Today, the Garvan Institute of Medical Research is recognised as one of Australia’s premier medical research institutes; however, its beginnings as a St Vincent’s Hospital clinical research unit were far more humble.

In 1963, when Garvan first opened its doors, only three endocrinology researchers occupied two ground-floor laboratories.

Nowadays, the 650-strong team working within the Garvan and The Kinghorn Cancer Centre (TKCC) are recognised as world leaders in the fight against the major diseases of our time - cancer, diabetes, obesity, osteoporosis, neurological diseases, and immune disorders.

Continued on pages 4 and 5.
It is easy to take modern medicine for granted. We now have relatively easy access to ubiquitous drugs such as antibiotics and advanced therapies for cardiovascular disease, cancer, and diabetes, just to name a few. It takes a person like Margaret Davis to remind us that these treatment options have only recently become available.

As a paediatric nurse in the 1940s, Margaret saw families experience the most unimaginable pain and suffering. “We would have to nurse sick children with meningitis for three weeks until the end.” It is incredible that in just one (very full) lifetime, there have been multiple, significant breakthroughs in medical research and Margaret has experienced firsthand how these changes can live. “The discovery of penicillin and streptomycin were remarkable, and put an end to nursing sick children in their final days of tuberculosis, and death from, in today’s terms relatively simple ailments such as a post orbital (behind the eye) abscess.”

Margaret speaks passionately about medical research as it has impacted her working life, her own health and the health of her family and friends. “Taking it easy” is not a phrase in Margaret’s vocabulary and she is fighting fit thanks to medical research. She was treated for a potentially life threatening heart condition in 1992 and then osteoporosis from 1995. Margaret has personally benefited from cutting edge discoveries and therapies for these conditions that would not have existed without medical research. Without these treatments Margaret would not be able to enjoy life as she does today, and certainly would not be as competitive in the Australian Crossword Club.

Margaret would like to see an improvement in cancer incidence for our next generations but she would also like to see a shift in the way some of the more obscure diseases like dystrophies and degenerative uraemic diseases are treated. She is optimistic about the new medical research discoveries that are just around the corner.

**Origins**

The Garvan journey began 56 years ago when funds raised in conjunction with the centenary celebrations of the founding of St Vincent’s Hospital by the Sisters of Charity were set aside “to provide a building to enable the establishment of a research unit.”" The illustrious committee formed to oversee the unit’s development included Sir John Eccles, the Nobel Prize winning physician, and Sir Edward Ford, Dean of Medicine at Sydney University. In 1961, a substantial donation of $100,000 was given to the fund by Helen Miles, the daughter of James Garvan (1843 – 96) who was one of the founders of the insurance industry in Australia. He was also a former Minister of Justice, Attorney General and Colonial Treasurer of NSW. And so the new St Vincent’s research unit was named ‘Garvan’ in his honour.

The newly built Garvan Institute of Medical Research, which stood on the corner of Victoria and Burton Streets and Chapel Lane in Darlinghurst, was formally opened by The Duke of Norfolk on February 17th 1963 at a ceremony attended by 1,500 supporters and dignitaries. The date was chosen to fit in with a lay-day in the Australia-England cricket test as the Duke was English team manager.

The first annual report noted with pride that the three Garvan researchers - Associate Professor John Hickie, Professor Lesslie Doolan, and Dr. Jim Biggs - had established a number of new projects including studies of aldosterone metabolism in cardiac failure, gonadotrophin in breast cancer, protein binding of steroid hormone, and iron metabolism.

**Growth, Expansion, and Change**

Research in the ‘60s and ‘70s was dominated by endocrinology, fostered by the presence of the State Reference Laboratory for endocrine assays**. The late ‘70s and ‘80s were characterised by expansion of the scientific staff including the arrival of a critical mass of key senior researchers many of whom are now recognised as ground-breakers in their field.

These included: Professor John Eisman, a world leader in bone mineral and Vitamin D research; the late Professor Rob Sutherland who established one of Australia’s most successful cancer research programs, initially in the fields of breast and prostate cancer but later diversifying into cancers of the pancreas, ovary, head and neck and lung; Professor Don Chisholm now a leader in diabetes research and care; and Professor John Shine, now the first to clone the insulin gene and who was Garvan’s Executive Director from 1990 to 2011.

In May 1984 the NSW Parliament incorporated Garvan as an autonomous non-profit research institute, “...to further knowledge in the field of human medicine by promoting the conduct of research in that field, being research which is consistent with the tenets of the Sisters of Charity.” At the same time Garvan and the University of NSW became formally affiliated, and the Garvan Research Foundation was established.

Perhaps the most significant event in the recognition of Garvan as a national leader in medical research took place in the early ‘90s when Garvan was awarded a National Health and Medical Research Council (NHMRC) block funding grant. Garvan became one of only five centres of research excellence in Australia, and the first Australian institute to receive block funding, and a subsequent infrastructure grant from the NSW government, allowed for the growth of the Garvan Institute into a world class research facility and the opportunity to increase the number of scientists towards 250.

In 1990, after 25 years of leading Garvan, Professor Lazarus retired and Professor John Shine took over as Executive Director. Professor Shine’s appointment coincided with the explosion of genetic technologies and the possibility of finally understanding the molecular basis of health and disease. To reflect this, Garvan’s scientific effort was divided into four domains: Gastrointestinal, Cancer, Neurobiology, and Metabolic Research. The Immunology Program was added in the mid-’90s. The mid to late-90s witnessed the completion and extension of Garvan facilities into the Frank Woolley designed building of today with the iconic staircase.

The year 2012 saw two new milestones in the Garvan journey. Firstly, in January, Professor John Mattick took up the role as Garvan’s new Executive Director following the retirement of Professor Shine after more than 20 years leading the Institute. Professor John Mattick’s appointment has made a significant contribution to the understanding of genetics and genomics through his pioneering discoveries on X-chromosome inactivation. And in late 2012, The Kinghorn Cancer Centre (TKCC), a joint venture between Garvan and St Vincent’s Hospital, opened its doors. TKCC’s vision is to realise the promise of innovation and personalised medicine for people affected by cancer and it will focus on translational research and personalised cancer care.

**Scientific Highlights**

Year after year, Garvan researchers continue to perform at the highest level, with competitive grants and publish innovative research in esteemed academic journals. Last year researchers published 219 peer-reviewed research papers in journals with an average impact factor over 8 (a measure of importance of a journal within its field). This places Garvan above internationally accepted benchmark levels and is testament to the excellence of Garvan science over the years.

It was the Diabetes and Obesity Program that first placed Garvan on the international medical research map. In the 1980s, Professors Ted Kneegen, Don Chisholm and Paul Compton developed a computer model of blood flow and insulin control which led to the first bedside insulin infusion system, or ‘artificial pancreas’. Research in the program then led to the first low-dose intravenous insulin therapy for diabetic ketoacidosis** - a discovery that has saved countless lives worldwide.

More recently, The Neuroscience and Immunology Programs collaborated to publish groundbreaking research that identified the pathway that reveals how stress can suppress the immune system. And in 2011, The NHMRC awarded pain researcher Dr Greg Neely a prize for the top grant application in the country for his ‘highly innovative and potentially transformative project’ which maps corresponding pain genes in fruit flies and humans.

The Cancer Program investigates the genetic, epigenetic, and cellular molecular biology of breast, colorectal, lung, ovarian, pancreatic and prostate cancers. The strength of Garvan’s cancer program is reflected in the opening of the TKCC which places Garvan cancer researchers at the national forefront of new diagnostics and therapeutics for cancer. Previously, the program was responsible for one of the top 20 advances in breast cancer of the 1990s when a group led by the late Professor Rob Sutherland, discovered the role of cyclins in breast cancer. More recently, Dr Alex Swarbrick found a way of shrinking tumours in certain cancers which are caused by a new class of genes known as ‘microRNAs’. He identified one particular microRNA (microRNA 380) that appears to disable the kind of tumour suppressors, the P53 gene. This finding holds promise for the future treatment of microRNA-induced cancers. Due to its expertise in pancreatic cancer research, in 2009 Garvan took a leading role in the Australian arm of the International Cancer Genome Consortium, a global body cataloguing the genome of the 50 most common cancers. Identifying whole genome cancer sequences will allow researchers to pinpoint the exact molecular aberrations of each tumour, and will therefore make it easier to target them with the most appropriate treatment.

The Immunology Program was established by a major bequest in 1998 and began with the recruitment of Professors Charles and Fabienne Mackay. It received a major boost in the mid-2000s with the recruitment of several new research groups headed by Emeritus Professor Antony Festen working on autoimmunity and allergy.

Research in the Immunology Program has led to the formation of a spin-out osteoimmunology company, 23 Therapeutics, which developed a monoclonal antibody therapy for rheumatoid arthritis. Clinical trials are currently underway. More recently, the current Program Leader, Associate Professor Robert Brink published innovative data explaining how injection can trigger B-cells to inappropriately launch an autoimmune attack, a process poorly understood until now.

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**50th anniversary edition**

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**1998** Identified the chromosomal region responsible for susceptibility to bipolar disorder

**1999-2005** Developed methods to culture adult nerve stem cells capable of generating new brain cells

**2000** Uncovered the role of abdominal fat in determining risk of Type 2 diabetes and influencing insulin resistance

**2000** First gene chip facility in Australia opened. Developed the largest prostate cancer tissue bank in the world (in collaboration with St Vincent’s Hospital)

**2006** Significant advances made in identifying the exact role of gene mutations in cancers through the use of large human tissue banks and patient databases
The chance to rub shoulders with clinicians at St Vincent’s Hospital was integral to Professor James’ early career. “You got to chat about the big picture, and learn about medicine and clinical application. It put everything into context. That had a very significant impact on me.”

It was this close interaction between scientists and clinicians and the fact that Professor James was a “Sydney boy” that eventually drew him back to the Garvan after completing postdoctoral training elsewhere and running labs in St Louis and Brisbane.

It was during his postdoctoral training that Professor James made what remains a landmark finding in diabetes research - how glucose is ferried from the blood stream into muscle and fat cells. By discovering GLUT4, the insulin-regulated glucose-transporter protein, “was like sitting on Mt Everest,” says Professor James.

Nowadays, the Garvan has over 100 people working on the problems of diabetes and obesity, and those in Professor James’ group are working to understand the complex interaction between the environment, especially increased food intake, and genetics. “We are at an historical moment in science. Genomics is about to become one tool in the physician’s toolbox. We can now sequence people’s genomes and phenotype people with diabetes much more accurately than just taking their blood glucose level. Already genomics and other ‘omics allow us to look more deeply and use information to predict what is going to happen later in the lives of patients,” says Professor James.

The challenge of research is “what gets me up in the morning,” says Professor James. But the success of “big data” research and its impact on diabetes and obesity depends not just on technology, but on the people in Professor James group. “We are only as big as the sum of the parts and we work together as a team.”

What are your thoughts when reflecting on Garvan’s history?

At the 50th anniversary, it is important to remember that the Garvan Institute has two special stories of origin. The first is the legacy left by the Sisters of Charity who believed it was important to not just treat disease, but to try and beat disease. And that spirit stays today. The second is to remember the Garvan family who made a special donation just over 50 years ago to establish a research institute in honour of James Patrick Garvan. It was a magnificent gift, and in a sense a seed was planted. That tree is alive and well and growing 50 years later, and will continue to give to the Australian population for many years to come.

What makes Garvan and The Kinghorn Cancer Centre so special?

We have a long history of research and innovation in cancer, diabetes and obesity, immunological diseases, neurological diseases, and osteoporosis. Garvan is one of the country’s, and the world’s, leading research institutes in these areas. And every one of these disciplines is a major problem, particularly in a population that is living longer because of past advances in medical research and treatment.

The Kinghorn Cancer Centre, which is a joint venture between the Garvan and St Vincent’s Hospital, is the first comprehensive cancer centre in the nation where clinicians who are treating cancer work side-by-side, day-by-day with cancer researchers who are working on new methods to diagnose and treat cancer. The establishment of this new centre coincides with a massive change in our scientific understanding of human genetics and the molecular basis of cancer. The Kinghorn Cancer Centre will lead the nation in the application of new genetic technologies to diagnose and effectively treat cancer.

Can you tell us a bit more about genomic medicine?

Genomics involves sequencing an individual’s entire DNA, as well as analysing their gene expression patterns. Having access to this information enables us to determine the full molecular signature of different cancers, and the best treatment options and approaches. Tumour sequencing has already been used to identify mutations and successfully inform treatment.

Soon, personalised genomic medicine will be routine. Doctors will use patients’ complete genetic sequences to factor in variations between individuals when deciding how to treat diseases. Within the next decade, we will be contemplating having everybody’s individual gene sequence as part of their medical records. Genomics will become an intrinsic part of the healthcare system.

Genomic medicine provides so many opportunities, but are there any challenges?

A challenge is an opportunity! If you can reasonably anticipate what is happening, then you have an opportunity to get ahead of the curve. One big challenge for the healthcare system is to embrace these innovations. Another challenge is how to assemble the information into usable databases. The information must be gathered, curated and translated into advice for the clinicians and patients. The technology is no longer the issue - it will be the gathering and provision of the information that will be critical.

Why does medical research need philanthropy?

Philanthropy has a dual purpose. Firstly, to underpin basic research programs, projects and infrastructure. But more importantly, it empowers the visionary individuals who have new ideas.

Philanthropy is critical because public funding alone can not meet the pressing needs in research and healthcare.

We have people who often have insights well ahead of the curve, and we need to have the resources to attract and equip them to invent the future. Philanthropy provides the bold, visionary solutions that have given us important breakthroughs.

What are the future holds.....

Executive Director Professor John Mattick AO FAA reflects on 50 years of research at the Garvan, and discusses what the next 10 years might hold.

The Kinghorn Cancer Centre
Identified the links between diet, gut bacteria and the immune system, highlighting the importance of insoluble dietary fibre in keeping many diseases at bay.

Demonstrated for the first time that a primary tumour can be shrunk by inhibiting a class of gene known as ‘microRNA’.

In Memoriam November 2012 - January 2013. Donations have been made in memory of:

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- Maureen Aronson
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- Stephanie S Waley
- Monty Walker
- Gordon Weeks
- Rene Wiecek
- Suzette Yuen

-- 2009 --

Identified the links between diet, gut bacteria and the immune system, highlighting the importance of insoluble dietary fibre in keeping many diseases at bay.

-- 2010 --

Demonstrated for the first time that a primary tumour can be shrunk by inhibiting a class of gene known as ‘microRNA’.

-- 2010 --

Showed for the first time that even modest weight loss of 6kgs reverses many of the damaging changes often seen in the immune cells of obese people.

-- 2011 --

Developed a reagent with the potential to prevent rejection of transplanted insulin-producing cells in people with Type 1 diabetes.