Insoluble dietary fibre, or roughage, not only keeps you regular, there is evidence to suggest it also plays a vital role in keeping many diseases at bay. Breakthrough research by a Garvan team describes a mechanism that links diet, gut bacteria and the immune system. For full details see page 5.
Two recent, closely related developments have highlighted exciting opportunities for the future direction of Garvan research.

Approval of the development application for the Garvan St Vincent’s Cancer Centre (GSVCC), now known as The Kinghorn Cancer Centre (see page 7), was formally announced by NSW Premier Kristina Keneally. By co-locating internationally leading cancer research with the very best in clinical care, we will be able to deliver on the promises of personalised medicine for prevention and treatment of many cancers.

As part of the new construction, the St Vincent’s Hospital Diabetes Centre is being temporarily housed in the Garvan. This provides an opportunity to consider ways in which our joint desire to maximise translational research activities in other areas on the campus can be enhanced. The Garvan and St Vincent’s have a long history of close association through the Diabetes Centre with all Centre medical staff having active research appointments at Garvan. The future structure of Garvan – St Vincent’s relationships in this area will now be expanded to ensure that, as with the Cancer Centre, research discoveries in diabetes can be quickly translated into the prevention and cure of diabetes.

Professor John Shine AO FAA
Executive Director

The Ritchie Family Fellowship

The Ritchie family has been associated with the Garvan for many years. Mrs Patricia Ritchie was initially impressed after attending one of our free public seminars.

In an endeavour to continue the philanthropic work of her husband, Bill Ritchie, after his death in 1990, Mrs Ritchie began looking for a forward thinking institution to which the Ritchie Family Foundation might contribute. After learning more about the Garvan’s track record, checking the Board of Directors and speaking with Professor John Shine, they established the Ritchie Family Fellowship.

“The fact that the Fellowship is invested in perpetuity was important to us,” says Mrs Ritchie. “The Garvan is held in such high respect and does all the right things, without being too showy. I like to think we share the same values.”

Mrs Patricia Ritchie AM – the Ritchie Family Fellowship supports a promising young researcher for one year

Quick Quiz
1. Insulin is an important hormone responsible for regulating our blood sugar. In which organ is it produced?
   - The pancreas
2. Over a ten year period, how many injections of insulin might a child have to endure to manage their type 1 diabetes?
   - Up to 14,500
3. What is one of the most common triggers of asthma?
   - Cigarette smoke

Answers: 1. The pancreas 2. Up to 14,500 3. Cigarette smoke
What is the current focus of your research?
My laboratory studies B lymphocytes (B cells), the white blood cells responsible for making antibodies against invading micro-organisms and vaccines. Most of the time B cells are passive, not producing antibodies but waiting for the signal telling them that their antibody is required. When this happens, the B cells become activated.

Our focus is on how B cells survive in the body and how they progress from the point of activation to eventual antibody production. We want to understand how these processes work under normal circumstances and how they can malfunction and cause B cells to contribute to disease instead of health. In particular, we are interested in how uncontrolled B cell survival can lead to B cell cancers such as lymphoma and myeloma and how misdirection of antibody responses against the body itself occurs in autoimmune diseases such as lupus and hemolytic anemia.

What are some of the recent findings from your work?
Our recent work on B cell cancers has identified a group of three proteins that control B cell survival and the molecular processes by which they operate. Mutations in the genes for any of these proteins lead to loss of the normal controls over B cell survival and so strongly predispose towards B cell cancer development.

Our work on antibody responses has identified how replicating B cells ‘split up’ into two groups that first generate a rapid antibody response to keep infections at bay followed by a later response that provides long-term immunity.

An exciting recent result was the successful testing of a system we have developed to study B cells making antibody responses directed against the body itself, an important step in our quest to understand autoimmune disease.

What is the biggest challenge in your area of research?
The biggest challenge in studying B cells is that the ones you are interested in make up such a tiny fraction of all the B cells in the body that they are virtually impossible to identify. We have worked towards circumventing this over many years and have developed experimental systems that now allow us to follow B cells right through the course of their responses. To use these systems we face the additional challenge of acquiring and maintaining several powerful but expensive technologies.

What do you enjoy doing away from the lab?
Spending time with my family, walking the dog, enjoying the beach...nothing very interesting I’m afraid!

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Researcher Profile:
Dr Robert Brink
Director Immunology and Inflammation Program

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askGARVAN

A number of our donors have expressed concern to us about the reported loss of donor funds held on investment at St Vincent’s Hospital.

While Garvan and St Vincent’s co-exist on the same campus and share a heritage through the Sisters of Charity, Garvan is an independent research institute. At no time are our funds ever comingle with St Vincent’s. In the case of our joint venture with St Vincent’s, the Cancer Centre, all funds donated are held by the Garvan on deposits with the four Government-guaranteed Australian banks.

Garvan supporters generously donate three different types of monies. Firstly, untied funds which allow the Foundation to make a most important annual grant to the Institute to support the running costs of our core scientific facilities - critical to the execution of all research at the Garvan. Secondly, donations directed towards a specific disease (such as cancer or diabetes, for example) which are distributed to fund needs in that program area - often for equipment or novel projects. Thirdly, gifts specifically identified for a particular research group, scientific position or piece of equipment which are transferred for that purpose to the appropriate cost centre within the Institute.

The Institute has an endowment fund and the Audit Committee of the Board oversees its management and sets our investment policies. Bequests will usually be held in this fund and research needs supported from the interest. Where it is appropriate to invest donor funds, it is Garvan policy to do this conservatively in externally managed public equities portfolios as well as cash and fixed interest deposits.
Garvan continued its excellent track record of research success in 2009. We published 172 peer reviewed research papers, with an ‘impact factor’ of 8 for the top 80% of our publications, well above the international benchmark. This represents 172 important new pieces of knowledge about the diseases we research. Here are some of the significant discoveries from 2009.

**Diabetes**
A group of researchers in Garvan’s Diabetes program, led by Professor David James and Dr Kyle Hoehn, identified a ‘free radical’ that appears to trigger insulin resistance, one of the first stages in the development of type 2 diabetes.

While we have known for decades that being overweight and eating too much sugar and fat can lead to insulin resistance, the process behind this has remained a mystery until now. Garvan researchers may have found the elusive switch.

Their research found that overeating may stimulate the conversion of oxygen in the air into toxic free radicals, leading to insulin resistance. They also discovered that by neutralising this ‘conversion pathway’ insulin resistance may be reversed in some animals.

The free radicals that cause insulin resistance appear to be superoxides made mainly in specific cellular compartments known as the mitochondria. The study highlighted that mitochondrial superoxides are a common feature in all instances of insulin resistance regardless of how it is induced; whether by pregnancy, lack of exercise or medical conditions.

By blocking or removing these superoxides, or the ability of the mitochondria to produce them, insulin action resumes, glucose transporters become more active and blood sugar levels return to normal.

This is a key finding, since many antioxidants available “off-the-shelf” may not work if they do not reach the mitochondria. And importantly, by identifying the mechanistic origin of insulin resistance, Garvan researchers have made the first step in identifying potential diabetes therapies with mitochondrial superoxides as their target.

**Neuroscience**
Researchers in Garvan’s Neuroscience program showed 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 chronic neurodegenerative diseases like Parkinson’s and Alzheimer’s.

Researchers have only recently been aware of the brain’s capacity to regenerate. Garvan scientists Drs Bryce 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 releasing Activin A. However, further experiments showed that the main role of Activin A was to block inflammation in the brain after neurodegeneration or injury.

**Alzheimer’s and motor neurone disease.** Dr Vissel and his colleagues 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.

In another significant finding in the Neuroscience program, Dr Paul Baldock demonstrated that the neurotransmitter NPY directly controls osteoblasts, the cells that make bone. It is now clear that the neural network, which controls appetite and energy, also alters bone density. This finding may give rise to new osteoporosis treatments able to safely block NPY receptors.

**Osteoporosis**
Research by Associate Professor Jackie Center and Dr Dana Bliuc found that bone fractures can double or triple mortality for up to 10 years post-fracture. Their findings show that osteoporotic fractures increase a person’s risk of dying, even after relatively minor fractures if that person is elderly. In the case of hip fractures, there is double the risk of death for women and three times the risk for men.

The premature mortality lasts for about 5 years after the fracture occurs, except for hip fractures when it lasts for around 10 years and then declines towards the background population level. If the fracture is substantial, the risk of mortality will rise again for the next 5 years.

This study was a first in many ways for Garvan researchers. Based on data collected from the internationally recognised Dubbo Osteoporosis Epidemiology Study, this was the first time researchers looked at long term data, and considered different age groups and the effects of minor fractures. It was...
Cancer
Professor Sue Clarke and Dr Rebecca Hinshelwood in Garvan’s Cancer program have described exactly what happens to a person’s DNA the moment at which a breast cancer suppressor gene is switched off – taking us one step closer towards finding ways to control the biochemical processes that ‘switch on’ bad genes and ‘switch off’ good ones. This field of research is known as epigenetics.

While it is possible to see the bead and string shape of DNA under a microscope, the molecular processes inside are not visible. To determine these, epigeneticists must measure and analyse biochemical changes, including ‘methylation’ (when groups of molecules attach to DNA and literally cause it to scrunch up or close down).

A Garvan Cancer research group has described exactly what happens to a person’s DNA the moment at which a breast cancer suppressor gene is switched off as an internal broom. When it arrives in the colon, bacteria convert it to energy and compounds known as ‘short chain fatty acids’. These are already known to alleviate the symptoms of colitis. Similarly, probiotics, prebiotics and food supplements that affect the balance of gut bacteria, reduce the symptoms of asthma and rheumatoid arthritis. Until now we have not known why.

Garvan researchers have solved this mystery by describing the mechanism that links diet, gut bacteria and the immune system. They have demonstrated that GPR43, a molecule expressed by immune cells and previously shown to bind short chain fatty acids, functions as an anti-inflammatory receptor. Mice lacking GPR43 have increased inflammation and a poor ability to resolve inflammation because their immune cells can’t bind to short chain fatty acids.

This research highlights the importance of eating considerably more unprocessed whole foods such as fruits, vegetables, grains, nuts and seeds.
Garvan Research Foundation is delighted to welcome Colin Biggers & Paisley Lawyers as our newest corporate partner in 2010.

Colin Biggers & Paisley (CBP), one of Australia’s oldest and most highly regarded law firms, has a strong engineering and construction group and for some years has been providing services on legal matters to the Garvan, including the construction of the Garvan St Vincent’s Cancer Centre; now known as The Kinghorn Cancer Centre.

Attracted by such a ‘premium brand’, CBP envisages a long term association with the Garvan. “We pride ourselves on the relationships we develop with our clients,” says Dunstan de Souza, Managing Partner. “We look forward to building a mutually beneficial relationship with Garvan.

Given our history with the Institute, it now makes sense to take this next step and become a financial supporter, both at corporate level and through staff involvement.”

In the current financial year, CBP’s involvement will include sponsorship of a young scientist and contribution to the purchase of a yellow/green laser – an essential piece of equipment for Garvan’s Flow Cytometry Facility.

In addition, CBP is in the process of setting up a Workplace Giving Program, which will facilitate individual (pre-tax) staff giving. Staff are looking forward to engaging with Garvan through volunteering opportunities such as Open Day. To launch the corporate partnership, Garvan Research Foundation CEO Carole Renouf was invited to speak to partners and staff in February.

What do you enjoy about working at Garvan?
I love working for such a prestigious Institute. It is a privilege to work for Garvan, and to help secure future funding in the form of a bequest. I also love the fact that the Garvan researches many of today’s prevalent disease.

Describe a typical day
Happily, I can report that there is no such thing as a typical day in my role at Garvan. After the mandatory ‘admin’ start to the day: reading emails, checking my calendar and work flow, my day can take me to many stops on the bequest route. Most days would involve establishing or maintaining relationships with people who have indicated they may consider supporting Garvan with a bequest through telephone calls or personal visits. In this way I hope to encourage these special donors to become one of our Partners for the Future (committed to a bequest). As a back-drop to this activity, I am usually progressing a direct mail campaign, updating materials for presentations to community groups, and organising tours and events.

What challenges are there working at Garvan?
As a new staff member one of my immediate challenges is recognising the faces of over 500 staff members. The other challenge is to learn as much as possible about the latest developments in Garvan’s research and what this means for humanity.

What do you enjoy doing away from Garvan?
I enjoy keeping active and fit. Every morning at six o’clock I can be seen running our local streets. I also work out at the local gym; all in the vain hope that I will be able to keep ageing at bay. The rest of my non-work time is spent enjoying my husband and son – and Molly the Moodle (our dog). I am also an active member of our local church, and ‘Reading through the Wines’ Bookclub.
Cancer Centre Milestones – DA Approval and a New Name

Garvan and St Vincent’s Hospital recently celebrated a number of important milestones in their joint mission to build a new Cancer Centre on the Darlinghurst campus. In January we welcomed the NSW Government’s approval of the development proposal lodged with the NSW Department of Planning. NSW Premier Kristina Keneally visited the precinct and made the announcement alongside Minister for Health, Carmel Tebbutt and Minister for Planning, Tony Kelly. Construction is now underway with completion expected by early 2012.

In another major milestone the Cancer Centre partners are delighted that the Kinghorn Foundation has chosen the Centre as the focus for its contribution to medical research. This is a critically important gift that has enabled us to complete our capital campaign and build a state of the art facility to realise the promise of personalised medicine for people with cancer.

The Kinghorn Foundation aims to make a profound difference in the community where there is a substantial need. Recognising that cancer is a national health priority, and inspired by Garvan’s track record of excellence in cancer research and the best practice cancer services at St Vincent’s, the Kinghorns have chosen the Cancer Centre as the beneficiary of this significant gift. The building will be known as The Kinghorn Cancer Centre.

2009: Thank you

We would like to thank the 8,400 individuals and organisations who contributed so generously to the progress Garvan scientists have made in 2009. You can read highlights of just some of the work you were part of on page 4.

Donations from the public are vital for Garvan’s work.

In Australia, the government supports medical research primarily through awarding grants from the National Health and Medical Research Council (NHMRC) on a competitive basis. As in other countries, including the US, government grants do not cover the full costs of conducting scientific research. Usually only approximately 60% of Garvan’s expenditure is covered by these competitive grants. This means that each year, for every dollar we receive from the NHMRC, we must raise nearly another 70 cents to be able to carry out our work. This is why your support is so vital.

In 2009, as well as our supporters making gifts which contributed approximately 10% of Garvan’s research costs, we were also very fortunate to be the beneficiary of a number of bequests. These bequests, valued at over $7 million, are currently held in the Garvan endowment fund. Bequests allow us to put in place major initiatives for Garvan’s future. For example, in 1998 a major bequest enabled us to set up the Inflammation and Immunology Research Program.

However you choose to give, and whatever the size, every donation helps us progress along the path that will ultimately lead to better diagnosis, treatments and cures for disease. Thank you.
Clinical Study: women with osteoporosis

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®, 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: October 2009 – February 2010

We gratefully acknowledge gifts received in memory of:

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- Barbara Craske
- Betty Hely
- Bill Atkinson
- Bill Babic
- Brenda Hoffman
- Dale Alexander Alderdice
- Dr Ralph Burley
- Ernest Kiss
- Gloria Waugh
- Greg Park
- Ian Bayley Doyle
- Jeannette Gordon
- Jenny Wareham
- Kerrie Shepherd
- Margaret Johnson
- Maria Kenyon
- Surrey Jacobs
- Mrs Bates
- Brenda Hoffman
- Stella Stavrianos
- Sue Hendry
- Neil and Molly Lamerton
- Noreen Smith
- Robert Rees
- Romeo Vassallo
- Stewart Charles Underhill
- Sue McIntyre
- May Farley
- Ellen Rogers
- Ena Schofield

Garvan Public Seminar Series

Our next events are Healthy Ageing (25th May) and Type 2 Diabetes (19th August). Seats are limited and registration is essential. Call (02) 9295 8110, or visit www.garvan.org.au.

Both seminars will be held from 10am -12pm at the Garvan Institute, NAB Auditorium 384 Victoria Street Darlinghurst.

All seminars are now available to listen or download on the Garvan website – visit www.garvan.org.au/news-events/podcasts.

Open Day 2010

Ever wondered what it’s like to see inside a world renowned medical research facility and meet scientists in action? Then mark Sunday 24th October in your diary, grab your friends and family and join us for a great day of discovery! Doors will open from 9am – 3pm. More details to follow in our next issue of breakthrough.

Clinical Study: women with osteoporosis

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