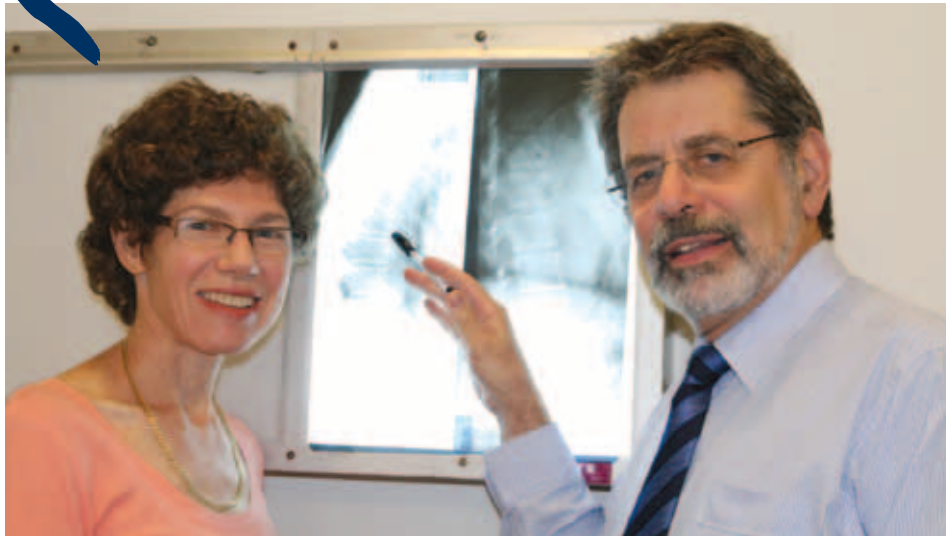




breakthrough

Associate Professor Jacqueline Centre and Professor John Eisman

Garvan researchers have found an unexpected benefit of osteoporosis treatment. People taking bisphosphonates are not only surviving well, and better than people without osteoporosis, they appear to be gaining an extra five years of life. Out of a cohort of around 2,000, a sub-group of 121 people were treated with bisphosphonates for an average of 3 years. When compared with other sub-groups taking other forms of treatment such as Vitamin D (with or without calcium), or hormone therapy, the longer life associated with bisphosphonate treatment was marked. This finding by Associate Professor Jacqueline Centre and Professor John Eisman reinforces the message that treating osteoporosis reduces fractures and reduces mortality. Currently only 30% of women and 10% of men with osteoporosis receive treatment.

making news

➤ Immunology researchers are closer to understanding how immune cells interact leading to Type 1 diabetes. In the disease, B cells see insulin-producing beta cells as the enemy and recruit T cells to help kill them. Researchers have identified two chromosomal regions in mice that control the ability of beta cell reactive B cells to interact with T cells, and determine whether or not Type 1 diabetes develops. The finding could help identify therapeutic targets to prevent Type 1 diabetes.

➤ Garvan researchers, using data from the Dubbo Osteoporosis Epidemiology Study, have found that beta-blocker use increases bone density and reduces the risk of osteoporotic fracture by around 50% in men and women.

➤ Garvan Immunologist, Dr Stuart Tangye has received the prestigious 2011 Gottschalk Medal from The Australian Academy of Science. Dr Tangye has made significant contributions to the understanding of various types of immune cells, and how these cells malfunction in rare immunodeficiency disorders.

➤ Garvan researchers have shown that children born of mothers with gestational diabetes will tend to become fat, and the worse mum's sugar levels during pregnancy, the fatter the child will be. The finding highlights how important it is for women to maintain healthy weight before and during pregnancy.

inside this issue

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➤ The mystery of why some people respond well to chemotherapy or radiotherapy for colorectal cancer and others don't may have been solved by researchers in Garvan's Cancer program. They have found that the gene 'MCC' is expressed at low levels in a subset of colorectal cancers, making them more responsive to radiotherapy or some types of chemotherapy.

➤ Garvan researchers have shown for the first time in mice that nasal stem cells injected in the inner ear have the potential to reverse or restore hearing during early onset sensorineural hearing loss.

opinion



After 20 years as Executive Director of the Garvan Institute many of you may be aware that I'm retiring from the position later this year and will spend more time at the laboratory bench.

It has been a privilege to be at the Garvan through a period of significant expansion and change over the last 20 years. Since 1990, the Garvan has grown from a staff of 113 to over 500, and an operating budget of \$400,000 to around \$50 million. It has been particularly pleasing for me to see our research scope and international standing increase significantly as we strive to improve the quality of life for all. This quest and our focus on the opportunities presented by closely linking basic research to clinical care will of course continue as we progress towards the opening of The Kinghorn Cancer Centre next year.

Without the generosity of our supporters much of these achievements would not have been possible. I thank all our loyal and committed donors - your support is critical to our success in achieving research breakthroughs.

The Garvan Board is currently undertaking a search for a new Executive Director. When this appointment is made later in the year I intend to focus on my research on adult neuronal stem cells. These cells have the potential to differentiate into any kind of nerve cell, and hold great promise as possible neuroreplacement therapies for those with neurodegenerative diseases such as Alzheimer's and Parkinson's disease.

I look forward to playing some small part in the worldwide effort to progress this important work and, like all Garvan scientists, remain committed to the advancement of medical research and the acquisition of new knowledge to fight the major diseases affecting our society.

Professor John Shine AO FAA
Executive Director

Donor Profile: Deanne Weir

Like many of our supporters, Deanne Weir has a deeply personal interest in Garvan's work. Ten years ago she lost her mother to ovarian cancer. For this reason, Deanne is committed to facilitating the discovery of early diagnostic tools and eventually finding a cure for this life-threatening disease.

Ovarian cancer is the sixth most common cause of cancer death in Australian women. It remains one of the hardest to detect in its early, curable stages with over 75% of sufferers being diagnosed at an advanced stage. This is because many of the early symptoms such as swelling and pain in the abdomen; changes in the usual menstrual pattern or postmenopausal bleeding; nausea and bloating; tiredness and appetite loss and unexplained weight loss or gain can occur in healthy women (especially those undergoing menopause). The problem is further compounded by there being no accurate non-invasive screening tests for the disease. After visiting the Garvan and meeting with our researchers, Deanne was



inspired to pledge ongoing financial support to our ovarian cancer research. And the timing of her generous donation could not have been better – in February, Garvan welcomed Dr Goli Samimi as the new Group Leader of the Ovarian Cancer Project.

Dr Samimi will focus on discovering novel prognostic biomarkers and new therapeutic targets for this disease. Deanne's funding will move us a step closer to our goal of curing ovarian cancer and is a wonderful tribute to her beloved mother, Evelyn.

ACRF Announces \$5 Million Grant



L to R: Garvan Chairman Bill Ferris AC, ACRF Chairman Tom Dery, Alicia McMahon, Melinda McMahon and Sr Anthea Groves, close friend to Lady McMahon.

The Australian Cancer Research Foundation (ACRF) has awarded its equal largest ever research grant of \$5 million towards the construction of The Kinghorn Cancer Centre. The ACRF grant honours the late Lady (Sonia) McMahon, life member and one of two joint founders of the Foundation (the other being the late Sir Peter Abeles). Lady McMahon

passed away last year at St Vincent's Hospital after a long battle with cancer. The announcement was made at a cocktail party at the Garvan attended by Lady McMahon's daughter Melinda and granddaughter Alicia. A plaque in Lady McMahon's memory was unveiled at the event.



The Foundation Welcomes Andrew Giles

The Garvan Research Foundation is pleased to appoint Andrew Giles as its new Chief Executive Officer. Since 2004 Andrew has been the CEO of the Prostate Cancer Foundation of Australia (PCFA) and led it through a period of remarkable growth into the peak body for prostate cancer in Australia. He oversaw such diverse activities as the *Be A Man: talk to your doctor* national TV campaign; the development of national support group networks with over 110 support groups across Australia and the development and growth of Movember (which is now the largest fundraising event for prostate cancer in the world). Prior to joining PCFA Andrew worked for a range of national and international not-for-profit organisations such as the University of Sydney, the University of NSW, AUSTCARE, Sydney Children's Hospital and the Yothu Yindi Foundation. Here Andrew shares his expectations in taking on this new role.

What inspires you about the work of the Garvan?

The Garvan is one of the most pre-eminent research institutes in Australia and, for someone like me with a passion for medical research, I consider it a great

privilege to be able to take on this role. For the past seven years, as the CEO of PCFA, I was fortunate to oversee the development of a world-class grant program to fund Australian researchers. This gave me an opportunity to meet many of the leading researchers in the cancer field in Australia, and see their incredible passion and dedication. It also gave me an insight into how tough it is to be researcher – and in particular to be regularly searching for funding. Equally inspiring is the passion of the donors who, not only give vital funds, but also give up their time to be part of the wider Garvan family through their attendance at events and seminars.

How important is the ongoing support and engagement of the community for the advancement of medical research?

I am always impressed by the level of understanding that the community has for research and researchers. I have long noticed that Australians don't tend to generally just give money and not care where it goes – they are concerned to see it goes to the right place. As such it is vitally important to ensure that the



community is regularly engaged and informed about the advances in medical research – advances and breakthroughs made possible through their support.

What are you most looking forward to in your first 6 months at the Garvan?

One of the greatest attractions to me about joining the Garvan is the diverse range of programs that it undertakes. So I am really looking forward to getting to meet the researchers and get a sense of the status of their work, their hopes and vision for their projects moving forward. I am also hoping to catch up with as many of our donors as possible through events like the AGM and seminars.

The difference you made in 2010

Finding cures needs more than just scientists. It also needs people like you. A heartfelt thank you to the 7,200 individuals and organisations who, through their thoughtful generosity, were a vital part of Garvan's research efforts in 2010.

Your kind gifts went towards covering vital costs across Garvan's five research areas: Cancer, Diabetes & Obesity, Immunology, Osteoporosis, and Neuroscience.

They helped us with:

- Establishment and maintenance costs of shared **state of the art scientific facilities**
- Funding of **novel projects** which are too early-stage to be eligible for government grants

- Costs of the **high tech IT** needed to run complex scientific analyses and databases
- Purchase of **equipment** vital to our work such as gene chip machines and microscopes
- Funding **specific research projects**
- Funding the construction of **The Kinghorn Cancer Centre**

Vital seed funding for our most innovative projects

One of the most important ways that public donations are used is to finance the exploration of new research ideas through our **New Projects Fund**. Before we can apply for government grant funding for new projects, a great deal

of work has to be completed to gather preliminary data. This work can take several years. Your donations to the fund allow our scientists to pursue exciting new ideas, explore possibilities, prove or disprove their theories. Otherwise, these opportunities would fall by the wayside. In 2010 work progressed on a wide range of innovative projects, any of which could one day lead to a medical breakthrough.

Without your support Garvan scientists would not be able to do their work. Thank you for your investment in the search for scientific knowledge that could benefit all mankind.

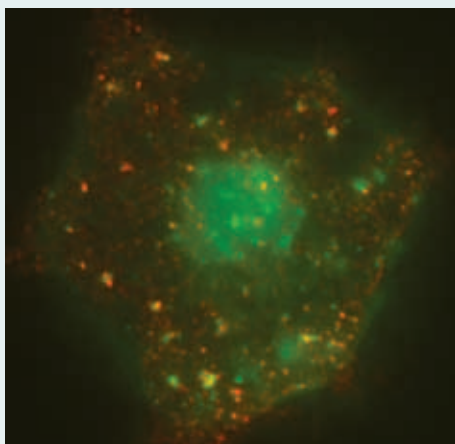
feature story: 2010 in Review

Modern medical research is driven by new creative ideas and collaborations in an environment of sophisticated technology. The Garvan acquired a number of vital pieces of equipment in 2010 thanks to our generous supporters including an electron microscope, two-photon microscope, mass spectrometer and cell sorting facility. This range of technology and imaging techniques is critical to apply to the complex diseases we research.

During the year Garvan published 201 internationally peer reviewed research papers with an average 'impact factor'* of 7.76 for the top 80% of publications. This is well above the international benchmark. Here are a few of the important discoveries from 2010:

Diabetes and Obesity

Researchers in Garvan's Diabetes and Obesity program have shown for the first time that even modest weight loss of about 6kgs reverses many of the damaging changes often seen in the immune cells of obese people,



Fat cell imaged under a microscope

particularly those with Type 2 diabetes.

Many different immune cells protect the body from germs, viruses and other

invaders, and they need to co-exist in a certain balance for good health. Factors such as diet and excess body fat can tip this balance, creating immune cells that can attack our body rather than protect it. Excess body fat, in particular abdominal fat, stimulates immune cells to become activated and 'pro-inflammatory'. These immune cells circulate in the blood and can promote coronary heart disease and other obesity-related illnesses. Other inflammatory immune cells, known as macrophages, are also activated within fat tissue.

Garvan's Associate Professor Katherine Samaras and Dr Alex Viardot studied the effect of weight loss on immune cells. Their study looked at obese people with Type 2 diabetes or prediabetes on a calorie restricted diet for 24 weeks. Gastric banding surgery was performed at 12 weeks to assist in restricting food intake.

Their results showed an 80% reduction of pro-inflammatory T-helper cells, as well as reduced activation of other circulating immune cells and decreased activation of macrophages in fat. They found that modest weight loss of 6 kg was enough to bring the pro-inflammatory nature of circulating immune cells back to that found in lean people. The researchers also showed that the activation status of immune cells found in fat predicted how much weight people would lose following a calorie restricted diet and bariatric surgery. Those with more activated immune cells lost less weight.

Excess weight disorders now affect 50% of adult Australians. These findings highlight the risks of carrying excess fat for the immune system and general health and wellbeing.

Cancer

Research by Dr Alex Swarbrick

from Garvan's Cancer program, in collaboration with colleagues from the Queensland Institute of Medical Research and the University of California, has identified a potential new way to treat certain cancers.

While studying the rare and aggressive childhood cancer of the nervous system, neuroblastoma, the researchers discovered that a new class of genes known as 'microRNAs' was driving the growth and survival of these cancers. Until recently microRNAs were dismissed as 'junk DNA', however it is now clear that they can interfere with how our genes are 'read'.

The researchers showed that one particular microRNA (microRNA 380) appears to disable the king of tumour suppressors, the P53 gene. This gene is so vital that it is also known as the 'guardian of the genome'. In many cancers P53 is either mutated or disabled.

In neuroblastoma, the researchers found that P53 was disabled by the overproduction of microRNA 380. However, by delivering an inhibitor of microRNA 380, effectively blocking its action, P53 production resumed, cancer cells died and tumours began to shrink.

The particularly exciting outcome from this research is that for the first time researchers blocked the primary tumour by the simple delivery of a microRNA inhibitor, which is the way it might be used in patients in a clinic, rather than using sophisticated genetic tricks.

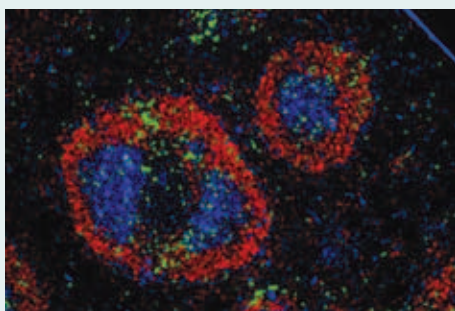
The researchers are keen to investigate whether these findings apply to other cancer types, including some adult brain cancers and melanomas, where this microRNA is produced in high numbers. Similarly, it may be possible to treat these more common cancer types with the microRNA inhibitor.



While this research is at an early stage, it holds much promise for the future treatment of early childhood neuroblastomas and other microRNA-induced cancers.

Immunology

A critical breakthrough at the frontier of immunology by Garvan researchers created a significant buzz in the field in 2010, and will translate to more



Germinal centres (blue) inside B cell follicle (red), with T follicular helper cells (green)

effective drugs and vaccines to fight autoimmune diseases.

Immunology researchers Drs Elissa Deenick, Stuart Tangye and Associate Professor Robert Brink have explained how a pivotal class of immune cells, T follicular helper cells, is generated. These cells are central to the normal function of our immune system, making it essential for us to understand exactly how they work. Their role is to help B cells (a type of white blood cell) make long-lived high-potency antibodies. Whenever we are infected, or vaccinated, many of our B cells migrate to the antibody-generated hot spots in lymph nodes known as 'germinal centres'. T follicular helper cells cluster around germinal centres, communicating with B cells and helping them make the best possible 'antigen-specific' antibodies.

Not only do these antibodies fight the current infection, but 'memory B cells' created in the process instantly recognise the same invader in the future. Without these cells our immune systems are severely compromised.

Without T follicular helper cells, there would be no germinal centres, no high affinity antibodies and no memory B cells, making it critical for us to understand exactly how they work. These cells were discovered around a decade ago, but until now scientists have not known how they are generated and how they function.

This discovery has shed light on a previously misunderstood area of the immune system and will help in the better development of drugs and vaccines to fight disease.

Osteoporosis

Garvan researchers identified surprising connections between the brain and the regulation of bone mass which may lead to new treatments for osteoporosis.

Our skeleton provides critical mechanical support for our body and to fulfill this role bone tissue modifies throughout our lives in response to changing body weight and activity levels. Bone mass increases as we gain weight and decreases as we lose it.

The findings by Dr Paul Baldock show that bone formation, far from being a straightforward mechanical process dependent on body weight, is delicately orchestrated by our brain, which sends and receives signals through the body's neural and hormone systems. It is now clear the neural network which controls appetite and energy also alters bone density. When we are starving, our brains don't allow us to waste energy on reproducing, making fat or creating new bone. When we eat too much our brains make it easier to do these things.

Dr Baldock's work has demonstrated in mice that the neurotransmitter Neuropeptide Y (NPY) directly controls osteoblasts, the cells that make bone. His research may lead to novel osteoporosis treatments in the future that safely block NPY receptors on osteoblasts.

Neuroscience

Researchers at the Garvan, in collaboration with American scientists, have uncovered a new mechanism of learning that may help people who have lost their capacity to remember as a result of brain injury or disease. The researchers, including Garvan's Dr Bryce Vissel, have shown that the way the brain first captures and encodes a situation or event is different to the way it handles subsequent learning of similar events. This second stage learning may hold promise if the process can be mimicked therapeutically.

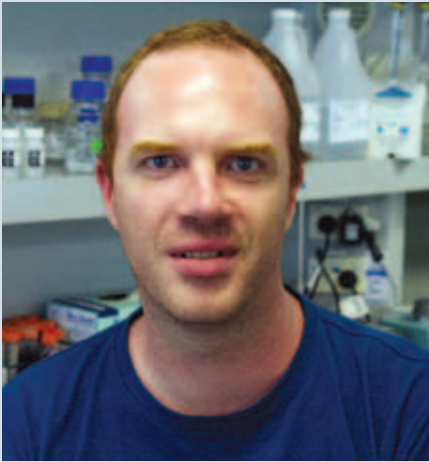
When a memory is first formed, a small protein involved in synaptic transmission, the 'NMDA receptor' is indispensable to the process. Activation of the NMDA receptor allows calcium to enter the neuron which triggers a chain of molecular reactions that help encode experience and consolidate memory.

Until now it has been assumed that learning cannot occur without the NMDA receptor. These new findings show that NMDA receptors are not essential in 'second-learning'. The researchers have identified another class of receptors that appear to take on this role, uncovering a whole new mechanism of learning.

While the work is still in discovery phase, this finding may offer a new target for drugs that are different from the standard class of cognitive enhancers. There are also possibilities for different styles of training that better activate this newly discovered mechanism.

*The impact factor of a scientific journal indicates its relative importance in a specific discipline. Research organisations use average impact factor measurements to determine the overall significance of their research output.

Researcher Profile: Dr Greg Neely



What are some of the recent findings from your work?

I have been using the simple fruit fly to learn about how our brains and hearts work. Even though they seem very different, our genome is around 70% the same as fruit flies; and fruit flies have brains and hearts that are evolutionary ancestors to our own.

In recent research we scanned the genome of fruit flies to investigate “pain” perception. I chose pain because if we can find new genes important for feeling pain, we can make drugs that block these genes

and possibly assist people with chronic pain. I was able to identify 580 genes out of 14,000 that were associated with pain after assessing the insects’ response to heat induced pain.

We honed in on one gene, known as $\alpha 2 \delta 3$, because it triggered the same cellular mechanisms as some existing painkillers. When we also investigated this gene in mice, we found they too felt less pain. Then through a collaboration with Harvard University, we were able to identify humans that have mutations near this gene, and they also felt less pain.

While studying this gene in mice, we found that a sensory stimulus (visual, touch, or heat pain) activated additional brain processing centers. The closest thing to this in humans is synesthesia, a condition where senses are partially crossed or additional sensory perception occurs. The most common form is when people perceive different numbers or letters as having different colours, so three might be yellow, whereas eight might be red. Alternatively, some people can visualise sounds and music. Synesthesia is linked to creativity, and so from this blind search in the fruit fly we may have found a mouse model for a fairly high level human phenomenon that only

really gained scientific acceptance 10 years ago through human brain imaging.

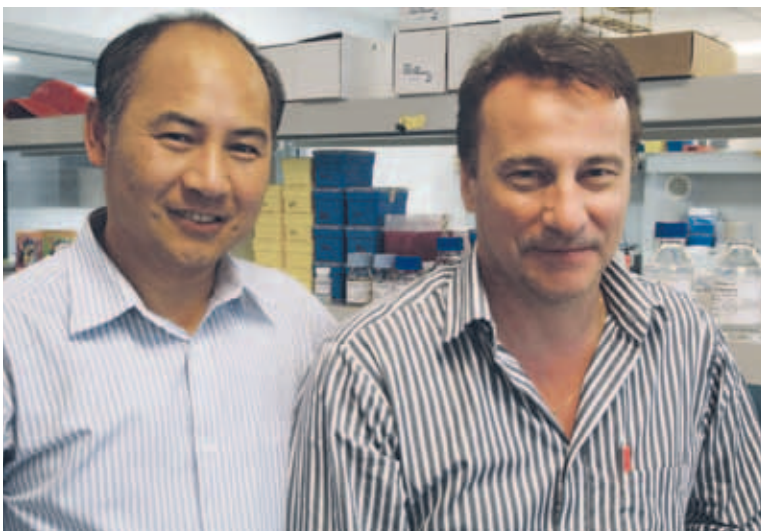
What is the biggest challenge in your area of research?

Funding for our research is always a challenge, so we are extremely grateful to Garvan’s generous supporters. Funding for novel research is particularly important – this is where some of the biggest discoveries can be made.

What do you enjoy doing away from the lab?

I love the ocean, the waves, surfing, swimming, snorkelling, scuba diving, sailing, just being in or around the water is so much fun. I am new to Australia so I haven’t spent too much time surfing, only a few days, but I want to change this. I like riding motorcycles but am kind of scared after some experiences driving through the Alps in Europe.

Reward for Innovation



Dr Shu Lin and Professor Herbert Herzog.

Professor Herbert Herzog, Head of the Neuroscience Research program, and Dr Shu Lin, from the Neuroscience Eating Disorders group, have received a cheque from Professor John Shine in recognition of their inventive contribution to a patent which has been licensed to Novo Nordisk A/S by St Vincent’s Hospital. St Vincent’s and Garvan co-own the patent.

Professor Herzog and Dr Shu Lin collaborated with Professor Sam Breit at St Vincent’s on increasing the understanding of the role that the protein MIC-1 plays in regulating appetite.

Garvan prioritises the effective management of intellectual property in order to promote research excellence for our scientists and to reward individuals for innovation. Garvan’s goal is to increase the relevance of Garvan research to clinical application.



A Peak Moment to Honour a Friend



Tarne at the summit with her picture of David.

Not one to be phased by a challenge, Tarne Usback chose climbing Africa's highest mountain Kilimanjaro to raise money in memory of her dear friend David Kerr who passed away from cancer in 2005. Her determination and courageous efforts to face the grueling physical challenge of climbing 5895 metres to the peak were rewarded on Christmas Day 2010, when she held David's photo on the summit.

"As I took my photo of David out of my backpack for 'our' summit shot I thought how seriously underdressed he was, yet how proud he would be to be there with me," said Tarne.

"Each painstaking step I took during the climb I thought about David and with his picture in my backpack I felt he was there to motivate me to be one of the small percent of people who manage to reach the summit," she added.

With the generosity of family and friends Tarne raised \$6,000 in support of The Kinghorn Cancer Centre. Tarne said: "I wanted to do something in David's memory and at the same time raise funds for an Australian organisation dedicated to researching cures for disease with a reputation for outstanding breakthroughs. The Garvan seemed like a logical choice. I hope it will bring us one step closer to finding a cure. I don't ever want to lose another David."

Raising money 'til it hurts!

When Paul Egan approached the Garvan last year to find out about our prostate cancer research little did we know that this would lead to him enduring lots of pain and suffering when he put his body on the line to ride 1350km in 10 days to support the Garvan.

On 1st April this year Paul joined 55 other riders to undertake a journey of a lifetime from Sydney to Melbourne by bicycle in the annual Tour de Cure.

"I was very excited to find the wonderful Garvan research team led by Associate Professor Lisa Horvath, and after sharing my goal to support Garvan with the Tour de Cure organisation and co-founder Geoff Combes, we decided to pledge part of our fundraising effort from this year towards a prostate cancer project she was heading up," said Paul.

Associate Professor Horvath and her research team will assess newly identified biological markers that may indicate if an individual's cancer is an aggressive or an indolent (slow growing) prostate cancer. Such research will determine how an individual's cancer is treated so that patients with low risk of developing secondary cancer have the option of deferring aggressive treatments and avoiding possible negative impacts on their quality of life.



Paul Egan

Prostate cancer patients identified at greater risk of developing secondary cancer would have treatments tailored accordingly.

Paul has had exposure to prostate cancer through his father and father-in-law, both survivors of this debilitating disease that affects almost 20,000 Australian men each year.

"I have seen the pain and suffering that prostate cancer can have on a man and wanted to do something to help. That's why I have been training for hours on end and am willing to put myself through the 10 days of pain to support such a great cause," said Paul.

To support Paul in his goal of raising \$20,000 please visit www.mytourdecure.com.au.

breakthrough

Clinical Studies

Study on Fat Metabolism

We have recently discovered that oestrogen may change how we burn and use fat as an energy source. Drugs that stop oestrogen action (tamoxifen) or prevent the production of oestrogen (letrozole) are widely used in the treatment of breast cancer and potentially can affect how fat is burned. We think that oestrogen regulates fat mass by interacting with other hormones, such as growth hormone, and that this interaction takes place in the liver.

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 fat burning in the body. 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 study 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 5 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).

Coming up

2011 Garvan Public Seminar

Garvan's next Public Seminar **Latest Advances in Cancer Research and Treatment** is on 13th September from 10am – 12pm at the Garvan Institute, 384 Victoria Street Darlinghurst. Seats for seminars are limited and registration is essential by calling (02) 9295 8110 or visit www.giving.garvan.org.au.

All Garvan seminars are available to listen or download on our website approximately one week after the event. Visit www.garvan.org.au/news-events/podcasts.

Garvan Gala

The inaugural **Garvan Gala** will be held on **Saturday 14th May 2011**, celebrating the Institute's proud history of research breakthroughs under the 20 year leadership of Professor John Shine. The event will be held at Byron Kennedy Hall, Moore Park Sydney. For more information go to www.giving.garvan.org.au/gala.

In memoriam:

November 2010 – February 2011

We gratefully acknowledge gifts received in memory of:

| | |
|------------------|------------------------|
| Katherine Alam | Giuseppe Merenda |
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| H Bertoz | Tapio Nurmi |
| Dorothy Brooker | Norman O'Hara |
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