A collaboration between US and Australian researchers, including the Garvan, has identified a particular microRNA (a recently discovered class of gene) as a therapeutic target in treating certain cancers, such as the childhood neural cancers known as ‘neuroblastomas’, some melanomas and some brain cancers. The microRNA appears to disable the king of tumour suppressors, the P53 gene. Findings in mice show that blocking the microRNA can restore P53 production and shrink tumours.

A joint finding by researchers from the Garvan and King’s College London shows that a gut hormone, peptide YY (PYY), released after we eat determines the speed at which we digest food and absorb nutrients across the gut into our blood. This in turn regulates our insulin and blood sugar levels. This new finding has deepened the understanding of conditions such as Type 2 diabetes.

Garvan researchers have made an important discovery at the frontier of immunology. They have explained how a pivotal class of immune cells, known as T follicular helper cells, is generated. These cells play a central role in helping B cells make long-lived high-potency antibodies. Future drug and vaccine development relies on a clear understanding of how the essential components of the immune system fit together at a molecular level.

Garvan researchers in association with US pharmaceutical company DiaKine Therapeutics have shown that a drug candidate, Lisofylline, could be useful in treating Type 2 diabetes. This is the first time that it has been suggested that the anti-inflammatory drug, undergoing clinical trials for other diseases, could be useful in treating Type 2 diabetes. Researchers believe it works by preventing the build up of certain by-products of fat metabolism.

By examining how we learn and store memories, Garvan researchers working with American scientists have uncovered a new mechanism of learning that might prove useful in helping people who have lost their capacity to remember as a result of brain injury or disease. They showed that the way the brain first captures and encodes a situation is different from the way it handles subsequent learning of similar events. It is this second stage learning that holds promise if the process can be mimicked therapeutically.

Researchers in Garvan’s Cancer Program have used sophisticated new protein screening technology to profile basal breast cancer, a particularly aggressive sub-type of breast cancer, identifying specific targets for future treatments.
The major diseases that challenge our health and well being such as cancer, heart disease, osteoporosis, Alzheimer’s and diabetes are complex. They arise from the interplay between our genes, lifestyle and the environment. However, sophisticated new technologies are proving to be a powerful weapon in the fight against these disorders. A very recent example from Garvan research has been the use of new protein screening technology to profile basal breast cancer, a particularly aggressive sub-type of breast cancer, identifying specific targets for future treatments.

Basal breast cancers represent approx 20% of all breast cancers, are resistant to hormone therapies such as Tamoxifen and also do not respond to Herceptin, a monoclonal antibody effective in treating a different subset of breast cancers. As a result, the dilemma for clinicians is that there is no effective ‘targetted’ therapy for basal breast cancer.

Cancers behave in extraordinarily complex ways, well below the cellular level. Each cancer type has a submicroscopic fingerprint defined by its particular mix of thousands of proteins – the molecules that carry out work in cells. Until now, basal breast cancer’s protein fingerprint has remained elusive.

Using this new technology, Garvan researchers have shown that basal breast cancers display a characteristic ‘signature’ or ‘fingerprint’ of phosphate molecules attached to proteins. In addition, these cancers show heightened activity of several different kinds of cellular enzymes known as ‘kinases’ responsible for attaching phosphate groups to proteins.

These findings suggest that we should stratify patients according to which kinases are active in their cancers. These kinases can then be targeted by specific therapies - and because several kinases are commonly activated in basal breast cancers, use of combination therapies that target more than one kinase, or multi-kinase.

Val Duncan had good friends among the doctors at St Vincent’s, and always used to say to them, “I’d love to have a look through the Garvan!” One day, the Garvan Research Foundation was able to arrange this and with a family interest in Type 1 diabetes, Val found her visit even more fascinating than she had foreseen. She then encouraged her husband, Peter, to come and take an interest too. In his typical, no-nonsense straightforward fashion, Peter’s response was, “What’s on the Institute’s wish list?”.

With his engineering background, he was particularly partial to considering making a gift to support the purchase of new equipment for the Garvan. At the time, the Institute wished to expand its core scientific facilities with the addition of a two-photon microscope. Unlike other microscopes which typically involve looking at frozen sections of tissue, two-photon microscopy allows us to image living tissue in great depth at very high resolution in real-time: viewing the activities of cells within a living system can teach us so much more. The only difficulty is that establishing a two-photon facility involves not just procurement of the microscope itself, but also a suite of peripherals such as an anti-vibration table and a special high powered ultrafast laser – requiring a significant commitment.

Brought up in families who simultaneously encouraged the values of thrift and giving to others, both Val and Peter were keen to make a big difference at the Garvan. One of Peter’s favourite sayings is: “It’s not what you spend, it’s what you save”. In keeping with this motto, Peter even became involved in negotiating for the Garvan with the two-photon suppliers and was instrumental in getting the very best deal. The two-photon has now officially been christened “Susie”, in honour of Peter’s mother, a very special lady who was always able to see what many others didn’t.
Dear Friends,

You may have heard that after five very full years at the Garvan, I am stepping down from the position of Foundation CEO as it is time for me to take up some new and different opportunities for growth. The Garvan is a wonderful place to work largely due to the quality of people with whom you come into contact. It has been a great honour and pleasure for me to serve in this position and to witness the incredible generosity shown to our cause by our supporters. Together, we have been able to make a real difference to our great scientists and their efforts to change our health future for the better. We can all be very proud of that.

While the Foundation Board begins the search for a new CEO, the strong and dedicated Foundation team will continue to ensure that every member of our Garvan community is well looked after and informed. As an interim strategy, Gabriella Lang will function as Acting CEO, working closely with Dimity Raftos as General Manager and Dianne Lavender heading up Public Relations.

Just some of the delights of working at the Garvan which I will miss are the treasure trove of medical research facts I have learnt from our scientists – such as butt fat is better than gut fat; osteoporosis affects elderly men just as badly as women; neuropeptide Y is a key player in stress, anorexia and just about everything; there are four, maybe five, known sub-types of breast cancer and more to be discovered; and T follicular helper cells are considered a ‘sexy’ area of immunology! Fortunately, as a supporter you can continue to accrue these riches – through this newsletter, by joining us on tours or at seminars - to drop on your friends over dinner!

The web of relationships formed between our supporters, scientists and the wonderful Foundation team is part of the Institute’s lifeblood and critical to our ability to continue generating research breakthroughs. Thank you for your ongoing loyalty to the Garvan and my very warmest wishes to you and yours.

Carole Renouf
CEO, Garvan Research Foundation

Running, Dancing, Cycling and Drinking Tea for Medical Research.

Garvan would like to say thank you to those energetic supporters who have held or participated in community fundraising events throughout the country to help in the fight against disease.

On 8th August, 50 Garvan staff participated in the City to Surf. The conditions were perfect for the 14 km run to Bondi and along with raising awareness of Garvan’s research, the ‘Garvan Giants’ won the registered charity section with times of 52 min, 56 min and 58 min for our first three runners.

The 2010 Young Garvan All Ribbons Ball, held on the 14th of August at the Sofitel Wentworth, was a tremendous success with over 430 people enjoying a fabulous night of fun, entertainment and fundraising. The black-tie dinner raised over $70,000 for the Young Garvan Post Doctoral Fellowship awarded jointly to Dr Matt Prior and Dr Liz Caldon. Young Garvan is a volunteer committee whose aim is to engage and educate young Sydney professionals as well as raise funds for the Young Garvan Fellowship.

We welcomed the beginning of spring with the Garvan High Tea. We invited our friends in the community to host High Teas in September to raise awareness and funds for our work. More than 140 people attended and contributed to High Teas raising more than $10,000.

In other community events, Gwenda Alderdice bravely cycled 548 kms from Cairns to Bowen to raise funds for Garvan’s pancreatic cancer research. To donate in support of this amazing effort visit www.giving.garvan.org.au/ridingforresearch. Kanat Wano organised a series of fundraising events in Townsville, known as FullBlack, to raise much needed funds for our research into Type 1 diabetes.

Thank you to all.

Karen Faulkner’s Garvan High Tea (l to r) are Karen, Dimity Raftos, Steve Ray and Elaine Beggs.
The increasing prevalence of neurodegenerative diseases such as Parkinson’s, Alzheimer’s and other dementias in our fast-ageing society is fuelling the need to find new and more effective therapeutic approaches for these disorders.

Dementia currently affects 250,000 Australians, with 1 million expected sufferers by 2050. More than 100,000 Australians are living with Parkinson’s disease, a figure estimated to increase by 4% each year. Garvan’s Neuroscience program is investigating these diseases from a range of approaches with the aim of better understanding the neuronal systems involved to ultimately pave the way for new therapies.

Alzheimer’s disease is a progressive illness marked by the degeneration of neurons in the cerebral cortex - an area of the brain vital for memory and other mental abilities. Plaques which contain misfolded proteins called beta amyloid form in the brain many years before clinical signs of the disease are obvious. Another protein, called tau, abnormally aggregates in the brain cells causing them to die. It is not known if this pathology, which is used to definitely diagnose Alzheimer’s after death, initiates the disease or results from the disease.

In the case of Parkinson’s, neurons in the part of the brain that control co-ordinated movement progressively degenerate. This creates a shortage of the brain signalling chemical (neurotransmitter) known as dopamine, causing the movement impairments that characterise the disease. The causes of both diseases are currently unknown. Although there is no cure, they can both be managed with drug treatments to alleviate symptoms. However, they come with side effects and do not alter the progression of the disease.

Research into adult neural stem cells as possible neuroreplacement therapies for Parkinson’s and Alzheimer’s is holding great promise, and Garvan is at the forefront of this field. There are many benefits in working with adult stem cells, the main one being their multipotent nature. This means that they can develop only into closely related cells - for example Garvan researchers have shown it is possible to convert sensory olfactory stem cells from the nose into hearing receptor cells known as hair cells. The other main advantage of sourcing adult stem cells from the same patient is that they do not carry the same risk of immune rejection and therefore anti-rejection drugs are not required.

Dr Kharen Doyle from Garvan’s Neuroscience program has been looking at the feasibility of using olfactory stem cells for conversion into the dopamine producing neurons lost in Parkinson’s disease (dopaminergic neurons). Ultimately, this work may lead to the ability to source olfactory stem cells from a patient, and convert them into dopaminergic neurons which would then be injected back into the area of the brain where these cells develop.

Dr Doyle is also seeking to understand the molecular process underlying adult stem cell differentiation, or in other words what is the trigger driving a particular differentiation pathway. By understanding how this process works, and the optimal environment for stem cell differentiation (or stem cell niche) it may then be possible to turn these triggers on within the brain without the need for transplantation. Dr Doyle hopes to apply the same research approach to differentiate olfactory stem cells into acetylcholine producing cholinergic neurons lost in Alzheimer’s disease.

In another approach to Parkinson’s disease research at the Garvan, Dr Antony Cooper’s lab is focusing on what causes neurons to malfunction and die at the earliest stages of disease progression.

Understanding the first domino to fall in the progression of neuron death has many benefits for Parkinson’s disease sufferers. Firstly, it will assist in identifying biomarkers for early detection of the disease, prior to the onset of symptoms. This is crucial given that Parkinson’s patients have lost at least 70% of their dopamine-producing cells by the time symptoms appear. Secondly, it may be possible to identify drug targets to inhibit the processes leading to cell death.

To understand what is going wrong within the cell at the early stage of disease progression, Dr Cooper is looking for...
new genes (and their proteins) with links to Parkinson’s disease. This will lead to a better understanding of why, when a particular gene is dysfunctional, the cell becomes more susceptible to failure leading to disease onset.

Dr Cooper’s research is also focused on the interaction between the genes known to play a key role in Parkinson’s, specifically PARK9 and alpha-synuclein. While little is known of PARK9, scientists have known for some time that over-expression of this protein is toxic and has been found in abundance in the brains of deceased Parkinson’s sufferers. In one of his recent findings using - of all things - yeast, Dr Cooper and collaborators discovered a critical connection between these two genes. Yeasts are single cell organisms that are widely used in biological research because their structure resembles that of cells found in animals and humans.

PARK9 is found in yeast and alpha-synuclein can be introduced to yeast, making it possible to analyse their function. He found that high levels of PARK9 in a cell significantly diminished the toxic effects of alpha-synuclein. PARK9 also appears to be a manganese pump capable in theory of removing excess levels of this metal from cells - an important finding because manganese poisoning can also cause Parkinson’s-like symptoms. This work showed for the first time the connection between three pieces of the Parkinson’s disease jigsaw (PARK9, alpha-synuclein and manganese), indicating that the research is on the right track to understanding what goes wrong in the disease.

Drs James Daniel and Bryce Vissel in the Neuroscience program have been looking at Parkinson’s disease from another perspective. Findings from their recent research have significantly advanced our understanding of dopamine release from nerve cells, and may speed the development of more effective drugs for treating Parkinson’s disease. The primary symptoms of Parkinson’s (rigidity, tremor and impairment of physical movement) are caused by the loss of dopamine producing nerve cells in the brain. Medicines used for treating Parkinson’s either provide extra dopamine or attach to the remaining nerve cells that release dopamine and regulate its release. In the latter case, no-one understands the mechanisms involved, or how to control them.

When an electrical impulse reaches the end of a dopamine nerve cell, called a synapse, it sometimes stimulates the release of dopamine. Yet more often, it doesn’t. Only about one in five impulses cause dopamine release, and the release rhythm is irregular. So the cell might release dopamine five times in a row, then not release twice, then release once, and so on.

Drs Daniel and Vissel have developed a mathematical model and microscopy method that reveal the mechanisms behind synaptic dopamine release – and the factors that govern the probability of release. Their work involved developing sophisticated statistical analysis protocols and mathematical models of synapses, to help de-mystify the part of the process that takes place at the dopamine nerve cell synapse. Their findings may help work out how drugs currently being used to treat Parkinson’s disease are regulating dopamine release. It will also open up new avenues for pharmaceutical development.

Further work in Dr Vissel’s lab has shown that nerve cells in the brain produce an anti-inflammatory molecule that allows the brain to repair itself, possibly changing the way we think about treating neurodegenerative diseases. Researchers have only recently been aware of the brain’s capacity to regenerate. Drs Vissel and Andrea Abdipranoto, seeking to understand what drives and blocks this regeneration, found high levels of a molecule known as Activin A being released from nerve cells whenever regeneration occurred in the brains of mice. It seemed that nerve cells may directly drive regeneration by released Activin A.

However, further experiments showed that the main role of Activin A was to block inflammation in the brain after neurodegeneration or injury. While inflammation is the body’s way of protecting itself against harmful irritants or damaged cells, these findings highlight that if left uncontrolled inflammation can prevent regeneration and healing. It is likely that inflammation aggravates existing damage in the central nervous system of people with Parkinson’s, Alzheimer’s and motor neurone disease. The researchers believe that chronic inflammation is probably providing a harmful feedback loop, preventing regeneration and contributing to progressive decline. If further research confirms that inflammation is blocking regeneration in these diseases, Activin A and derivatives need to be investigated as potential therapeutics.

Work by Garvan’s Neurosignalling group led by Dr Adam Cole also has potential impacts for sufferers of neurodegenerative disease. Dr Cole investigates the molecular mechanisms involved in synaptic plasticity - the part of the brain that is changeable and increases our ability to learn and adapt to new things. This is particularly active in our early development. However, in the ageing brain synaptic plasticity decreases and in neurodegenerative disease deterioration of this function is dramatic.

By understanding how synaptic plasticity works in a healthy brain it may be possible to develop strategies to enhance brain function and specifically the ability to learn new things, retain and recall information. For sufferers of neurodegenerative diseases this understanding may assist to delay or prevent the onset of disease and possibly help compensate for the loss of brain function.

The Neurosignalling group is focused on 3 enzymes (CdK5, GSK3 and PCTK2) known as kinases found in the brain which are important for neurotransmission (communication between neurons) and regulation of synaptic plasticity. The group is working to better understand how these proteins regulate neurotransmission in healthy brains, but also why changes to their activity contribute to brain dysfunction during ageing and in dementias such as Alzheimer’s disease. In previous research Dr Cole discovered a brain protein called CRMP2 that is excessively modified in the brains of Alzheimer’s disease patients. He found that his occurred early in the disease process and was specific for Alzheimer’s disease, giving it great promise as a diagnostic biomarker for early and specific detection of Alzheimer’s disease.

In recent work he discovered a similar brain protein called β-adducin that is also found in red blood cells. Since blood is more accessible for diagnostic purposes, this poses the exciting possibility that β-adducin might serve as an early stage, blood-based biomarker for Alzheimer’s disease. If so, this would greatly assist in earlier diagnosis of Alzheimer’s disease, when patients are more receptive to drug therapy.
Helping Hands for The Kinghorn Cancer Centre

Generous supporters of The Kinghorn Cancer Centre and staff from its partner organisations, the Garvan and St Vincent’s Hospital, are not afraid to get their hands dirty to share in community spirit. Together with students from local Darlinghurst Primary School, they have created a unique community mural, “HELPING HANDS, HEALING HANDS”, which features hundreds of hand prints of St Vincent’s and Garvan staff, students, Kinghorn Cancer Centre Patron Delta Goodrem, Jill Kinghorn and other generous supporters and embodies not only community connectivity but also the importance of making major inroads in the fight against cancer for future generations.

“I am so proud that my hand print is going to be on The Kinghorn Cancer Centre. For me it represents a symbolic connectivity to a project that I am very close to as we work towards finding better cancer treatments for our community and beyond,” said Patron Delta Goodrem.

The mural has been erected along Victoria Street on the hoarding of the construction site of The Kinghorn Cancer Centre for the 18 month duration of the Centre’s construction.
In an effort to break the Guinness World Record™ for the largest model of DNA in the world, the Garvan has constructed a 25.66 metre long replica of the neuropeptide Y gene (NPY), with the help of 150 school students from Sydney Boys High, Sydney Girls High, SCEGGS Darlinghurst, Sydney Grammar School, Ascham and Cranbrook Schools.

The model was an added attraction for attendees at Garvan’s Open Day, who battled bad weather to spend a day discussing the latest breakthroughs in medical research with our scientists, touring the building and listening to a series of Breakthrough Talks. We were delighted to welcome many new visitors to the Garvan on Open Day.

Over 100 scientists, staff and volunteers not only from Garvan, but from Colin Biggers and Paisley and National Australia Bank happily gave their time creating a great spirit of enthusiasm and collaboration. We wish to thank donors and their friends and families who joined us to find out more about our research.

If you missed Open Day you can watch videos of the Breakthrough Talks at www.giving.garvan.org.au/openday.

Visitors to Open Day check out the mini-expo.

Breaking Records and Open Day

The 25.66 metre long DNA model hanging through Garvan’s atrium.

What is Garvan’s position on gene patenting?

The Garvan supports the appropriate use of patenting of true gene related inventions as a means to help develop research discoveries into practical treatments and to ensure industry does not make inappropriate profits from tax payer funded research.

By protecting our research discoveries in this way, industry must “pay back” the public good institutions’ investment in the original research. However, a close working relationship with industry is essential to ensure that research discoveries born in our laboratories are quickly translated into new improved treatments for disease.

A good example of appropriate patenting today would be for the engineering of a new antibody to a cell receptor (a novel invention). It is not possible to patent a gene. A patent can only be issued for a true invention, not just isolation of an existing gene.

As with any rapidly developing technology, the science behind gene research is always ahead of the legal and patent issues. This is why the patent system provides for legal review and challenge to ensure that patents are not enforced on standard processes and tests.

Garvan supports the recent court decision in the US to overturn the issuing of patents for diagnostic tests for a breast cancer gene to Myriad Genetics.
Osteoporosis Clinical Study

Osteoporosis is a major disease causing disability and death especially as we get older. Excellent medications to stop progression of the disease have been available for some years. The most common medications must be taken fasting and in a very specific way, and sometimes cause side effects. Unfortunately sometimes people can forget to take their medications; a common problem when the medications are to prevent diseases rather than treat present symptoms.

In view of very encouraging results from an earlier study of a medication given as an injection to treat osteoporosis in women, Garvan is now recruiting patients for a new study to look at women being treated for post menopausal osteoporosis who have had problems taking an existing oral medication regularly i.e. alendronate (Fosamax®, Alendro®, Adronat®, Alendrobell®, Alendronate sodium). Participants will be asked to either have an injection every 6 months or take another effective treatment by mouth on two days per month. The aim of this 12-month study is to compare the effect of the two medications on bone structure and strength and to see if the participants prefer the injections to the tablets.

For further information please contact Ruth Toppler on (02) 9295 8269, or email r.toppler@garvan.org.au or Dr Yvonne Selecki on (02) 9295 8269 or email y.selecki@garvan.org.au.

In memoriam: 25 June – 30 October 2010

We gratefully acknowledge gifts received in memory of:

- Dale Alderdice
- Elstatios Amanatidis
- Robyn Stewart Barratt
- Janet Blake
- John Burne
- Colleen Calaghan
- Alexander Canaris
- Joan Chapman
- Richard Clegg
- Patrick Coyne
- Margaret Anne Dilosa
- Cherie Ditrich
- Sue Dowlan
- Judith Ann Dunbar
- Frances Fazzino
- Marie Suzon Chantal Fricot
- Fred Gernhoefer
- Steve Goracz
- Kevin Graham
- Gary Gray
- Paul Hosford
- Françoise Hulme
- Djuro (George) Kijurina
- Tsung Cheng Lin
- John Lowe
- Bunty Mantel
- Geoffrey Mason
- Dorothy Maitland
- George McCall
- Bruce Moody
- Annemarie Nanasi
- Peter O’Grady
- Lawrence Patrick
- O’Donoghue
- Rosemary Pang
- Greg Park
- Christine Pegler
- Sue Punch
- Dawn Schultz
- Gloria Elizabeth Smith
- Chris Soupisid
- Andrew Stewart
- David Stroke
- Christopher John Vincent
- Doug Waitley
- Fred Wrigley
- Hugh Norman Wrigley
- Evangelos Xenoulis

2011 Garvan Public Seminars

The 2011 program of Public Seminars will include: The Ageing Brain – Latest Breakthroughs in Neurodegenerative Disorders (24th March) and Latest Advances in Cancer Research and Treatment (13th September). Both events are held from 10am – 12pm. Seats for seminars are limited and registration is essential by calling (02) 9295 8110 or visit www.giving.garvan.org.au. Garvan will also host a public lecture by the Garvan International Fellow, a renowned scientific expert in 2011. Stay tuned for information about this lecture online at www.giving.garvan.org.au.

In memoriam: 25 June – 30 October 2010

We gratefully acknowledge gifts received in memory of:

- Dale Alderdice
- Elstatios Amanatidis
- Robyn Stewart Barratt
- Janet Blake
- John Burne
- Colleen Calaghan
- Alexander Canaris
- Joan Chapman
- Richard Clegg
- Patrick Coyne
- Margaret Anne Dilosa
- Cherie Ditrich
- Sue Dowlan
- Judith Ann Dunbar
- Frances Fazzino
- Marie Suzon Chantal Fricot
- Fred Gernhoefer
- Steve Goracz
- Kevin Graham
- Gary Gray
- Paul Hosford
- Françoise Hulme
- Djuro (George) Kijurina
- Tsung Cheng Lin
- John Lowe
- Bunty Mantel
- Geoffrey Mason
- Dorothy Maitland
- George McCall
- Bruce Moody
- Annemarie Nanasi
- Peter O’Grady
- Lawrence Patrick
- O’Donoghue
- Rosemary Pang
- Greg Park
- Christine Pegler
- Sue Punch
- Dawn Schultz
- Gloria Elizabeth Smith
- Chris Soupisid
- Andrew Stewart
- David Stroke
- Christopher John Vincent
- Doug Waitley
- Fred Wrigley
- Hugh Norman Wrigley
- Evangelos Xenoulis