a Foundation Professorship in Molecular Biology, and at the same time, to start a new centre in molecular biology.

"By the end of the first five years, we were self-sufficient. A few years later, we had more research income than another local university. It was due to the vision we set out and judicious appointments of gifted people. This is a great formula, and the Centre matured into the Institute for Molecular Bioscience (IMB), now recognised as one of Australia's best.

"After heading IMB and its forebear for 18 years, I realised that I had three big jobs. I was running an institute of over 400 people. I had research I wanted to pursue, because I thought I had seen something nobody else had - that human genetics had been misunderstood for the past 50 years. I also had an extremely supportive family that I wanted to give more time to. I was confident that I could do any two of those jobs well. However, by trying to do all three, I was compromising all of them.

Professor John Mattick AO FAA
Image courtesy of Paul Harris, seesaw photography

"There was really no choice. In 2006 I elected to go back to research for a while, as I did not want to die wondering," said Professor Mattick.

It is this research that has transformed the way scientists now think about the human genome, our evolution and our brain. Previously, it was believed that only a few per cent of the genome (the protein-coding part and nearby regulatory sequences) was actually useful. The rest was labeled "Junk DNA". By challenging this long-held belief, Professor Mattick was able to show that this "Junk DNA" actually specifies a massive hidden layer of regulation that directs the processes of our development from a single cell to a finely sculpted organism of 100 trillion cells that can walk and talk. This insight has made scientists re-think biology and consider a previously unknown level of the genetic programming of our development and cognitive complexity. It also opens many avenues for entirely novel therapeutic approaches.

Of Garvan's future, Professor Mattick says, "There is presently a great opportunity to do 'next generation' science and medicine, using the amazing advances in technology that have occurred over the past decade, especially in DNA sequencing, and thereby to connect our capabilities directly with the health and medical concerns of the community. I think this will be the true flowering of medical research institutes, and I want Garvan, through its close collaboration with St Vincent's Hospital, and the opportunities presented by the joint Kinghorn Cancer Centre, to lead the way."

Cures can take more than a lifetime

The late Gay Marx

Gabriele (Gay) Marx is described by her godson, Mark Hedges and wife Robyn as, "a formidable lady with a heart of gold."

"She was always a forthright, business-like woman, but if you took the time to get to know her, it was well worth it. I feel a great deal of warmth and respect for Gay," said Mark.

A very successful businesswoman, Gay ran a bookkeeping service in Sydney for almost 30 years.

Mark's mother shared a life-long friendship with Gay, who was considered part of the Hedges family, and they were part of hers. Gay never married, and with no children, asked Mark and Robyn to be the executors of her estate. This included managing a generous bequest to the Garvan.

Gay was reasonably healthy, but over the years her health deteriorated. "I think that's where the interest in medical research came from. She supported a range of medical charities during her life (including Garvan), and she left the bulk of her estate to medical research," said Robyn.

TIP: ***When shares have been left to a charity, consider transferring them directly to the charity. Selling shares within a estate, then forwarding the funds can result in capital gains and transaction tax implications that can have a significant impact on the final value of the bequest as charities are exempt from capital gains and transaction tax.***

Including a charity in your will

include a charity
Help the work live on.

Sadly, only 7.5 per cent of Australians leave a bequest to charities in their will. If this figure doubled, it would result in an additional $440 million each year to assist the work of not-for-profit organisations. Garvan has joined with more than 100 other organisations in the Include a Charity initiative, promoting philanthropic bequests.

Leaving a bequest to Garvan is a wonderful way to make a significant and enduring contribution to the future of medical research.

For more information about leaving a bequest to Garvan, please contact Carol O'Carroll on 02 9295 8117, or email c.ocarroll@garvan.org.au

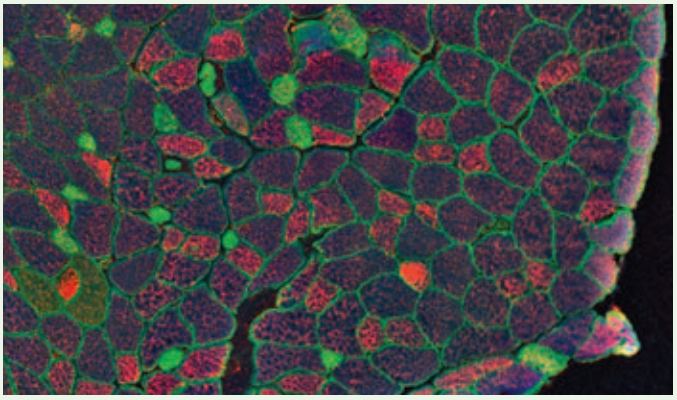
Feature *Type*

Almost a million Australians are currently living with diabetes, and a further 275 develop diabetes every day.

Significant Garvan Research Discoveries in Diabetes and Obesity

- Low dose insulin infusion can help people in diabetic comas saving thousands of lives since 1973.
- Abdominal fat is a key risk factor for insulin resistance and Type 2 diabetes.
- Fish oil in the diet increases insulin sensitivity and reduces the risk of diabetes.
- Modest weight loss reverses damaging changes seen in the immune cells of obese people.
- Development of a simple 'field friendly' tool to identify individuals at high risk of Type 2 diabetes in low income countries.
- PYY, a hormone released by the gut, can be used to treat obesity and Type 2 diabetes.
- Isolation of small molecules from the vegetable bitter melon that improve insulin sensitivity.
- Discovery of new actions of insulin using proteomics including regulation of mRNA processing and autophagy.
- Insulin resistance in human muscle is highly selective for carbohydrate metabolism providing new insights into the mechanism of the disease and how it should be treated more effectively.
- Too much fat in the diet kills insulin producing pancreatic beta cells and the discovery of new genes that might reverse this effect.
- Contrary to dogma, strategies that increase fat burning do not necessarily lead to reduced whole body fat mass.

story: 2 diabetes



Muscle Tissue. Muscle responds to insulin and takes up glucose from the blood. It is one of the critical tissues for controlling blood glucose levels.

What is Type 2 diabetes and how did I get it? After eating, we need insulin, a hormone made in the pancreas, to channel sugar from our blood into our cells. In Type 1 diabetes, a less common form of the disease, the part of the pancreas that manufactures insulin is accidentally destroyed by the immune system leading to a complete lack of insulin. In Type 2 diabetes, which accounts for around 90% of all diabetes, the pancreas still produces insulin, but not enough to properly regulate sugar metabolism because our cells do not respond properly to insulin. Therefore, in Type 2 diabetes, there are defects in our tissues and in the pancreas leading to elevated blood sugar levels.

Type 2 diabetes is often, but not always associated with obesity and this is why obesity is a major risk factor for diabetes. Obesity is a result of an overconsumption of food and/or not enough exercise, which can explain why Type 2 diabetes has been referred to as the 'scourge of modern life'.

Obesity and Type 2 diabetes are heritable disorders. Studies in identical twins reared apart from birth show that genes, rather than environment, is the major determinant of body mass. Does this mean that a human's genes have changed in the last 50 years? Not necessarily, but the environment has changed and it has impacted most on those who have a genetic predisposition to eating more food and/or doing less exercise. What we all have in common is the drive to eat and to reproduce, and this is "hard-wired". For some reason, many of us now eat too much, thus defying physiological processes that would normally inform the brain that we have eaten enough.

Dieting is extremely difficult and usually fails because our bodies are programmed to defend an increased body weight rather than a decreased body weight. This is because storing extra fat traditionally provided protection against times of food shortage.

Garvan researchers are using a large arsenal to tackle this problem. The body's response to food is complex. If we overeat, the extra calories are rapidly absorbed and stored by our adipose tissue. Indeed our body fat stores can increase considerably in just a few days of overeating. Normally our fat cells send signals to the brain to cut down on eating, but for some reason this wiring system can go wrong in certain people. One of the consequences of overeating is insulin resistance, a phenomenon where insulin is secreted from the pancreas, but it doesn't work efficiently due to a block in the insulin regulated machinery in muscle, fat and liver cells as well as in the brain. Garvan researchers are at the forefront of mapping pathways that underpin insulin resistance.

Not all insulin resistant people develop diabetes, but some do, and this may represent the interplay between genes and the environment. Hence, it is important to identify those genes so that we can determine which individuals are most at risk. Garvan scientists are gearing up for an ambitious venture to identify these genes in Australians with Type 2 diabetes.

Unlike Type 1 diabetes, Type 2 diabetes is reversible. This gives us hope that we can do something to help people, no matter how far along they are in the course of the disease. One way is to reverse the insulin resistance, and the other is to make the pancreas more efficient at producing insulin. Garvan scientists have discovered a novel gene that regulates pancreas development and this gives us new insight into the malleability of this process.

Type 2 diabetes and obesity are NOT due to a lifetime of slothfulness and gluttony. This is one of the major myths about metabolic diseases like diabetes. We are controlled by our genes and these may work differently, depending upon the environment they are exposed to. This is why some people can avoid the temptation to overeat, while others cannot. It is an unavoidable consequence of modernisation.

You don't die of diabetes! True - what you do die of is the heart disease, the kidney failure, a stroke, or possibly cancer that you acquire as a consequence of your diabetes. Worst of all, as the excesses of the western world spread across the globe, diabetes, and all of these other problems, are rapidly following.

Garvan scientists are using sophisticated technologies to unravel the complex relationship between genes, food and health. We believe the solution to this problem will be neither simple nor immediately forthcoming, but it is achievable and we must urgently find it. It will require time, resources and commitment to embrace this challenge.

Staff Profile: *Dr Ann McCormack*

What is the current focus of your work?

My primary research interest relates to the pituitary gland. The pituitary gland is located in the brain and has been affectionately coined "the master gland". It regulates other important glands in the body such as the thyroid, adrenal and reproductive organs. One area of my research focuses on pituitary tumours. Pituitary tumours are common and cause headaches, visual loss and/or hormonal dysfunction. The hormone dysfunction has far reaching effects with patients having increased rates of diabetes, osteoporosis, and infertility, to mention a few. Patients with pituitary tumours have an increased mortality compared with the general population and have a significant reduction in quality of life.

One in every 1000 individuals has a clinically significant pituitary tumour. However, data from autopsy and imaging studies have found that, in fact, 20% of the population harbour a pituitary tumour.

I am currently leading a project investigating the use of pathological markers as a predictive tool to help us determine which tumours may become an aggressive cancer. I have also set up a project to investigate the Australian prevalence of mutations in a newly recognised gene implicated in familial pituitary tumour syndromes. The future of pituitary tumour research will be greatly facilitated by the development of a National Pituitary Tumour Registry and biobanking, which I am actively involved in establishing. The other exciting emerging area of research I am pursuing aims to gain a better understanding of the role that hormones derived from the pituitary, as well as hormones that communicate with the pituitary, have in a number of other diseases such as cancer, osteoporosis, obesity and diabetes. It is hoped that this will identify treatments that can modulate the hormonal environment and thus offer improved outcomes for the millions of patients with these diseases.

What are some of the recent findings of your work?

In my doctorate I studied a gene (MGMT) whose expression predicts response to a chemotherapeutic agent used to treat aggressive pituitary tumours. We determined that the best way of assessing this gene was by using the technique of immunohistochemistry, a common tool used by pathologists. This biomarker has now reached clinical practice in the assessment of an aggressive pituitary tumour. In addition, we have found that the MGMT gene probably plays an important role in the development of an aggressive pituitary tumour.

In other work, we have identified a new inherited mutation in the AIP gene in a young patient suffering from gigantism, a condition resulting from a growth hormone secreting pituitary tumour. We are now about to embark on screening other members of this patient's family for the same mutation. The hope is that identification of the mutation in other family members may lead to earlier detection and treatment of a pituitary tumour.

What is the biggest challenge in your area of research?

Like all other researchers, finding funding for research is a battle, particularly in the early stages of establishing a research career. However, for my work, an added difficulty is the lack of awareness of the pituitary gland. With the right support, we can increase the understanding of this vital gland and the hormones it produces. I believe benefits for patients with a range of conditions will transpire as a result.

What do you enjoy doing away from the lab?

I am a mother of two young children and I thoroughly enjoy the time I have with them. This doesn't leave much spare time, although I always look for excuses to travel. I am a keen skier and love to spend time dreaming about which mountain to explore on the next ski holiday.

Congratulations to the many individuals and teams who have recently laced up their running shoes, and hit the road in support of Garvan Institute of Medical Research. Special mention should be given to Jane Hemstritch who, along with her team, 'Team Phil', participated in the Run Melbourne event. So far, Jane has raised more than $75,000 for the Australian Pancreatic Cancer Genome Initiative (APGI). This initiative is part of the International Cancer Genome Consortium, and APGI is co-led by Professor Andrew Biankin from the Garvan, and Professor Sean Grimmond from the Institute of Molecular Bioscience in Brisbane. Team Phil is named in memory of Jane's late husband, Phil Hemstritch who lost his battle with pancreatic cancer in 2010. Congratulations to Jane and Team Phil for their passion and commitment.

Jane Hemstritch (centre) and Team Phil'

Ask Garvan

Q: How did Garvan get its name?

A: In 1957, when the Sisters of Charity were looking to raise funds for a research institution, a lady by the name of Helen Mills offered to donate a sum of £100,000 in the name of her late father, James Patrick Garvan.

James Patrick Garvan

James was born in Ireland in 1843, and came to Sydney with his family in 1847. A successful businessman, he established the Australian Terminating Building Society, and the North Shore Steam Ferry Co Ltd. He also founded the City Mutual Fire Insurance Co. Ltd and the City Mutual Life Assurance Society Ltd. Later, he founded the Citizens' Life Assurance Co. Ltd, which later became MLC (a major supporter of the work of the Garvan).

James was a leading parliamentarian, and also a keen sportsman. At one stage, he held the record for throwing a cricket ball the furthest (121 yards).

On his death in 1896, Sir Edmund Barton acknowledged his, "entirety of life, adorned with consistent principle, filled up in the discharge of virtuous duty, with nothing to conceal, no friendship broken, no confidence betrayed, no timid surrender to popular clamour, no eager reaches for popular favour."

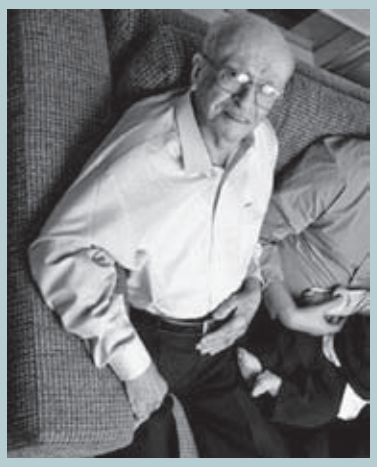
Topping Out Ceremonies

First glimpse inside The Kinghorn Cancer Centre

Events held in late August and early September gave Kinghorn Cancer Centre visionaries, as well as St Vincent's and Garvan cancer staff the opportunity to don a hard hat and get their first glimpse inside The Kinghorn Cancer Centre. Guests received an insight into the layout of the ground floor, as well as a very special trip to the "top" of the site.

Left to right: Professor John Shine AO FAA, Mr John Kinghorn, Mrs Jill Kinghorn and Mr William (Bill) Ferris AC

In memory of a ***remarkable man***



Marko Berger

Joshua Berger, Director of Fivex Commercial Property, describes his late father Marko (Mordechai) Berger as, "A down-to-earth gentleman. A very remarkable, uncomplicated man."

To honour the memory of Marko, and his extraordinary life, Joshua makes an annual contribution to Garvan's Neurodegenerative Disorders research group, headed by Dr Bryce Vissel.

Marko was born in Czechoslovakia in 1920, the youngest of seven children. When World War II began, Marko joined the Czech Jewish Army. He was injured and managed to hide from the Germans for a year, until he was eventually captured. He spent the rest of the war in various concentration camps, and emerged weighing 35kg, and with no hair. While Marko, his parents, and two of his sisters survived the war, tragically three brothers and another sister did not.

Following the war, Marko not only survived – he flourished. In 1948, he married Lily, the love of his life. In 1955, with their son Joshua, the family moved to Australia. Arriving in Australia with little in his pocket, Marko set about selling shoes at Paddy's Markets. It was not long before he had established a successful business.

Marko lived life to the full, enjoying every moment.

Of his contribution to Garvan, Joshua says, "My dad was successful in the way he lived his life in the field of business and in general. He always wanted to be an inventor, yet that is one area of his life that he did not actually succeed in. I think he'd have a chuckle to think he was participating in the process of invention by proxy!

"He set the standard and tone of our family, and he is terribly missed. However, his spirit lives on through his family, and his memory lives on through this contribution to the work of the Garvan."

Announcing Garvan Australian Proms

Stars of Australian opera, musical theatre and jazz will join forces at Sydney Town Hall on Saturday 28th April 2012 for the inaugural Garvan Australian Proms.

Featuring the Sydney International Orchestra and the Garvan Proms Choir, this event will be a celebration of the Australian spirit and Australian talent. Importantly, it will also help to raise vital funds for cancer research at the new Kinghorn Cancer Centre. More details will be released soon, so mark the date in your diary and keep an eye out for more information, including how to buy your tickets, at **www.giving.garvan.org.au**

Don't forget to bring your Australian flag for the rousing finale!

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).

Diabetes Study

Are you interested in improving the control of your diabetes? We are studying the effect of the amino acid glutamine on glucose control in Type 2 diabetes. We are looking for people with Type 2 diabetes for less than five years, males and females ages 40-75 years, only on Metformin (ie not taking insulin or other diabetes medications).

For more information contact:
Renee Richens on (02) 9295 8215, email r.richens@garvan.org.au
(St Vincent's Human Research Ethics Ref H07/059 version 1).

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
Vanessa Travers (02) 9295 8232 or v.travers@garvan.org.au
(St Vincent's Human Research Ethics Ref HREC/10/SVH/133).

Coming Up

Garvan's 2012 free public seminar series has been announced. Join us to hear about the latest developments in diagnosis, treatment and prevention of some of the most widespread diseases affecting our community today. Full details for each seminar will be available on Garvan's website shortly.

29 March – Immunology. 10am – 12 noon.

24 May – Ovarian Cancer. 10am – 12 noon.

9 August – Osteoporosis and Bone. 10am – 12 noon.

20 September – Alzheimer's disease and other neurodegenerative disorders. 10am – 12 noon.

14 November – Type 2 diabetes and obesity. 10am – 12 noon.

Registrations are now open for all seminars. Please note that registration is essential. To register, visit **www.giving.garvan.org.au/seminars** or phone **(02) 9295 8110**.

In Memoriam July 2011 – October 2011. Donations have been made in memory of:

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Gordon Adamson
Daniel Anisimoff
Doug Bailey
Betty Bale
Moses Bainy
John R Barbour
Bob Bauza
Lynda Beattie
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Rhea Tahn
Adrian J Taylor
Klara Torheiden
David Victor Torr
Jenny Wareham
Judith Ann Waters
Rosemary Wheen
Harry Widdup
Margaret Peggy Wilson

BREAKING NEWS! **For the first time, Garvan's 2012 seminars will also be available as live webcasts via www.giving.garvan.org.au/seminars**

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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