Research carried out by the Australian Pancreatic Cancer Genome Initiative (APGI – a joint venture between the Garvan Institute and Brisbane’s Institute of Molecular Bioscience), and published in *Nature* shows there are more than 2,000 mutated genes that contribute to the development of pancreatic cancer. Using this information, researchers now plan to commence a pilot clinical trial using genomic sequencing to direct treatment selection for patients with advanced pancreatic cancer.

In a three-year study, Garvan researchers have identified a microRNA that is strongly associated with prostate cancer prognosis. The gene in question, miRNA-205, was ‘silenced’ in prostate cancers, particularly in aggressive or metastatic cancers. Researchers now aim to use this potential translational biomarker to screen a much larger clinical cohort, investigating how it might be used in the management of prostate cancer.

Dr Nike Krautler, in collaboration with colleagues from Switzerland, has demonstrated how follicular dendritic cells (FDCs) play a critical role in allowing us to fight infection and create a strong armory of antibodies for future use. Dr Krautler has shown that FDCs arise from the ‘mural cells’ that surround our blood vessels. The next step is to investigate the role of follicular dendritic cells in germinal centres, both in healthy immune responses and in disease.
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Prime Minister officially opens The Kinghorn Cancer Centre

On Tuesday 28 August, Prime Minister, The Hon. Julia Gillard MP officially opened The Kinghorn Cancer Centre, a joint venture between the Garvan Institute of Medical Research and St Vincent’s Hospital. The $128 million Centre has been funded through a $70 million Federal Government grant from the Health and Hospital Fund as well as major philanthropic support. The Centre incorporates several sophisticated technological and design-firsts that will transform both care delivery as well as the research undertaken.

250 researchers and clinicians from across the St Vincent’s campus will work together at The Kinghorn Cancer Centre, allowing clinical challenges to directly drive laboratory research, and enabling research findings to be rapidly translated into clinical application for the prevention, diagnosis and treatment of cancer patients.

The Prime Minister toured the new facility, taking the time to speak with researchers, clinicians and patients. In one of the new, state-of-the-art labs, researchers from the Garvan Institute explained their work to the Prime Minister, including Dr Alex Swarbrick who showed the Prime Minister breast cancer cells through a multi-headed microscope. Professor Andrew Biankin discussed his team’s ground-breaking work in pancreatic cancer research; while Dr Goli Samimi explained her team’s research to find an accurate, simple and non-invasive test for early ovarian cancer.

The Prime Minister breast cancer cells through a multi-headed microscope; Professor Andrew Biankin discussed his team’s ground-breaking work in pancreatic cancer research; while Dr Goli Samimi explained her team’s research to find an accurate, simple and non-invasive test for early ovarian cancer.

TRIBUTES TO PROFESSOR ROB SUTHERLAND

“Seen through the prism of the Garvan Institute, Rob leaves a powerful legacy in his internationally acclaimed cancer research; in his unstinting leadership on the Garvan and St Vincent’s campus; in his inspirational work for The Kinghorn Cancer Centre, and in the enduring example of just what a good doctor and scientist can achieve in a lifetime,” Mr Bill Ferris AC Chairman, Garvan Institute of Medical Research.

“Rob was one of a kind. He was frighteningly bright and capable, with a global reputation as a researcher. Yet, he was someone who exuded humility and who discounted his past achievements as not worthy of discussion. In all, he stood behind the legacy of being a role model that we should all aspire to be like – driven to make a difference, but not so full of our self-importance that we forget about the simple pleasures in life, and the simple acts of common humanity to others.” Mr Daniel Petre AO Board Member, Garvan Institute of Medical Research, Head of the Petre Foundation which funds a chair in breast cancer research at the Garvan, and a chair in prostate cancer research.

Prime Minister Gillard looking at breast cancer cells with Dr Alex Swarbrick

Delta Goodrem performs at the opening of The Kinghorn Cancer Centre

The St Vincent’s Campus is home to St Vincent’s Hospital, Garvan Institute of Medical Research, The Victor Chang Cardiac Research Institute, and now The Kinghorn Cancer Centre. At the official opening, Prime Minister Gillard described the campus as, “Per square metre, perhaps the greatest concentration of medical care and research excellence in the nation.”

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Feature story: Osteoporosis and Bone Biology Research

As part of its quest to better understand osteoporosis, the Garvan Institute of Medical Research established the Dubbo Osteoporosis Epidemiology Study (DOES) in 1989. Now the world’s longest running, large-scale epidemiological (i.e. the causes, distribution, and control of disease in populations) study of osteoporotic fractures in men and women, DOES aims to better understand the complex web of genetic, environmental, medical and lifestyle factors involved in osteoporosis.

Ultimately, DOES aims to help doctors, specialists and the general public recognise who is at greatest risk of developing osteoporosis and why; how those at risk can be identified; and how the disease can be managed so those who are, or most likely to be affected, can continue to remain healthy.

In this article, we examine what osteoporosis is, as well as some of the findings from DOES relating to the effects of the disease and the benefits of treatment. We look to the future, and examine other areas of research into which Garvan’s Osteoporosis and Bone Biology research division plans to expand.

What is osteoporosis?
Osteoporosis is a disease characterised by low bone mass associated with declining bone strength. Common fractures include wrist, arm and leg ribs, as well as the hips and spine. Osteoporosis is often called “the silent thief” because bone loss occurs without symptoms. Individuals may not know they have osteoporosis until their bones are so weak that a simple strain, bump or fall causes a fracture.

Our bones grow in size, density and strength as our bodies develop through childhood and adolescence, with bone mass reaching its maximum at around 25 years of age, from where it gradually proceeds to lessen. So, achieving lower peak bone mass in younger years puts individuals at greater risk of developing osteoporosis in later life.

Risk factors for osteoporosis include:
- Gender – females are more likely to develop osteoporosis, however one in three fractures occur in men.
- Menopause – the loss of oestrogen after menopause is a major risk factor as is lack of testosterone in men.
- Family history – inherited factors account for a major part of an individual’s risk.
- Limited physical activity and inadequate vitamin D intake.
- Cigarette smoking and excessive alcohol intake – even in teenage years – can influence peak bone mass.
- Prolonged use of certain medications such as high dose cortisone.
- Some diseases including hyperparathyroidism and intestinal malabsorption.

Research findings – effects of osteoporosis and its treatment
The results of DOES have, and continue to not only change the way the world thinks about the biology of osteoporosis, but also our knowledge of the effects of the disease and its treatment.

For example, DOES set out to examine the long-term risk of subsequent fracture following an initial osteoporotic fracture in men and women. These findings have shown that osteoporosis is not just a disease of elderly women. Once men over the age of 60 have had a fracture, the risk of a second fracture increases three to four fold, while for women, the risk of a second fracture doubles.

So, while women are initially twice as likely as men to have a fracture, once a first break occurs, the risk of a second fracture increases substantially more for men and the protective effects of being male disappear altogether. In fact, a 60 year old man who has had their first fracture is at the same risk of a second fracture as a 80 year old man who has not yet fractured.

Currently, the majority of postmenopausal women and older men who have a fracture fail to get proper treatment that could help prevent a subsequent fracture. Part of the problem lies in educating physicians and the public to make the link between having a fracture and osteoporosis.

Associate Professor Jackie Center, the leading author of this study says, “Anyone, a man or a woman, over 50 years of age, with a fracture of any kind resulting from minimal injury – say, tripping on a footpath – needs to be investigated and treated for osteoporosis because, there are good treatments available that can have the likelihood of a subsequent fracture.”

Another DOES project looked at the long-term mortality risk in women and men following all osteoporotic fractures, and aimed to assess the association of subsequent fractures with that mortality risk. The results again demonstrate how important it is to take all fractures very seriously, particularly in the elderly.

Alarming, the study shows that any osteoporotic fracture in a person over the age of 60 years increases that person’s risk of dying prematurely, even after a relatively minor fracture. More specifically, with hip fractures, there is double the risk of death for women, and three times the risk for men.

This study was the first time osteoporosis researchers had looked at long-term data in different age groups and had shown the effects of minor fractures; and examined subsequent fractures in relation to mortality.

In women over the age of 75, there is about a 40 per cent increase in mortality after even a minor fracture, such as a wrist fracture. That risk can double for vertebral fractures, and increase two and a half fold for hip fractures.

For men, increased mortality is a little higher – around 80 per cent higher than the general population for minor fractures in men aged over 75, about double for vertebral fractures; and approaching threefold for hip fractures.

Importantly, among the younger of the participants aged 60-75 years, there was also premature mortality following all but the most minor fragility fractures.

This study also looked at the factors that are associated with premature mortality after a fracture. Thigh muscle weakness and having a subsequent fracture are important factors among both men and women, and low bone density was an additional factor in women.

DOES has also identified a surprising side-effect, a remarkable benefit, of osteoporosis treatment – that people taking bisphosphonates are not only surviving well (better than people without osteoporosis), they appear to be gaining an extra five years of life.

Out of a total cohort of around 2,000, a sub-group of 121 people were treated with bisphosphonates for an average of three 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 and clear.

In a group of women with osteoporotic fractures over the age of 75, 50 per cent would be expected to die over a period of five years. Among women in that age group who took bisphosphonates, the death rate dropped to 10 per cent. Similarly, in a group of younger women, amongst whom 20-25 per cent would be expected to die over five years, there were no deaths.

Study leaders, Associate Professor Jackie Center and Professor John Eisman are intrigued by these findings. “We speculate that it may have something to do with the fact that bone acts as a repository for toxic heavy metals such as lead and cadmium,” said Professor Eisman.

“Also, when people get older, they lose bone. When this happens, these toxic materials are released back into the body and may adversely affect health. By preventing bone loss, bisphosphonates prevent some of this toxic metal release. While we know this is the case, we don’t yet have evidence that this produces the survival benefit.”

Like any pharmaceutical product, bisphosphonates may have unpredictable side-effects in a small minority of people and should only be used for their approved purpose.

The road ahead
In the future, Garvan hopes to also look at younger people within the families of the original DOES participants, in the hope of:
- Developing and expanding public health approaches to high-risk groups.
- Analysing the incidence of fracture and bone density in younger women and men;
- Continuing participation in international studies to identify genes that contribute to, or protect against the risk of developing osteoporosis.

Garvan’s Osteoporosis and Bone Biology division is also planning to broaden its research base to include tumour-induced bone disease. The combined expertise of Professor Peter Croucher, head of Garvan’s Osteoporosis and Bone division, and Professor Mike Rogers (see Meet the Researcher article in this issue) will allow Garvan to explore new ways to treat and prevent the devastating bone disease that commonly occurs in cancer patients when tumour cells spread to the skeleton.

It will do this by focusing on interactions between cells of the immune system, tumour cells and bone cells, allowing Garvan’s bone researchers to work closely with Garvan’s researchers in the Cancer and Immunology Divisions. This research is using cutting-edge techniques to study signalling pathways and mechanisms of drug action in the bone-tumour microenvironment.

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Q. What is your role at Garvan?
For five years at the University of Aberdeen (Scotland), I headed the Musculoskeletal Program, a multidisciplinary group of about 60 lab and clinical scientists. At Garvan I am establishing a brand new group within the Osteoarthritis and Bone Biology division. My focus is on finding new ways to treat and prevent the devastating bone disease that commonly occurs in cancer patients when tumour cells spread to the skeleton. I am particularly interested in the interactions between cells of the immune system, tumour cells and bone cells, so I want to work closely with researchers in the Cancer and Immunology Divisions to develop cutting-edge techniques to study signalling pathways and mechanisms of drug action in the bone-tumour microenvironment.

Q: What are you enjoying most about working at Garvan?
Talking science with like-minded people! In my previous university post, a large portion of my time was spent in a management role and I had little time to devote to research. At Garvan I’m really looking forward to throwing myself straight back into lab research. Going around Garvan and The Kinghorn Cancer Centre and meeting both senior and junior staff from the other divisions is great fun - I’ve already had some fantastic conversations about great science and my head is spinning with ideas.

Q: So far, what are you enjoying most about living in Australia?
After living in the North East of Scotland for 15 years, I have to say, “the weather.” The winter in Sydney is better than the summer in Aberdeen! I love the outdoor lifestyle, and the food and laid-back attitude are fantastic. My family has settled in easily and we’re looking forward to weekends at the beach and exploring the national parks and outback.

Q: What is the biggest challenge facing your area of research?
Bone is a particularly difficult part of the body to study, because the cells are difficult to isolate, grow and manipulate in the laboratory. In the past, the role of the immune system in the spread of cancer cells to bone has largely been ignored, but it is becoming clear that immune cells play a fundamentally important role in this.

The biggest challenge is to understand the complexity of the interactions between these different cell types in bone in a 3D environment (rather than just in a culture dish, which doesn’t recapitulate the spatial and physical influences that are present in the whole skeleton).

Q: What do you enjoy doing away from the lab?
Rather worryingly for someone who’s just moved here, I do love the snow and I’m a very keen snowboarder (so I’m hoping that will help when I try surfing!). I’ve brought three kayaks and canoes with me from the UK and I love paddling in wild places, especially with a camera slung around my neck (check out my website, www.lightandthelens.com).

I’m a guitar junkie too - rip-roaring solos or bluesy ballads from the ’70s and ’80s are best.

2012 Garvan Spring Dinner

After a year’s absence while the spectacular Park Hyatt Sydney was being refurbished, Garvan Research Foundation was pleased to again host its annual Spring Dinner. With Sydney Harbour as the backdrop, this was an opportunity to showcase some of Garvan’s brightest early career researchers and hear about their most recent scientific breakthroughs in a relaxed and intimate setting. It was also an opportunity for Garvan Research Foundation to personally thank a group of donors who support those researchers who spoke on the night.

The Spring Dinner was made possible thanks to the generosity of Park Hyatt Sydney, a long-time supporter of Garvan, having provided stunning venues and services for a range of fund and awareness raising events over many years. Garvan Research Foundation sincerely thanks Park Hyatt Sydney for its ongoing generosity and for recognising the importance of medical research.

There are many ways to support the work of the Garvan, and Park Hyatt Sydney’s ‘in-kind’ support – donating relevant resources and services in a way to reduce expenses – is one way.

For more information about providing in-kind support to Garvan, please contact Garvan Research Foundation on (02) 9295 8110. For more information about the newly refurbished Park Hyatt Sydney, visit www.sydney.park.hyatt.com

Luxi Zhang has received the $10,000 (USD) Castle Harlan Award for being the most outstanding early career PhD student at the Garvan Institute in 2012. The award can be used for anything that might help career development, such as travel to overseas conferences or laboratory expenses.

Castle Harlan Inc is a US-based private equity firm that supports medical research like that carried out at Garvan. The award was presented to Luxi by Mr Leonard Harlan (Chairman, Executive Committee of Castle Harlan).

A member of Garvan’s Signal Transduction Group headed by Professor Roger Daly, Luxi’s work focuses on protein kinases, which comprise the largest enzyme family.

During Luxi’s PhD, she developed a kinase capture reagent capable of isolating significantly more kinases from cells than previously possible. This development has dramatically improved the identification and characterisation of kinases by mass spectrometry.

Luxi is currently applying the kinase profiling method to identify the global impact of Src on the expressed kinome (a subset of the genome consisting of the protein kinase genes). Over 70 per cent of the expressed kinome can be detected by Luxi’s approach, and she has determined that approximately 100 kinases, or 20 per cent of the total kinase repertoire, respond to Src activation.

Importantly, many of the Src-regulated kinases that Luxi has identified are poorly understood. Further functional characterisation of these kinases will provide major insights into the mechanisms underlying Src-mediated cell transformation, and potentially identify new therapeutic targets or alternative treatment strategies for cancers expressing active Src.

Luxi intends to use the Castle Harlan Award to attend the 17th European Cancer Congress to be held in Amsterdam in September 2013, where she will present her research findings. This will also allow her to gain valuable feedback from experts in different fields of cancer research.

In addition, Luxi also plans to visit the laboratory of Matthias Mann in Germany, in order to gain experience in targeted mass spectrometry. This will greatly assist her in the final part of her PhD, and importantly, will allow Luxi to share this knowledge and experience with other Garvan scientists who are using mass spectrometry, including members of Garvan’s Cancer and Diabetes and Obesity Divisions.

2012 Castle Harlan Award Winner Announced

2012 Garvan Spring Dinner

Ask Garvan

Q. I am thinking of leaving a bequest to the Garvan Institute of Medical Research. Can I leave my gift to a particular area of research?
A. Typically, our bequests are invested through our endowment fund, which means that the gift will provide income in perpetuity, enabling us to plan with security as well as fund new research projects with greater ease and speed. However, we are also extremely conscious of the need to respect your wishes as expressed in the terms of the Will. Therefore, if your Will specifies an area of research to support, this will certainly be upheld. When you are considering your very personal gift, please keep in mind that research needs can change over time, and what may be a priority today, may not be in the future.

If you have any questions about the scope of our work, and whether it matches your desires, please telephone our Bequest Officer, Carol O’Carroll. (See details across.)

Q. Should you tell us that you have left a gift to the Garvan in your Will?
A. Of course this is very much a personal decision, however, at the Garvan Institute of Medical Research, we take great delight in honouring bequests. We love the opportunity to say “thank you” in your lifetime. One way we do this is by placing your name on the Honour Board situated in our Galleria. You will also receive invitations to special morning teas and other events.

However, if you wish to remain anonymous, we will certainly respect your wishes. If you would like to let us know about your bequest, or if you are thinking about including a gift to Garvan in your Will and would like to receive our bequest booklet, please telephone our Bequest Officer, Carol O’Carroll on (02) 9295 8117, or email: bequests@garvan.org.au

Staff Profile: Professor Mike Rogers

For more information about providing in-kind support to Garvan, please contact Garvan Research Foundation on (02) 9295 8110.
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).

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 Jen or Renee, (02) 9295 8216, jevans@garvan.org.au (St Vincent’s Human Research Ethics Ref HREC/10/SVH/131).

Osteoporosis Study

Are you female and over 60? Have you had a vertebral (spinal) fracture due to osteoporosis? We are looking for volunteers to be part of a clinical trial that compares a new osteoporosis treatment to a current medication. Both are designed to stop further fractures. For further information please contact Dr Yvonne Selecki on (02) 9295 8276 or y.selecki@garvan.org.au, or Vanessa Travers on (02) 9295 8269 or email v.travers@garvan.org.au (Southern Health HREC Ref HREC/12/SHA/6).

Pre-diabetes Study

We are looking for healthy male volunteers who have close relatives with Type 2 diabetes for a study investigating the role of the autonomic nervous system activity in the development of the disease. The study involves visiting the Garvan Institute in Darlinghurst for one morning during working hours. If you are willing, aged 50 to 60 years and healthy, please contact Lynne (02) 9295 8231 or Dorit (02) 9295 8309 or email crf@garvan.org.au (St Vincent's HREC Ref HREC/12/102).

BE PART OF PROGRESS

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OR Please deduct the above amount ☐ once ☐ monthly ☐ annually from my ☐ Visa ☐ MasterCard ☐ Amex ☐ Diners

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Donations of $2 and above are tax deductible. 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.

In Memoriam July - October 2012. Donations have been made in memory of:

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Lindsay Alderton
Bernie Alleck
Anita Austin
David Baldwin
Mrs Barkhausen
Susan Bayley
Mrs Bentley
Kenneth Berthold
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