Garvan’s mission is to make significant contributions to medical research that will change the directions of science and medicine and have major impacts on human health. Garvan strives to enhance and develop research programs that combine fundamental science with strong clinical interactions.
Who we are, What we do

Significant breakthroughs have been achieved by Garvan scientists in the understanding and treatment of diseases such as:

- Cancer
- Diabetes and obesity
- Alzheimer’s and Parkinson’s disease
- Osteoporosis
- Arthritis and asthma
- Pituitary disorders

Garvan’s ultimate goal is prevention and cure of these major diseases.
Chairman’s Report

2009

I am pleased to report that Garvan continued its excellent record of research success in 2009, as measured by grants, publication impacts and international awards, and we are justly proud of our faculty and staff.

Several important strategic initiatives were consolidated during the year, including:

- Planning approval and funding for the new Garvan St Vincent’s Cancer Centre
- Implementation of all the major recommendations arising from the Strategic Review of the Institute completed by the international panel, and
- A highly successful first year of operations for Australian BioResources, our major breeding and holding facility for experimental mouse models in the Southern Highlands.

Financial Performance
Garvan’s operating income grew to approximately $64m in 2009 from $46m in the previous year, an increase that is testament to the quality of Garvan research. Philanthropic support through the Garvan Research Foundation, essential for providing critical equipment and facilitating new initiatives, continued to be strong, with over $5.3m in general and specific grants contributed to research programs and almost $6.4m into the long term endowment of the Institute.

Our People
Garvan has been very well served for many years by the commitment and counsel of an outstanding Board of Directors. There were several Board changes during 2009 as longstanding members Graham Bradley and Professor Ron Trent resigned to be replaced by the incoming Chair of the Foundation, Geoff Dixon, and Dr John Horvath. During Graham Bradley’s time as Chair of the Foundation for the past decade, the Endowment Fund grew from ~$4m to nearly $28m. We also welcomed Anne Keating and Jillian Segal as nominees of the NSW Government and the University of New South Wales (UNSW) respectively. The Institute is most grateful for the contributions made by the outgoing directors, Lisa McIntyre, Chair of our Business Development Advisory Council, and Peter Smith, Dean of Medicine at UNSW, were both reappointed for a further term. I was also honoured to be reappointed as a nominee of the Trustees of St Vincent’s Hospital.

Garvan St Vincent’s Cancer Centre
The mission of our Centre is to create a facility of international standing and best practice in translational cancer research which will accelerate the rate at which new discoveries can be trialed in the clinic.

2009 witnessed extraordinary and exciting progress for the Garvan St Vincent’s Cancer Centre. The architects (Bligh Voller Nield) completed the design work based on our detailed functional and design briefs and development approval was finally granted in late December. Importantly, we also received a $70m grant from the Federal Government’s Health and Hospitals Fund and a $2.5m grant from the Australian Cancer Research Foundation; we also accumulated philanthropic support of nearly $40m plus the commitment of the land from the Trustees of St Vincent’s Hospital. Together with the funds raised from the inspiring “Nuns Run” and the St Vincent’s Garvan Gala Dinner, we were able to reach our goal of $110m needed for the construction and fit-out of this important and innovative facility. The Centre should be ready for occupancy by early 2012.

We were particularly pleased to name the Centre The Kinghorn Cancer Centre: a joint facility of the Garvan Institute of Medical Research and St Vincent’s Hospital in recognition of a most generous donation of $25m from the Kinghorn Foundation.

Business Development
Garvan’s success in basic research continues to be matched by progress in translating research “discoveries” into real outcomes for patients. 2009 saw excellent progress in several collaborations with the biotech industry. Positive early results were generated from the research collaboration with US west coast biotech, Kai Pharmaceuticals, to develop a potential Type 2 diabetes therapeutic. This project is testing a molecule that may be effective in blocking “PKC epsilon” (PKCe), an enzyme that is active during diabetes and which reduces the availability of insulin.

Similarly the licence to Danish-based Novogene A/S of the hormone galanin which is being developed as an epilepsy therapy continued its progression towards phase 1 clinical trials. Other exciting collaborations are detailed in this Annual Report.

2010

Australia wide, medical research can proudly boast its continuing discovery record in causes of, and potential cures for, many of the world’s diseases. I take this opportunity to add Garvan’s thanks and congratulations to the extraordinary efforts of Elizabeth Blackburn, Australia’s most recent addition to its long list of Noble laureates.

Given this performance, it is especially disappointing once again to be obliged to observe the appalling lack of funds in this State and in this country for the operating support (often referred to as infrastructure funding) necessary to run the laboratories. Scientists in universities and medical research institutes depend on success in the NHMRC research grants scheme for their salaries. But for every dollar of such grants we need about another 70c for day to day lab and Institute operating expenses. We, like all others in research, are currently relying on past endowments and current donations to find this 70c to keep the doors open. This is not a long term solution for Garvan or the research platform of this nation.

The Board is confident that, with the support of government and the community, our research will continue to have a growing impact on human health, particularly as we integrate it even more closely with health care delivery.

Once again my sincere thanks and admiration are extended to Professor John Shine, his senior management team, faculty and staff.

Bill Ferris AC
Chairman
Garvan Institute of Medical Research
Executive Director’s Report

2009

2009 was another very productive year for Garvan in terms of significant research findings, success in obtaining competitive grants and growth in the number of papers accepted for publication in prestigious international journals. We published 176 peer reviewed research papers, the top 80% in journals with an average impact factor of 9.2. This remains above internationally accepted benchmark levels and is testament to the excellence and commitment of our researchers.

Research publication productivity was matched by success in applications for competitive grants. Our funding from the National Health and Medical Research Council (NHMRC) rose to a record $19.1m, up from $18.7m in 2008. Overall, peer reviewed grant funding increased to approximately $30.2m.

Of particular importance was Garvan’s role as a lead partner in the pancreatic cancer arm of the International Cancer Genome Consortium. The Consortium brings together the world’s leading scientists, through 11 funding organisations in 8 countries, and aims to catalogue the genetic changes of the 50 most common cancer types.

The Australian team will be led by Professor Andrew Biankin from Garvan and Professor Sean Grimmond from the University of Queensland’s Institute for Molecular Bioscience in Brisbane. It also involves collaborative contributions from the Walter and Eliza Hall Institute of Medical Research in Melbourne, Johns Hopkins University in Maryland, the Ontario Institute for Cancer Research and the University of California, San Francisco.

Garvan has also played a leadership role in the International Human Epigenome Consortium (IHEC). Professor Susan Clark, Head of our Epigenetics Group, was a founding member of the small National Institutes of Health USA (NIH) funded task force that initiated the project. This new initiative to map the epigenetic modifications of the human genome was officially launched in Paris in January, with Professor Clark on the interim steering committee.

Staff numbers across the organisation grew to a total of 504. Growth was particularly strong in our Cancer, Immunology and Diabetes and Obesity Programs, reflecting ongoing success in competitive grant applications for new and existing projects. After nearly a decade at Garvan, two of the Institute’s leading immunology groups, led by Professors Charles and Fabienne Mackay, relocated their research to Monash University in Melbourne. Although their direct input into Garvan research will be missed, they will retain honorary appointments at Garvan and continue their strong collaborative research activities with several Garvan groups. Following an international search, we were very fortunate to appoint Dr Robert Brink as the new Immunology Program Leader. Dr Brink brings exceptional skills and a universally respected reputation to the role, which will increasingly focus on a closer integration of immunology across the spectrum of Garvan research programs.

Australian BioResources (ABR)

The state-of-the-art holding and breeding facility for experimental mouse lines at Moss Vale provides critical infrastructure for Australian innovation. The facility completed its first full year of operation in 2009, reaching 50% of total capacity (approximately 25,000 mice). It now holds all major breeding colonies for Garvan and 7 partner institutes.

Strategic Review

During 2009 the final recommendations of the international review were implemented. The smaller research units of autoimmunity and pituitary research were integrated into the Immunology and Neuroscience Programs respectively. A Scientific Advisory Council of eminent international and national researchers was formally established and will hold its inaugural meeting in October, 2010. The Council will help advise the Institute on current and future research directions.

Campus Developments

An active member of the St Vincent’s Campus, Garvan values its historic and ongoing close association with St Vincent’s Hospital and its commitment to the values of the Sisters of Charity.

Our joint venture with St Vincents & Mater Health Sydney to establish a Garvan St Vincent’s Cancer Centre, made exceptional progress in 2009 and is detailed elsewhere in this report. As part of the demolition of existing buildings during construction of the Cancer Centre, the St Vincent’s Hospital Diabetes Centre is being temporarily housed in the Garvan building. This provides the opportunity for us to explore even more effective ways of translating the findings of diabetes and obesity research into improved patient outcomes.

2010

The upcoming years promise much for Garvan, with the addition of approximately 250 new researchers in the Cancer Centre, expansion of our Neuroscience, Immunology and Diabetes and Obesity Programs, and consolidation of the long-running translational research activities emanating from the Osteoporosis Study based in Dubbo. Such expansion places extra pressure on our already minimal infrastructure resources – a challenge that the Board and staff are committed to overcoming.

During 2010 we will remain clearly focused on elucidating the fundamental basis of disease. We will also drive the translation of our research discoveries into new and improved ways to prevent and treat the major diseases that challenge our society.

John Shine AO FAA
Executive Director
Garvan Institute of Medical Research
Chairman’s Report

After taking over the Chair in April, I am very pleased to report that the Foundation’s results have surpassed budgeted expectations for 2009 with a total income of $13.6m. This marks a fourth consecutive year of growth for the Foundation and is testament to the fact that the combination of a loyal community of informed donors, a premium brand and a dedicated team can, together, surmount even a global financial crisis. We are deeply indebted to our supporters and our staff for this result and proud of the contribution we have therefore been able to make to Garvan’s science.

Gift income
We are especially indebted to a wonderful Garvan supporter by the name of Margaret Benning, who sadly passed away in 2008 and wanted her estate deployed to further our research into better methods of diagnosis, prognosis and treatment of most of the major diseases affecting our society today. This thoughtful bequest has brought the Foundation's bequest income for 2009 to a total of $7.8m, which will grow the Institute’s reserves in the endowment fund maintained to address special needs or emergencies and foster new directions. Additional gifts totaling $5.8m were generously donated, mostly by individual supporters, and we thank each and every one of them.

Capital campaign
In a challenging economic climate, the Foundation also carried responsibility for fundraising for our capital project, the Garvan St Vincent’s Cancer Centre. A number of supporters have helped us reach the campaign goal, but none more so than the Kinghorn Foundation. Following an initial gift made in 2008, John and Jill Kinghorn committed an extraordinary gift of a further $20m to the Centre. This is an example of the type of transformative philanthropy we see only seldom in Australia, and it is hard to express our gratitude adequately.

Events
The Foundation’s activity levels were at an all-time high in May and June this year due to the inaugural Nuns’ Run. This was a daring, creative and multi-faceted event which involved 11 Sisters of Charity walking 400 km from Dubbo to Darlinghurst to raise funds for the Cancer Centre. Along the way, the Sisters engaged in high teas and dinners, memorial services and even a drumming circle with regional communities who supported their endeavours to the hilt. Ms Delta Goodrem, Patron of the Centre, attended both the start event in Dubbo and the finale in Sydney. A number of sponsors contributed most generously to make the event possible; for example, the essential support vehicles were donated by Citroen Australia. I would particularly like to thank M & C Saatchi for their generous provision of in-kind support for the Nuns’ Run and development of the larrkin and eye-catching logo.

Planning, administration and risk management of the Nuns’ Run took up many of the Foundation’s resources during the busiest time of our year and peak period for donations. The team deserves to be congratulated on their multi-tasking ability, a fitting complement to the Sisters’ fortitude. The final fun run in Centennial Park was greatly enjoyed by staff of both the Garvan and St Vincent’s and their dogs, and a total of over $200,000 raised towards the Cancer Centre.

Board and staff movements
I wish to take this opportunity to thank my fellow Directors for the welcome offered to me as incoming Chairman and for the support they offer to the Foundation.

I would especially like to highlight the exceptional service provided by Mr Graham Bradley AM over a term of ten years as Foundation Chairman from 1999 to 2009. Mr Bradley oversaw and encouraged much forward progress during this period thanks to his dedication to the philanthropic cause. His stature as a Director and Chair and his corporate expertise have been recently recognised by his appointment as President of the Business Council of Australia.

I also acknowledge the contribution as a Director made by Mr Alexander Brennan (2000–2009); Mr John Koch (2000–2009); and Ms Meredith Hellicar (2002–2009). It is also my pleasure to have welcomed to the Board this year Mr Simon Mordant.

I am pleased to report that the Foundation team’s membership has remained stable in 2009, with the addition of two new fundraising positions (Ms Gabriella Lang joined in January, and Ms Georgie Le Poer Trench in September) as a necessary response to the additional responsibility of the Cancer Centre. I also welcome Ms Lynell Riley, who started as Assistant to the CEO in November.

I am impressed with the efficiency of Foundation operations and proud to say that all Garvan donors can have absolute confidence in the leadership of our CEO and the determination of her team to achieve maximum support for Garvan’s science coupled with well-controlled expenditure.

I look forward to getting to know our supporters in the year ahead and to playing my part in what I fully believe will be the bright future of the Foundation and the Garvan Institute.

Geoff Dixon
Chairman
Garvan Research Foundation
Garvan at a Glance

Research Collaborations
Patent Portfolio by Category

<table>
<thead>
<tr>
<th>Portfolio</th>
<th>Percentage</th>
<th>Number of Patents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutics</td>
<td>4%</td>
<td>1</td>
</tr>
<tr>
<td>Drug discovery tools</td>
<td>11%</td>
<td>3</td>
</tr>
<tr>
<td>New treatments</td>
<td>19%</td>
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</tr>
<tr>
<td>Therapeutic target</td>
<td>36%</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Scientific Publications

Impact factor of scientific publications

Each paper published constitutes a new piece of knowledge, and scientists aim to publish in the most highly regarded journal in their area of research. Each journal has an “impact factor” which is a common measure of its relative importance within a specific discipline. Research organisations use “average impact factor” measurements to determine the overall significance of their research output. For example, in 2009 Garvan achieved an “average impact factor” of 9.2 for the top 80% of its publications. This is a very respectable tally, well above the international benchmark.

Phanilanthropic Support

Total Income (excluding bequests) received by Garvan Research Foundation

- $3,539,000
- $2,790,000
- $4,158,000
- $5,370,000
- $6,966,000
- $5,806,000

Donations are particularly important in two respects:

- They provide seed funding for novel work, which may not attract other support for several years
- They fund core items of equipment that are typically not covered by research grants

Peer Reviewed Grant Income

<table>
<thead>
<tr>
<th>Year</th>
<th>NHMRC</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>9,244</td>
<td>6,222</td>
</tr>
<tr>
<td>2005</td>
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<tr>
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<td>9,159</td>
</tr>
<tr>
<td>2009</td>
<td>19,094</td>
<td>11,061</td>
</tr>
</tbody>
</table>

One of the major challenges facing successful research institutes around Australia remains the “gap” between the total costs of doing research and the funding provided by competitive research grants. For every dollar of research funding awarded, another 70 cents is required to carry out the research.

Staff Profile

- Researchers: 2008 314, 2009 296
- Students: 2008 68, 2009 87
- Scientific Facility Staff: 2008 62, 2009 68
- Secretarial & Admin: 2008 35, 2009 39
- Foundation: 2008 7, 2009 11
- DVDC: 2008 2, 2009 3

Total: 2008 488, 2009 504

Demographics

- Average age: 37
- Researchers from 55 countries
- Research Staff: 37.75% male, 62.25% female

Operating Income

2009 $64 Million

- Peer reviewed grants: 47%
- Other grants: 26%
- Donations: 11%
- NSW Government: 6%
- Industry partners: 1%
- Other income: 12%
Garvan Institute of Medical Research
Board of Directors
- Chairman: Mr Bill Ferris AC
- Executive Director: Prof John Shine AO FAA

Board Committees
- Business Development Advisory
- Finance & Audit
- Investment
- Remuneration

Institute Committees
- Executive Research
- Appointments & Promotions
- Scientific Advisory Council
- RTP Policy Advisory
- Higher Degrees
- Information Technology
- OHS Consultation
- Operations Advisory
- Seminar Program
- Common Users of Building Equipment (CUBE)

St Vincent’s Research Precinct (SVRP) Committees
- Animal Ethics
- Human Research Ethics
- Institutional Biosafety
- SVRP Management
- SVRP CHS

Garvan is a partner in the CRCs for Asthma and Biomedical Imaging Development. Garvan is a shareholder in the spin-out company G2 Therapies Ltd.
Research Highlights

- Discovered a promising therapeutic target for prevention of Type 1 diabetes, a molecule known as BCMA, which effectively subdues the immune cells that cause the disease.
- Extended our prognostic models for predicting fracture risk for men and women, implemented in www.fractureriskcalculator.com, widely used by doctors and patients worldwide.
- Found that sex hormones and the neurotransmitter neuropeptide Y (NPY) work together to control fat levels and bone density in the body.
- Used new protein technology to identify that a specific group of cell signalling proteins, Src family kinases, represent potential therapeutic targets in basal breast cancer, an aggressive sub-type of breast cancer.
- Showed new ways of artificially boosting the numbers of a certain class of immune cells (regulatory T cells), a process which could be used to prevent the rejection of organ transplants or the development of autoimmune diseases.
- Identified new serum biomarkers for therapeutic response to the chemotherapy drug docetaxel in advanced prostate cancer.
- Showed that over-eating generates the production of toxic oxygen scavenging molecules, or ‘free radicals’, in the intracellular energy warehouse of cells, the mitochondria. These free radicals trigger insulin resistance.
- Demonstrated that extensive gene silencing is common in cancer, encompassing many tumour suppressor and neighbouring genes, non-coding RNA, intergenic regions and microRNAs. Up to 3% of the genome may be affected by epigenetic remodelling in cancer cells.
- Found that fats disrupt movement of protein out of the cellular protein-folding compartment in pancreatic insulin-producing cells, triggering cell death.
- Showed that the three signalling molecules, TRAF2, TRAF3 and cIAP, function together to control B cell survival and are all potential B cell tumour suppressors, so they may prevent development of cancer in these cells.
- Identified the specific neuronal pathways in the brain that respond to pancreatic polypeptides and reduce appetite. This highlights a potential new way of treating obesity.
- Reported findings of initial clinical studies with a novel treatment that reduces bone breakdown, and which has major potential in osteoporosis treatment.
- Showed that different forms of the PKC enzyme family cause insulin resistance in different ways, raising the potential for combination therapy.
- Demonstrated that neurotransmitters in the brain play a critical role in the regulation of bone mass, a function that has been considered purely mechanical. Specifically, neuropeptide Y (NPY) directly controls the cells that make bone, increasing bone mass in line with body weight.
- Advanced candidate biomarkers of therapeutic responsiveness into national and international clinical trials of personalised medicine strategies for pancreatic cancer. The Garvan led consortium called PRIMe (Pharmacogenomic Research for Individualised Medicine) is a new multi-institutional initiative funded by a program grant from the Cancer Council NSW.
- Demonstrated that a tiny genetic irregularity in the gene encoding for the growth factor IL-21 greatly boosts its expression, leading to the development of Type 1 diabetes in mice. The absence of the irregularity, on the other hand, keeps IL-21 at normal levels and prevents development of the disease.
- Proved that inflammation in the brain prevents stem cell proliferation and neural repair, a finding that will have important therapeutic implications for Parkinson’s and Alzheimer’s disease.
- Demonstrated that ‘short chain fatty acids’ (the by-products of bacterial fermentation of insoluble dietary fibre in the gut) bind to GPR43, a molecule expressed by immune cells that acts as an anti-inflammatory receptor.
- Characterised a new 5 biomarker panel that predicts outcome in early breast cancer.
- Showed that NPY receptors in the body, rather than the brain, regulate fat burning and storage, and that blocking them can prevent fat gain.
- Identified that the oncogenic signalling protein Gab2 plays an important role in early breast cancer development.
- Showed that SERMs, a class of synthetic oestrogens commonly used in medical treatment, block the ability of growth hormone to burn fat and build muscle.
- Demonstrated that burning fats, as opposed to carbohydrates, is not enough to promote fat loss because the body compensates by converting the unburned carbohydrate into fat.
Program Overview

Although derived from normal cells, cancer cells have distinctive features that can be exploited to aid diagnosis, prognosis, treatment and prevention. To do this, we need to know much more about the fundamental processes that govern cell behaviour: their division, their survival, their motility and their differentiation into complex tissue structures. With this knowledge we will be better able to stop the formation, spread and early growth of cancers.

As well as basic research into genetics/epigenetics and the cellular and molecular biology of cancer, the Cancer Program has six translational research groups that study a number of the most commonly diagnosed and most lethal cancers: breast, colorectal (bowel), lung, ovarian, pancreatic and prostate.

Program Highlights

- Demonstrated how the protein Bag-1 inhibits apoptosis (cell death) in normal breast epithelial cells and how it may play a role in the early development of breast cancer.
- Used new protein technology to identify that a specific group of cell signalling proteins, Src family kinases, represent potential therapeutic targets in basal breast cancer, an aggressive sub-type of breast cancer.
- Showed that cell cycle genes, cyclin E1 and cyclin E2, which are usually co-regulated and so are believed to be functionally very similar, are regulated differently in breast cancer cells.
- Identified that the MCC protein, which we had already shown to be "switched off" in colon cancer, is important for the protection of DNA from environmental damage.
- Demonstrated that extensive gene silencing is common in cancer, encompassing many tumour suppressor — as well as neighbouring — genes, non-coding RNA, intergenic regions and microRNAs. Up to 3% of the genome may be affected by epigenetic remodelling in cancer cells, resulting in a brake in activity in those cells.
- Discovered a novel microRNA pathway regulating the p53 tumour suppressor protein in cancer cells. It could be argued that p53 is the most important tumour suppressor, sometimes referred to as "the guardian of the genome".
- Identified novel microRNAs that are commonly epigenetically deregulated in bladder and prostate cancers — providing exciting new diagnostic targets for detection.
- Identified that the oncogenic signalling protein Gab2 plays an important role in early breast cancer development.
- Identified CCBE1 as a potential tumour suppressor gene in ovarian cancer that is inactivated by epigenetic changes in DNA.
- Demonstrated the importance of transcription factor GATA-2 in the transition to aggressive prostate cancer, which is resistant to hormone treatment.
- Identified that the Runx2 gene, well known as a master controller of bone development, also controls normal breast development, and is a potential mediator of breast cancer progression.
- Undertook a major review of breast cancer resistance to commonly used endocrine therapies (such as tamoxifen) which highlighted the potential for emerging technologies to help us better understand this major limitation to the successful treatment of breast cancer.
- In collaboration with Professor Wayne Tilley, University of Adelaide, we identified the mechanism of androgen receptor inhibition of oestrogen action in breast cancer.
- Demonstrated a partial loss of the SATB1 protein in lung cancer, and showed that this loss indicates a poor prognosis.
- In collaboration with Dr Erik Knudsen, Kimmel Cancer Center, Philadelphia, we identified that the cell cycle protein cyclin D1b is a marker of poor prognosis in breast cancer.
- Identified new serum biomarkers for therapeutic response to the chemotherapy drug docetaxel in advanced prostate cancer.
- Characterised a new 5 biomarker panel that predicts outcome in early breast cancer.
- Identified roles for aberrant expression of Bag-1, CAIX, beta-catenin, Notch-1, Her-2, Gab2 and several components of the PI3 kinase pathway in defining cancer types and outcomes in breast cancer patients.
- In collaboration with Dr Karen Knudsen, Kimmel Cancer Center, Philadelphia, we documented how the
various proteins (splice variants) that can be encoded by the cyclin D1 gene function in prostate cancer.

- Developed new technology and methodology for analysis of the human epigenome — in other words, for all the reversible chemical modifications to DNA and its associated proteins that determine when genes can be expressed

- Developed a novel algorithm and web-based software program that helps identify genetic subtypes of cancer

- Identified pathways (myc/E2F) that provide new therapeutic targets for non-oestrogen responsive breast cancers, for which no targeted therapies currently exist

- Identified that the degree of clearance around a tumour when removed surgically is important for the long-term survival of patients treated for pancreatic cancer, and that this finding should inform future clinical trials involving radiotherapy

- Advanced candidate biomarkers of therapeutic responsiveness into national and international clinical trials of personalised medicine strategies for pancreatic cancer. The Garvan-led consortium called PRIMe (Pharmacogenomic Research for Individualised Medicine) is a new multi-institutional initiative funded by a program grant from the Cancer Council NSW

- Showed that standardised reporting in pancreatic cancer histopathology increased the accuracy of diagnosis. We then facilitated the Australia-wide implementation of the approach

- In collaboration with the Cancer Council NSW developed a multimedia/DVD support package for patients with pancreatic cancer and their families.

People Highlights

- Dr Alison Butt was appointed President of the Australian Society for Medical Research (ASMR).
- Professors Andrew Bankin, Rob Sutherland and Susan Clark, in conjunction with Associate Professor Sean Grimmond from the Institute for Molecular Bioscience, University of Queensland, were awarded an NHMRC Medical Bioinformatics, Genomics and Proteomics Program Grant worth $27.5m to establish the Australian Pancreatic Cancer Genome Initiative. This effort aims to characterise fully some 400 pancreatic cancers at a genomic, epigenomic and transcriptomic level as part of the International Cancer Genome Consortium (www.icgc.org). The project brings together major international centres for pancreatic research including Johns Hopkins University and the University of Verona.
- Dr Lisa Horvath, Professor Rob Sutherland and Professor Roger Daly, in conjunction with Dr Michael Boyer at the Sydney Cancer Centre, were awarded a Cancer Australia grant to identify and target Docetaxel resistance in hormone refractory prostate cancer.
- Professor Susan Clark received Australia’s “Top Ten” National Health and Medical Research Council (NHMRC) Scientist Award for 2009 and was promoted to Senior Principal Research Fellow at Garvan.
- Professor Andrew Bankin was awarded co-lead of the Australian Pancreatic Cancer Project, Clinical Lead of the Australian Pancreatic Cancer Genome Initiative, member of the ICGC Tissue and Clinical Annotation Working Group and member of the writing team for the ICGC Marker Paper to be published in early 2010.
- Cancer Program senior scientists are members of several major national and international networks. Professor Susan Clark is President of the Australian Epigenome Alliance, the Australian Member and Representative of the Asian Epigenome Alliance, and a Steering Group Committee Member of the International Human Epigenome Consortium; Dr Alison Butt is a member of ASMR and Women in Science, Environment Network, Inc.; Professor Marie Dizadek is a member of the Australian Research Council (ARC)/NHMRC Research Network in Genes and Environment in Development, and Professor Rob Sutherland is a member of the International Breast Cancer Study Group, TRANSHERA and the National Breast Cancer Foundation Novel Concept/Pilot Study Award Sub-Committee.

Three Cancer Institute NSW infrastructure grants totalling $1m were awarded to the Cancer Research Program, two to continue support of the ACFP Genomics Facility and one to develop primary pancreatic cancer xenografts with detailed genetic and molecular information.

- The Cancer Program’s application to the International Cancer Genome Consortium (ICGC) was awarded a Genomics Cancer Alliance Network Grant worth $3m to establish the Australian Pancreatic Cancer Genomics Research Lab at Garvan.

- Dr Alex Svarbrick, in conjunction with Dr Robert Brink from the Immunology Program, was awarded an NHMRC Project Grant to study the genes controlling multiple myeloma.

- Dr Matthew Naylor was awarded a UNSW Goldstar Award.

- Andrew Bankin and James Kench were promoted to Conjoint Professor at the University of NSW (UNSW) and University of Sydney respectively.

- Professor Rob Sutherland was made a Life and continued

- Reviews in Oncogenesis to the Editorial Board of Australia’s “Top Ten” National Health and Medical Research (NHMRC) Scientist Award for 2009 and was promoted to Senior Principal Research Fellow at Garvan.

- Professor Roger Daly was appointed in conjunction with Dr Michael Boyer at the Sydney Cancer Centre, were awarded a Cancer Australia grant to identify and target Docetaxel resistance in hormone refractory prostate cancer.

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- Several members of the Cancer Program served on grant review panels: Professor Rob Sutherland as a member of the Advisory Group for the Foundation for Science and Research Technology, Wellington, New Zealand; Professor Susan Clark on the NHMRC Disciplinary Panel 1; and the NIH review panel for the Epigenetics Roadmap Technology Development Group in Washington, USA; Associate Professor Chris Ormandy for the Victorian Breast Cancer Research Consortium (VBCRC) Program Review Board; Professor Marie Dizadek for the ARC Future Fellowships Selection Advisory Committee; and Dr Alison Butt for the NHMRC.

- Dr Marcel Coolen was awarded a five year tenure-track Research Fellowship at The Radboud University Nijmegen Medical Centre, Netherlands to start 2010.
addition, we have identified a novel effect of another signalling protein, cortactin, on the cell cycle machinery of head and neck cancer cells that leads to their increased proliferation. Finally, we have established new methodologies to characterise global alterations in protein phosphorylation associated with cellular signalling events. These are being used to identify novel therapeutic targets and prognostic markers in cancers refractory to current treatment regimens. For example, we have identified that basal breast cancers are characterised by a Src kinase signalling network, and related research projects on pancreatic cancer, docetaxel-resistant prostate cancer and hormone-insensitive breast cancer are underway.

Epigenetics Group
Group Leader Professor Susan Clark

Cancer cells can modify the expression of critical cancer genes independently of the DNA sequence, using two epigenetic biochemical processes called DNA methylation and histone modification. Our research aims to understand the mechanism that triggers abnormal methylation and histone modification between normal and cancer cells. We have developed different methods to detect methylation changes during early cancer development and have discovered that these epigenetic changes can take place not only in single genes, but can also occur across very large regions of DNA during the spread of cancer. These changes provide novel tumour “signatures” for cancer diagnosis as well as potential targets for cancer therapy. We are now trying to determine which changes are specific to breast and prostate cancer and the sequence of events that trigger these changes so that we can try to reverse the process. This is a large and complex project and our work forms part of the international effort on unravelling the human epigenome.

Development Group
Group Leader Associate Professor Chris Ormandy

Development of the mammary gland occurs in defined stages that are governed by the hormones that regulate reproductive events. We hypothesise that genes controlling normal mammary development can become mutated or deregulated in breast cancer and thus contribute to the disease process. We have discovered that the transcription factor E115 controls the development of the mammary gland during pregnancy and also regulates the proliferation and function of breast cancer cells. We are investigating how E115 exerts these effects to provide a way to therapeutically target this mechanism.

Tumour Progression Group
Group Leader Dr Alex Swarbrick

Most aggressive cancers have two features in common: they proliferate endlessly (have high self renewal) and contain mostly unspecialised, poorly differentiated cells. We are investigating genes that control self renewal and differentiation in cancer, with a particular focus on breast cancer. Together with the Breast Cancer Group and external collaborators we have discovered that several genes are key regulators of the growth and metastasis (spread) of poorly differentiated cancers. These include the transcriptional regulator Id1, the Hedgehog signalling protein, and also the non-coding microRNA-380. Understanding the contribution of these genes to cancer progression will help us predict the behaviour of aggressive metastatic cancers and may ultimately lead to the development of new drugs to stop their growth.
Integrin and Cell Biology Group  
Group Leader Dr Matthew Naylor  
Our research aims to understand the mechanisms that regulate cell fate decisions during the progression of cancer to metastatic disease. Integrins mediate the adhesion of cells to the extracellular matrix and provide cells with a positional identity in addition to coordinating growth factor and hormone signalling to control cell function. Modulation of integrin expression and function can alter the cancer phenotype. We are currently investigating integrin function during mammary and prostate gland development and in experimental models of carcinogenesis and metastasis. We are also investigating the role of several cell fate transcriptional regulators during mammary gland development, cancer and metastasis.

Translational Cancer Research  
Breast Cancer  
Group Leader Professor Rob Sutherland FAA  
In association with clinicians at several teaching hospitals in Sydney (St Vincent’s, Royal Prince Alfred/Sydney Cancer Centre and St George) and major national and international trials groups (Australia New Zealand Breast Cancer Trials Group and International Breast Cancer Study Group) we have developed large tissue banks and patient databases that are being used to identify markers of disease subtype, disease progression and response to particular therapies. A major joint project with the Cell Cycle, Apoptosis and Steroid Hormone Action Groups is identifying molecular markers of tamoxifen resistance, since loss of response to tamoxifen is a major reason for treatment failure. We are also conducting collaborative studies in-house and with other institutions to define the role of newly-discovered breast cancer genes in the disease process.

Lung and Colorectal Cancer  
Group Leader Dr Maja Kohoren–Corish  
Our area of expertise is colorectal and lung cancer genetics and epigenetics. We examine the gene profiles of resected tumour tissues and correlate them with patient clinical outcomes. The challenge is to work out which key gene alterations and biomarkers are the most useful for determining prognosis and treatment outcomes, in order to improve the clinical management of patients. We have identified new genes that are inactivated through epigenetic mechanisms in cancer. In lung cancer we have analysed genes on chromosome 3p, an area of the genome important in lung cancer development. We have shown that aberrant methylation may be synchronised in this region and that the presence of this defect in the cancer is associated with poor patient prognosis.

Ovarian Cancer  
Group Leader Dr Philippa O’Brien  
Our group works in collaboration with the Gynaecological Cancer Centre at the Royal Hospital for Women. Our major research goal is to use our combined expertise and knowledge to identify new ways to diagnose women with early stage curable ovarian cancer. To this end we utilise a number of different approaches to identify the genes involved in the development of ovarian cancer, particularly its early stages. Our primary focus is the identification of genes with altered methylation patterns that have potential as blood-based diagnostic markers for early stage ovarian cancer. We also aim to understand how such genes influence ovarian cancer development, which may additionally identify new treatment targets for women with advanced disease.

Prostate Cancer  
Group Leader Professor Rob Sutherland FAA  
Our group is concerned with the identification of markers for therapeutic responsiveness, prognosis and early prostate disease. We take a multidisciplinary approach that utilises expertise from a number of cancer researchers within and outside the Garvan, as well as clinicians and pathologists, particularly colleagues at the St Vincent’s Prostate Cancer Centre and the Sydney Cancer Centre, Royal Prince Alfred Hospital. We aim to identify genes and pathways whose expression changes can predict the development of aggressive life-threatening prostate cancer or resistance to chemotherapy used for the treatment of advanced stage prostate cancer.

Pancreatic Cancer  
Group Leader Professor Andrew Biankin  
Pancreatic cancer is the fourth leading cause of cancer death in Western societies, with a five year survival rate of less than 5%. The treatment and survival of patients with pancreatic cancer has not changed for over thirty years because there has been little research into the molecular and cell biology associated with it. Our projects focus on improving outcomes for patients by defining molecular phenotypes of pancreatic cancer using biomarkers to guide therapeutic decisions and personalise therapies for pancreatic cancer. In addition, we are investigating molecular mechanisms of pancreatic carcinogenesis which may lead to the development of novel therapeutic strategies.

Cancer Development Laboratory  
Research Director Professor Marie Dziadek  
The Cancer Development Laboratory is investigating the potential for developing new cancer drugs against molecular targets expressed by cancer cells. Our current project aims to block the activity of a key enzyme that is highly expressed in many different types of cancer. This enzyme allows cancer cells to produce the energy that is essential for their growth. We undertook a high throughput screen of a chemical library in collaboration with the Walter and Eliza Hall Institute (at the WEHI-Bio21 HTS facility) in Melbourne and identified potent inhibitor compounds that showed efficacy in blocking cancer cell growth. These compounds will be further developed in collaboration with commercial partners.
By the end of 2009, we had raised the necessary capital to build our proposed translational cancer research centre — an exciting joint initiative with St Vincent’s Hospital. Known as the ‘Garvan St Vincent’s Cancer Centre’ during the planning phase, the Centre will be named in honour of the Kinghorn Foundation, which made a very generous and significant donation.

The Kinghorn Cancer Centre will provide over 10,000 m² of research and clinical space. Adjoining Garvan, and a short walk from St Vincent’s Hospital, the Centre will bring together around 250 cancer researchers, clinicians and support staff within a single location.

Vision

The vision is to realise the promise of personalised medicine for cancer patients by creating a world-renowned facility where research findings move quickly into clinical care and clinical challenges drive laboratory research.

The Centre will complement other cancer initiatives being planned around Australia, all of which have different emphases and strengths.

Design and Inclusions

Architectural practice Bligh Voller Nield (BVN) has designed an environment of warmth and life, by using timber and other natural finishes and by maximising natural light and a sense of space.

Clinical areas including outpatient chemotherapy, consulting rooms and a Wellness Centre will have a view over gardens, a feature proven to benefit patients’ wellbeing. A central atrium will provide a focal point and collaborative hub for patients, visitors, clinicians and researchers. State-of-the-art research areas and core scientific facilities will be situated on the upper and lower levels of the Centre, visible from the atrium and a physical representation of the Centre’s aim to build bridges between cancer research and patient care.

Contributing to the Vision

The cost of building and equipping The Kinghorn Cancer Centre will be around $110m. The Centre is now fully funded, thanks to a $70m grant from the Commonwealth Government’s Health and Hospitals Fund; the generous support of many private donors, and the Trustees of St Vincent’s, who have provided a site.

Building works started in March 2010. Completion is expected in the latter half of 2011.
Program Overview

The growing incidence of obesity is driving a worldwide epidemic in Type 2 diabetes, a disease that already affects 1 in 10 Australians. Research in this program is focused on the molecular regulation of body weight and fuel metabolism, and on obtaining a better understanding of Type 2 diabetes at multiple levels. There is a particular emphasis on the release of insulin and its mode of action in normal and disease states. Research strengths include live cell microscopy, the use of mass spectrometry for the discovery of new molecules affected by metabolic disease, in vivo gene manipulation and metabolic studies in humans.

Program Highlights

- Showed that overeating generates the production of toxic oxygen scavenging molecules, or ‘free radicals’, in the intracellular energy warehouse of cells, the mitochondria. These free radicals trigger insulin resistance and overriding their production is of benefit in animal models.
- Showed that fats disrupt movement of protein out of the cellular protein-folding compartment in pancreatic insulin-producing cells, triggering cell death.
- Showed that different forms of the PKC enzyme family cause insulin resistance in different ways, raising the potential for combination therapy.
- Identified a novel role for the scaffold protein, actin, in controlling the insertion of glucose transport molecules into the cell surface of fat cells, one of the most important actions of insulin.
- Showed that increasing the delivery of fat into muscle mitochondria reduces insulin resistance.
- Demonstrated that burning fats, as opposed to carbohydrates, is not enough to promote fat loss because the body compensates by converting the unburned carbohydrate into fat.
- Indicated that diets high in medium chain fats (such as coconut oil) have a less detrimental effect on insulin action in muscle than long chain fats (animal fats).

People Highlights

- Associate Professor Trevor Biden and Dr Georg Ramm were awarded NHMRC project grants.
- Dr Ross Laybutt was awarded a project grant from the Juvenile Diabetes Research Foundation.
- Dr Carsten Schmitz-Peiffer and Associate Professor Trevor Biden signed a collaborative agreement with the Californian company Kila Pharmaceuticals to test PKC epsilon inhibitors in models of Type 2 diabetes.
- Dr Alex Viardot successfully obtained his PhD degree and was awarded an NHMRC travelling fellowship.
- Jamie Lopez was awarded his PhD and a postdoctoral fellowship from NHMRC to undertake postdoctoral study at the Peter Mac in Melbourne.
- Yvonne Ng was awarded her PhD from UNSW.
- Professor Ted Kraegen spent several months on sabbatical leave with Professor Keith Frayn, University of Oxford UK. During this time, Professor Kraegen gave a number of invited seminars to UK research groups.
- Dr Jiming Ye was appointed Associate Professor at RMIT University in Melbourne, where he will continue his work on traditional Chinese medicine.
- Dr Kyle Hoehn, a postdoctoral fellow in the James lab was appointed to a prestigious position at the University of Virginia in Charlottesville, where he will commence his career as an independent research scientist.
- Yvonne Ng and Alex Rowland delivered oral presentations at the American Diabetes Association meeting in New Orleans.
Research Groups

Appetite and Adiposity in Pre-diabetes and Prader Willi Syndrome (PWS)
Group Leader Professor Lesley Campbell

Our group focuses on the underlying defects in metabolism and appetite control in pre-diabetes and in the commonest genetic obesity disorder, Prader Willi Syndrome (PWS). The latter is associated with relentless weight gain after childhood and can be very difficult to manage. We undertook clinical studies in collaboration with Royal Prince Alfred Hospital PWS Clinic and in collaboration with Professor Herzog of Neuroscience we examine the role, and possible control, of satiety hormones and involvement of inflammation in PWS.

In the pre-diabetes area, we examine heritable factors in individuals predisposed to Type 2 diabetes. For example, overfeeding studies undertaken in 2009 showed that people with relatives with Type 2 diabetes, who are otherwise healthy, gained more weight and showed more metabolic decline than similarly healthy people whose relatives did not have Type 2 diabetes.

Fat and Insulin Resistance
Group Leader Professor Don Chisholm

We study patients with Hepatitis C, which is associated with insulin resistance and predisposition to Type 2 diabetes. We have shown the insulin resistance is, surprisingly, in muscle rather than liver and is reversed with successful treatment of the virus. We are now examining the molecular mechanism involved. We also continue our work on abdominal obesity, examining the role of a transcription factor, IGF1, unique to visceral fat. We use adipose tissue transplantation in mice to examine interactions between adipose tissue and nervous and endothelial cells in the generation of insulin resistance.

Molecular Metabolism
Group Leader Associate Professor Greg Cooney

Fat accumulation causes problems with metabolism that can lead to Type 2 diabetes, heart disease and stroke. The major focus of the Cooney group is to understand factors (genetic and environmental) that control fat accumulation in muscle and liver and to use this information to devise strategies to reduce fat in these tissues and improve insulin action. When fat enters a cell from blood there are two major choices for its fate. It is either stored as an intracellular lipid or it is channelled into the mitochondria, where it is burnt to produce energy. We are studying the regulation of glucose and fatty acid metabolism and energy production by mitochondria and how tissue metabolism changes at different times of the day. This could help explain the contribution of increased food availability and altered eating habits to the rapid increase in obesity and metabolic disease.

ER Stress and Protein Misfolding
Group Leader Associate Professor Antony Cooper

Our group aims to understand how cells cope, or fail to cope, with the stress that can result from the over-production of proteins and misfolding of proteins within a cellular compartment called the endoplasmic reticulum (ER). ER stress is directly applicable to a growing number of diseases including diabetes, as well as many diseases of the brain like Huntington’s, Parkinson’s, Alzheimer’s and motor neuron disease. Either the cell ‘burns out’, generates an excess of harmful products, or accumulates unmanageable amounts of unusable proteins, which ultimately lead to cell death. If the mechanisms by which these stressors induce cell death can be elucidated, this may enable identification of potential points of intervention to help cells deal with extra demands.

Human Physiology
Group Leader Dr Jerry Greenfield

In collaboration with the Cellular Systems Biology group, we are undertaking a major study to identify defects in insulin signal transduction in skeletal muscle from at-risk individuals. We are also examining the characteristics of a group of obese people who seem to be protected from developing insulin resistance and diabetes. In addition, studies have been established examining the effects of glutamine, an amino acid, on metabolism, both in isolation and in combination with a new diabetes medication. Glutamine appears to have a promising effect on glucose lowering after a meal and may offer a simple, novel and effective treatment in Type 2 diabetes. In another study, we are examining the possible role of the autonomic nervous system in the development of diabetes and obesity.

Phospholipid Biology
Group Leader Dr Wil Hughes

Phospholipids are the basic building blocks of cell membranes but, as is becoming clearer, some are also dynamically regulated to enable control of many of the major functions of cells. Two such examples are the stimulated secretion of insulin from pancreatic beta cells after a meal, and the movement of glucose transporter GLUT4 to the plasma membrane in muscle cells to allow glucose uptake in response to insulin. We continue to use state-of-the-art live cell microscopy to see where and when in individual cells the dynamic changes in phospholipids occur to determine how they may regulate insulin release or GLUT4 movement. In collaboration with the Cellular Systems Biology and Molecular Metabolism groups, we aim to identify precisely which intracellular processes may be defective in diabetes.
Islet Biology
Group Leader Dr Ross Laybutt

Pancreatic beta-cell failure is fundamental to the development of diabetes. Our goal is to identify mechanisms responsible for the beta-cell destruction and the loss of insulin secretion that cause diabetes. The major hypothesis under investigation is that in Type 2 diabetes a gradual rise in blood glucose (hyperglycaemia) and lipid levels leads to a loss of the unique expression pattern of genes necessary for appropriate insulin secretion. This worsens hyperglycaemia, which causes further beta-cell dedifferentiation and eventually beta-cell death. Studies have also made important contributions to understanding how cytokines, lipids and high glucose induce stress within the endoplasmic reticulum (ER) and are investigating ER stress as a potential mechanism for beta-cell dysfunction and destruction in Type 1 and Type 2 diabetes.

Insulin Signalling
Group Leader Dr Carsten Schmitz-Peiffer

We focus on the lipid metabolites that disrupt insulin signalling and how these contribute to insulin resistance. This year we demonstrated the effectiveness of blocking the accumulation of such intermediates with a novel compound, which represents a new approach to treating insulin resistance. Another interest of our group is the protein kinase C (PKC) family of enzymes, and we have shown that while two distinct PKC members (PKCd and PKCe) each play a role in generating insulin resistance due to fat oversupply, they do so in different ways, either by promoting lipid synthesis or by affecting its partitioning in insulin-sensitive tissues. Proteomic approaches indicate that PKCs control the levels of several enzymes involved in lipid metabolism. In addition, PKCe regulates the insulin receptor itself, promoting its cellular internalisation to reduce its downstream signalling.
Diabetes Vaccine Development Centre

CEO Ms Rowena Tucker

Overview

The Diabetes Vaccine Development Centre (DVDC) was established in 2003 through a major joint initiative of the National Health and Medical Research Council (NHMRC) and the New York based Juvenile Diabetes Research Foundation (JDRF).

With the assistance of a grant from the NSW Government, DVDC relocated from Melbourne to Garvan in 2007. It became a company limited by guarantee with Garvan as the sole member in 2008.

DVDC is governed by a Board representing its major stakeholders (Garvan, JDRF and NHMRC), as well as internationally recognised scientists and biotechnology executives with expertise in the fields of diabetes and vaccine development.

Originally, the Centre’s mission was to accelerate the development of one or more vaccines that would prevent or delay the progress of Type 1 diabetes, however the DVDC Board decided to broaden the focus to include clinical research on interventions and complications of Type 1 diabetes.

DVDC has substantial in-house experience for the conduct of clinical trials, and coordinates a network of 10 trial sites across Australia and New Zealand.

DVDC received confirmation of a further $5m over three years from JDRF to support DVDC activities.

Scientific Program

Type 1 Diabetes Prevention Study, INIT II

This is a Phase 2, multi-centre, randomised, double blind, placebo-controlled trial of intranasal insulin (440IU) in children and young adults at risk of Type 1 diabetes. The aim of this project is to determine whether the administration of insulin via an intranasal route will result in a protective immune response.

Pepidia-1, Phase 1b Study of Proinsulin (P1) Peptide Immunotherapy in New-onset Type 1 Diabetes

Peptide immunotherapy represents a novel approach to preventing loss of insulin production from the pancreas in Type 1 diabetes. The Pepidia-1 study, which is being conducted in the UK, aims to address the safety issue of whether, in patients with residual beta-cell function (new onset disease), P1 peptide administration adversely affects the rate of beta-cell loss.

Use of BAFF Blockers to Prevent Type 1 Diabetes in Man

DVDC is supporting pre-clinical studies aimed at testing a therapy targeting the B cell arm of the immune system. Using non-obese diabetic mice, this study aims to test the hypothesis that B-cell depletion, by way of BAFF-blockade, will restore tolerance to islets and prevent diabetes occurrence.

Highlights

- Received confirmation of a further $5m over three years from JDRF to support DVDC activities.
- Invested in the development of a new database for the management of its INIT II clinical trial which will serve as a platform for the management of other clinical trials in the future.
- Employed a Senior Clinical Research Associate which now enables DVDC to undertake its own trial monitoring, and provide additional support and advice to the network of INIT II investigators and study coordinators.
- Received a number of Expressions of Interest seeking DVDC involvement in multicentre Type 1 diabetes trials — evidence that the DVDC profile is growing.
- Successfully held the INIT II Annual Meeting 26–27 November 2009 in Melbourne.
- Worked closely with JDRF Australia in the further development and implementation of its research strategy, including a substantial proposal for an enhanced and inclusive network of clinical trial sites linking investigators, study nurses, and hospitals in each state around Australia.

Membership of the DVDC Scientific Advisory Committee

Professor Ian Frazer FAA (Chair)
Director, Diamantina Institute for Cancer Immunology & Metabolic Medicine

Dr Robert A. Goldstein, MD, PhD
Senior Vice President, Scientific Affairs, Juvenile Diabetes Research Foundation International (JDRF)

Professor Chris Goodnow FAA, FRS
Director, Immunogenomics Laboratory
& Director, Australian Phenomics Facility, John Curtin School of Medical Research & The Australian National University

Professor Ian Frazer FAA
Director, Diamantina Institute for Cancer Immunology & Metabolic Medicine

Stephen Higgs
Director, Business Development & Legal Affairs, Garvan

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Immunology Program

Program Overview

Our immune system is designed to protect us from dangerous attacks whether they come from outside the body in the form of infections, or from inside the body in the form of cancer. At the same time, the system must learn to avoid attacking our own tissues or reacting to minor threats like pollens and house dust mites. When this balance is upset and the controls fail, the outcomes are diseases ranging from life threatening infections and spreading tumours to autoimmune conditions (eg rheumatoid arthritis and Type 1 diabetes) and allergies (eg asthma).

The work of the research team in the Garvan Immunology Program is divided between studying how a normal immune system functions in a balanced way and what goes wrong when disease occurs. To this end, use is made of the latest models of human diseases to improve our understanding of their pathology and devise better ways of treating them. Close ties therefore exist between the Program and Garvan’s biotech company, G2 Therapies Ltd, which is currently commercialising a range of therapeutic antibodies made within the Immunology Program’s laboratory.

Staff in immunology interact with colleagues from the Cancer, Neuroscience and Diabetes Programs. This reflects the importance of immune mechanisms in many different diseases and the value of immunological techniques when studying the differences between normality and disease in a wide range of target tissues.

Program Highlights

- Discovered a promising therapeutic target for prevention of Type I diabetes, a molecule known as BCMA, which effectively subdues the immune cells that cause the disease.
- Showed new ways of artificially boosting the numbers of a certain class of immune cells (regulatory T cells), a process which could be used to prevent the rejection of organ transplants or the development of autoimmune diseases.
- Defined a role for ‘lipid rafts’ — tiny fat-enriched platforms in cell membranes that appear to ramp up the sensitivity of killer T cells — in helping us mount an immune response to viruses and cancers.
- Elucidated and patented methods for improving the stability of antibody therapeutics, a novel class of drugs with more than US $20 billion sales each year.
- Every month the prestigious Journal of Immunology features a previously published paper, which is selected as a ‘pillar of immunology’ article by the editors for its “enormous impact on the field of immunology.” In November 2009, a paper co-authored by Dr Robert Brink and Professor Tony Basten and published in Nature in 1988 received this accolade. Cited 944 times it describes the development of the most widely used transgenic mouse model for studying the control of antibody responses.
- Identified checkpoints during the development of B cells (immune cells which make antibodies), when any rogue cells present that can attack ‘self’ are destroyed, so helping protect us against autoimmune diseases.
- Identified a role for the EBI2 gene, that produces a B cell surface protein of previously unknown function, is required to co-ordinate B cell migration and differentiation during the early phases of antibody responses.
- Showed that the three signalling molecules, TRAF2, TRAF3 and cIAP, function together to control B cell survival and are all potential B cell tumour suppressors, so they may prevent development of cancer in these cells.
- Revealed that the body usually manages to deploy a class of T cells (known as T follicular helper cells) to help B cells produce high quality antibodies against ‘enemies’ (foreign pathogens) and at the same time prevent them from producing antibodies against “self” (our own tissues).
- Showed that a gene known as STAT3 is critical in regulating the production of antibodies, which explains why people with certain rare immunological

Dr Robert Brink
disorders, where that gene is mutated, cannot produce functional antibodies to protect themselves against disease.

Demonstrated that a tiny genetic irregularity in the gene encoding for the growth factor IL-21 greatly boosts its expression, leading to the development of Type 1 diabetes in mice. The absence of the irregularity, on the other hand, keeps IL-21 at normal levels and prevents development of the disease.

Identified high levels of a particular immune cell — a ‘T helper cell’ — in the pancreatic insulin-producing cells of mice and humans prone to develop Type 1 diabetes. These cells appear to originate in the gut and migrate to the pancreas, where they produce large quantities of the IL-21 gene and so contribute to disease onset.

Demonstrated that ‘short chain fatty acids’ (the by-products of bacterial fermentation of insoluble dietary fibre in the gut) bind to GPR43, a molecule expressed by immune cells that acts as an anti-inflammatory receptor.

People Highlights

- Professor Jonathan Sprent was awarded an NHMRC Senior Principal Research Fellowship.
- Dr Shane Grey was awarded both an Australian Research Council 2009 Future Fellowship and an NHMRC Senior Research Fellowship (he accepted the latter).
- Kenneth Ho was awarded the Novartis Young Investigator award by the Endocrine Society of Australia for the best presentation at the annual scientific meeting in August 2009.
- Dr Cecile King, Dr Shane Grey and Professor Tony Basten were invited to speak at the Australasian Autoimmunity Workshop.
- Dr Daniel Christ was an invited speaker at Lorne BDI conference in Victoria and at MedImmune (Cambridge). He was also session chair (Antibody engineering) at OzBio meeting.
- Dr Daniel Christ and Professor Jonathan Sprent received a Cancer Institute New South Wales grant for translational studies on Interleukin-2.
- Dr Tin Phan was an invited international speaker at the 16th Germinal Centre Conference, Frankfurt, Germany.
- Kip Dudgeon received a Cancer Institute NSW - 2010 Research Scholar Award.
- Helen McGuire and Kendle Maslowski were chosen to present in the prestigious Young Investigators Forum at the Annual ASI Scientific Meeting, Gold Coast.
- Helen McGuire received a travel grant from the UNSW Graduate Research School (PRSS).
- Tyrion Chan received two travelling scholarships for the Keystone B cell conference: the Keystone Symposia Travel Scholarship 2009 and the UNSW Postgraduate Research Scheme Travel Scholarship 2009.
- Kendle Maslowski: received this year’s Castle Harlan Award of $10,000 for the best 2nd year PhD student at the Garvan Institute.
- Professors Jonathan Sprent and Tony Basten were invited to speak in symposia at the Korean Association of Immunologists meeting, Seoul, Korea.
- Professor Tony Basten was a participant in the Cambridge Immunology Forum, UK.
- Dr Kylie Webster won a St Vincent’s Research Symposium Award for Oral Presentation and a TSANZ (Transplant Society of Australia and New Zealand) Young Investigator Award.
- Tyrion Chan won the NSW Flow Cytometry Prize for her work on early B lymphocyte responses.
- Dr Sandra Gaudin was awarded an NHMRC Overseas Biomedical Fellowship.
- Dr Dominique Gatto was awarded a one year pilot grant by the Alliance for Lupus Research (US).
- Dr Jenny Gunton was awarded a two year JDRF grant for translational studies in islet transplantation in Type 1 diabetes.
- Dr Shane Grey gave a public seminar for Diabetes Australia (Pushing the Boundaries day) on the Australasian clinical islet transplant trial.
- Dr Jenny Gunton was elected Honorary Secretary of the Australian Diabetes Society, and Program Organising Committee Chair for the ADS annual scientific meeting. She also became a Board Member of Diabetes Australia and was an invited speaker at the Endocrine Society of Australia Seminar.
- Drs Cecile King, Robert Brink and Stuart Tangey were awarded Project Grants from the NHMRC.
- Dr Cecile King was invited to give a plenary talk at the annual Immunology of Diabetes Society meeting in Malmo, Sweden in May.
- Dr Robert Brink was an invited keynote speaker at the Australasian Society for Immunology NSW Branch Meeting, Bowral.
- Dr Robert Brink was an invited plenary speaker at 39th Annual Conference of the Australasian Society for Immunology, Gold Coast.
- Vivian Turner received a Cancer Institute NSW – 2010 Research Scholar Award.
Our team is interested in the development and fate of T cells — white blood cells that participate in a variety of immune responses but can somehow distinguish between self and foreign antigens. One of the unknown questions that is central to maintaining the immune system’s homeostasis is how are these cells destroyed once their mission is complete and infections are overcome? We know that most self-destruct within a few live on to become memory T cells, which are activated by a re-infection, but we don’t know the factors that determine their destiny. Application of our work lies in harnessing the immune system to boost its attack on cancerous tumours and, conversely, dampening down the immune response to treat autoimmune diseases.

**B Cell Immunobiology**

**Group Leader** Dr Robert Brink and Emeritus Professor Antony Basten AO FAA FTSE

B lymphocytes (B cells) produce secreted antibodies in response to the entry of foreign substances and microorganisms into the body. Antibodies bind specifically to these foreign "antigens" and target them for destruction and elimination. Autoimmune diseases such as immune thrombocytopenic purpura, myasthenia gravis and haemolytic anaemia can arise when B cells produce rogue antibodies that attack the body itself instead of the foreign invaders. The growth and survival of B cells can also become dysregulated, leading to B cell malignancies such as lymphoma and multiple myeloma. Our laboratory has developed a unique system that allows the detailed characterisation of B cells participating in all phases of an immune response. This system is used to identify the genes, signalling pathways and intercellular interactions that regulate B cell survival, proliferation, and differentiation in the body. By understanding how B cells function we hope to reveal new strategies for improving vaccines, controlling autoimmune disease, and treating B cell cancers.
Gene Therapy & Autoimmunity
Group Leader Dr Shane Grey

Our laboratory is interested in the how and why of the immune system’s attack on the body’s tissues as it occurs during the rejection of organ grafts and in autoimmune disorders like Type I diabetes where the insulin-producing beta cells are destroyed. Approaches include examining factors that regulate the immune attack on our own cells and investigating the molecular changes that occur in the tissue being attacked in the hope of, one day, being able to genetically engineer tissues that could withstand the assault. This strategy would alleviate the need for the toxic immunosuppressive drugs currently required to promote successful organ transplantation and, in the case of Type I diabetes, enable creation of a ‘death-defying’ beta cell as a novel cure.

Immunobiology
Group Leader Dr Stuart Tangey

Our focus is on understanding the development of B cells — the population of white blood cells responsible for the production of protective antibodies — and the regulation of antibody responses. We are particularly interested in finding out how the immune system responds to infections or vaccinations by providing us with a ‘memory’ of the response so that we cope faster and better following subsequent exposure to the same infectious agent. The development of immunological memory involves interactions between B cells and helper T cells — another subset of immune cells. Thus, a major focus of our work is to understand exactly how helper T cells instruct B cells to produce antibodies. We are also studying several genetic conditions of the immune system, and corresponding mouse models, that result in immunodeficiencies — disorders whereby affected individuals are unable to mount appropriate immune responses following exposure to some infections or pathogens. These include X-linked lymphoproliferative disease, common variable immunodeficiency and hyper-IgE syndrome. Overall, we hope to identify means to improve the immune response in individuals with immunodeficiencies and, conversely, ways in which the immune system of patients with autoimmune diseases could be controlled.

Mucosal Autoimmunity
Group Leader Dr Cecile King

Our laboratory is interested in the autoimmune responses that cause destruction of tissues at the mucosal interface between the body’s own tissues and the environment. Broad-based immunosuppression is commonly used to treat the more serious autoimmune diseases and transplant recipients, but it has an obvious drawback since we need a functioning immune system in order to thrive. The aim of our research is to identify target molecules that will enable the selective suppression of self-tissue-destructive cells.

Antibody Engineering
Group Leader Dr Daniel Christ

Our laboratory is working on the development of novel antibody therapeutics. In particular, we are interested in the engineering of human antibody fragments, which are considerably smaller than current monoclonal antibodies. Human antibody fragments (such as domain antibodies) can be generated by genetic engineering technology, completely bypassing the use of animals. These fragments can be produced in large quantities in bacteria and open up promising new routes for non-intravenous applications, imaging and therapy. We are applying our technology to targets in cancer and inflammatory diseases.

B Cell Tolerance and Autoimmunity
Group Leader Dr Pablo Silveira

Our ultimate goal is to prevent the immune system attacking the insulin-producing beta cells of the pancreas, which leads to Type 1 diabetes. Our research aims to identify the faulty mechanisms that allow the B cells recognising beta cell proteins to persist and thus activate the destructive T cells. We also aim to identify novel genes that control the generation and function of this aberrant population of B cells, findings that could form the basis for new therapies to prevent or reverse Type 1 diabetes in humans.

Diabetes and Transcription Factors
Group Leader Dr Jenny Gunton

The causes of beta-cell failure are not well understood, but we know there are changes in these cells’ gene expression that can yield clues about what is going wrong. Through the use of a variety of tissue-specific knockout and transgenic mice we hope to identify why beta cell failure occurs as well as ways to improve beta cell function and thereby treat human diabetes. We are currently focusing on a gene called ARNT, which is decreased by 90% in the beta cell containing islets of people with Type 2 diabetes. It seems to be a master gene that controls other genes involved in beta-cell function, including glucose breakdown and insulin production. We are now looking at ways to control ARNT.

Translational Immunology
Group Leader Professor Charles Mackay FAA

Professor Mackay took up a Chair at Monash University at the beginning of this year. However, he continues to run an active group of students and postdocs at the Garvan. Their research has led to development of antibodies that can intervene in the inflammatory process, the final common pathway for many diseases, and are being developed by G2 Therapies Ltd. They are also studying the link between diet, fatty acid binding proteins and asthma, and looking more broadly at the links between inflammatory and metabolic diseases. The outcome is a new hypothesis suggesting that gut microbes in conjunction with our diet, determine the nature of inflammatory responses.

A node of the Cooperative Research Centre for Asthma and Airways
Head Professor Charles Mackay FAA Group leader Dr David Zahra

Our group focuses on the development of a promising therapeutic that neutralises the function of the cytokine GM-CSF. GM-CSF has been linked to a number of inflammatory diseases including asthma and rheumatoid arthritis, and we have developed an antibody that blocks this cytokine. The antibody has been successfully humanised and the epitope that our antibody binds on GM-CSF has been defined. The potential therapeutic is protected by two provisional patents and is now ready for pre-clinical and toxicology studies. A feasibility study is being conducted in collaboration with a major pharmaceutical company with the aim of fully licensing the therapeutic for pre-clinical and clinical development by the end of 2009.
Program Overview

The Neuroscience Research Program aims to increase our understanding of the neuronal systems involved in disorders such as Parkinson’s disease, Alzheimer’s disease, schizophrenia, eating disorders and hearing loss. We also investigate neuro-endocrine defects caused by the loss of growth hormone function. We aim to identify new therapeutic approaches in these areas, with a special interest in regeneration of the nervous system for therapeutic purposes. Much of our research strives to achieve a better understanding of the brain’s control of body functions including the regulation of energy balance (intake and expenditure), which affects fertility, mood, and weight gain.

Program Highlights

- Found that sex hormones and the neurotransmitter neuropeptide Y (NPY) work together to control fat levels and bone density in the body.
- Showed that NPY receptors in the body, rather than the brain, regulate fat burning and storage, and that blocking them can prevent fat gain.
- Identified the specific neuronal pathways in the brain that respond to pancreatic polypeptides and reduce appetite. This highlights a potential new way of treating obesity.
- Discovered the exact location of adult taste bud stem cells, making it easier to access and use them in transplantation.
- Proved that inflammation in the brain prevents stem cell proliferation and neural repair, a finding that will have important therapeutic implications for Parkinson’s and Alzheimer’s disease.
- Revealed that NPY plays a central role in the correlation of bone mass with body weight.
- Made significant advances in our understanding of dopamine release from nerve cells, knowledge that should speed up the development of more effective drugs for treating Parkinson’s Disease.
- Demonstrated successful survival of transplanted adult human olfactory stem cells in a mouse model of age-related hearing loss.
- Showed the first evidence that growth hormone enhances sprint capacity, a selective aspect of physical performance.
- Demonstrated that Beta-blockers, a commonly used blood pressure medication, cause obesity by slowing down metabolism and diminishing physical activity.
- Identified new growth hormone-responsive genes that breakdown fat.
- Showed that SERMs, a class of synthetic oestrogens commonly used in medical treatment, block the ability of growth hormone to burn fat and build muscle.
- Demonstrated that measuring gene expression changes in blood cells is not as effective as a growth hormone doping test than measuring blood proteins.

People Highlights

- Professor Herbert Herzog was an invited plenary speaker at the 17th International Symposium on Regulatory Peptides in Santa Barbara, California, USA where he also received the Victor Mutt Award.
- Professor Herbert Herzog was also an invited plenary speaker at the 30th Winter Neuropeptide Conference Breckenridge, Colorado, USA; the 16th Obesity meeting in Kagoshima, Japan; the 1st International Neuropeptide Festival in Salzburg, Austria; and the 1st Annual Meeting of the Austrian Association of Molecular Life Sciences and Biotechnology, Innsbruck, Austria.
- Associate Professor Amanda Sainsbury-Salis was invited to present the Keynote Seminar at the 26th Annual Kinesiology Conference of the Australian Kinesiology Association in Sydney.
- Dr Sharon Oleskevich was an invited speaker at the Hearing and Balance Centre, St Vincent’s Hospital.
- Dr Bryce Vissel was appointed to the Scientific Advisory Board for Parkinson’s NSW; the Editorial Board of Journal of Neurochemistry; to the clinical trials group of the
Research Groups

Adult Stem Cell Research
Group Leader Professor John Shine AO FAA

Neural stem cells can be isolated from the adult olfactory neuroepithelium (situated in the nose) and grown in the laboratory in the form of olfactory neurospheres. These structures are three-dimensional aggregates of cells that are able to grow into neuronal and non-neuronal cells. The identity of the cell type within the olfactory neuroepithelium that gives rise to these neural stem cells remains elusive. Our group studies the basic biology of adult olfactory stem cells with the aim of identifying, isolating and propagating these cells, and to determine the conditions needed to transform them into the different types of nerve cells found in the brain, for example, those lost in Parkinson’s or Alzheimer’s disease.

Eating Disorders Research
Group Leaders Professor Herbert Herzog and Associate Professor Amanda Sainsbury-Salis

One of our laboratory’s major goals is to understand how appetite and body weight are regulated. Deficits in the brain pathways that regulate these processes may be responsible for causing wasting conditions such as anorexia nervosa and cancer cachexia as well as the metabolic resistance to weight loss occurring in overweight or obese people.

Our main focus is on neuropeptide Y (NPY) and its Y-receptors, since many of the molecules that regulate appetite and body weight do so via this system. Our research findings have implications for the treatment of obesity, infertility, poor lactation, dwarfism, and osteoporosis, as well as anorexia nervosa and cancer cachexia.

Hearing Research
Group Leader Dr Sharon Oleskevich

Many forms of hearing loss result from the degeneration of hearing receptors (hair cells) in the inner ear. Hair cells degenerate with aging and exposure to excessive sound. We are exploring the transplantation of adult stem cells to help repair the hearing receptors. We have discovered that taste stem cells have a positive effect on hearing levels following transplantation into a mouse model of noise-induced deafness. In the past year we have extended this research to transplantation of human olfactory stem cells into a mouse model of age-related hearing loss. We are also exploring how deafness can change the way nerve cells in the brain communicate with each other. An international collaboration is underway to determine the anatomy and physiology of these changes.

Neurodegenerative Disorders — Repair and Regeneration
Group Leader Dr Bryce Vissel

The Neurodegeneration Research Group identifies approaches for better understanding and treating Parkinson’s disease, Alzheimer’s disease and spinal disorders. Our goal is to harness the nervous system’s own repair systems and stem cells in order to stimulate the formation of new nerve cells and their connections. We also investigate how to block nerve cell loss. Our team has identified new mechanisms for stimulating brain repair from stem cells in the brain and has also discovered potential ways to block neurodegeneration. Our research outcomes have significant clinical implications for the lives of people who confront devastating neurodegenerative diseases.

Pituitary Research Group
Group Leader Professor Ken Ho

The pituitary gland produces key hormones that control body growth, strength, appetite, metabolism, mood and reproduction under the control of the brain. An over or under active pituitary gland can produce problems such as obesity, osteoporosis and sarcopenia (muscle wasting).

Projects include the investigation of the sympathetic nervous system (SNS) in the control of body fat and muscle. One aspect looks at the metabolic consequences of beta-blockers, which are a class of drugs commonly used to treat blood pressure.

Complementary work in the laboratory addresses the cellular and molecular mechanisms by which sex steroids modify the action of growth hormone and seeks to identify novel growth hormone regulated genes.

Another project aims to develop new approaches for the detection of growth hormone doping and for studying the effects of growth hormone on performance.
Osteoporosis & Bone Biology Program

Program Overview

Osteoporosis affects the capacity for independent living and also contributes to premature mortality for men and women, younger and older. As prevention is the best strategy for reducing this large human and financial burden, we need to improve our knowledge of the risk factors for fracture; find ways to better assess treatments; increase our understanding of bone biology and help identify new treatment possibilities.

Program Highlights

- Demonstrated the association between fragility fracture and premature mortality in both old and younger men and in women.
- Extended our prognostic models for predicting fracture risk for men and women, implemented in www.fractureriskcalculator.com, widely used by doctors and patients worldwide.
- Validated our nomograms for absolute fragility fracture risk in collaboration with colleagues in Canadian Multicentre Osteoporosis Study (CaMOS) data. Similar collaborations are underway with the Geelong Osteoporosis Study (Melbourne), CAIFOS study (Perth) and other major cohorts in New Zealand, Norway, UK and Holland.
- Reported findings of initial clinical studies with a novel treatment that reduces bone breakdown, and which has major potential in osteoporosis treatment.
- Identified novel chromosomal regions that harbor osteoporosis genes in the world’s first search for osteoporosis genes, as part of international collaborations using genome wide analysis advanced technology.
- Demonstrated the frequency of vitamin D insufficiency in general populations and in severely ill individuals in hospital. These findings suggest that vitamin D deficiency contributes to in-hospital mortality.
- Demonstrated that neurotransmitters in the brain play a critical role in the regulation of bone mass, a function that has been considered purely mechanical. Specifically, neuropeptide Y (NPY) directly controls the cells that make bone, increasing bone mass in line with body weight.
- Identified the ability of bone cells to fine tune the brain’s signals at a local level, increasing bone mass in parts of the body exposed to greater weight, or load.
- Initiated collaboration with a group in Strasbourg to study the action of endorphin receptors in the control of bone mass.
- Developed a collaborative relationship at Royal North Shore Hospital to investigate the role of NPY in osteoarthritis.
People Highlights

_ The Bone Biology Group received an NHMRC project grant for the 5th consecutive year. The current application is to investigate the interaction between sex steroids and neural pathways in the control of bone mass.

_ Professor Tuan Nguyen collaborated with colleagues at the Pham Ngoc Thach University of Medicine, Ho Chi Minh City (Vietnam) to examine the effects of vegetarian diets and micronutrients on bone health. He is also working to help them design new studies on the effects of vitamin D on bone health and infectious diseases.

_ Professor John Eisman chaired the development group for Guidelines for Osteoporosis Management, supported by the Federal Department of Health through the Royal Australian College of General Practitioners. The final draft is with the NHMRC at present.

_ Dr Paul Baldock gave the Plenary Symposium of the 2009 annual conference of the American Society of Bone and Mineral Research in Denver Colorado. He also gave a Plenary Symposium Presentation at the 41st International Symposium on Endocrinology & Metabolism in Prague. He was an invited oral presenter at the International Pituitary Society meeting in Washington.

_ Dr Nguyen Nguyen won The Outstanding Abstract Award of the 2009 ANZBMS annual meeting.

_ Bone Program students had the following successes: Bich Tran, the ASBMR Christine & T Jack Martin Research Travel Grant; Iris Wong, a Young Investigator Award at the ASBMR Annual Scientific Meeting, Denver, USA; and Dana Bluc, the Stuart Furler Travel Award to attend the ASBMR Scientific Meeting. Young researchers Dr Frank Driessler and Dr Nguyen Nguyen and students Bich Tran and Iris Wong were awarded a Qantas Travel Grant each for 2009.

Research Groups

Population, Individual and Genetic Determinants of Osteoporotic Fracture Risk and their Outcomes

Group Leaders Professor Tuan Nguyen and Associate Professor Jackie Center

The Dubbo Osteoporosis Epidemiology Study (DOES), which began in 1989, is the world’s longest running large-scale epidemiological study of osteoporotic fractures in men and women. The data from this study has allowed us to develop powerful predictive models to identify men and women at high risk of fracture, who would benefit most from preventative interventions. Our search for new osteoporosis genes is continuing in large-scale international collaborations. We are developing tools to predict those at high (and low) risk for osteoporosis and fractures. This insight will direct the focus of preventative activities on osteoporosis or other health concerns, as most appropriate. Establishing how clinical factors and genetic factors interact to affect bone biology will help identify those individuals who would most benefit from existing therapies, as well as helping to identify targets for novel therapies.

Bone Biology

Group Leader Dr Paul Baldock

Osteoporosis is characterised by a reduction in bone density and therefore strength. It is caused by an imbalance between bone production and bone loss. Our group’s research is primarily focused upon investigating the influence of brain signals on bone formation and strength. Much of this work makes use of transgenic mouse models and is carried out in collaboration with researchers in the Neuroscience Program. Our investigations involving the effect of neurotransmitter neuropeptide Y (NPY) have identified a novel and powerful pathway for stimulating the production of bone and increasing bone strength, suggesting an approach to new treatment. Recent work has identified major interactions between the NPY pathway and body weight and responses to stress.

Fracture Prevention — Clinical Studies

Group Leader Professor John Eisman AO

Our clinical studies group continues to participate in multicentre international clinical trials evaluating potential osteoporosis treatments that are in the final stages of pharmaceutical development. Involvement in these studies helps ensure we remain at the cutting edge of knowledge of novel therapies and provides an entry pathway to pharmaceutical interest in our novel developments.
Technology is an important component of being competitive in medical science. Garvan’s core research facilities contain state-of-the-art equipment that enables our scientists to perform the necessary experiments to understand disease processes better. Highly trained managers oversee the facilities which are also available to external researchers.

Australian BioResources (ABR) facility, based in Moss Vale, holds mouse production colonies under clean room conditions for Garvan and other medical research organisations in NSW. Services offered include the import and export of mice, rederivation and embryo freezing. The Biological Testing Facility, located at Garvan in Darlington, receives mice from ABR for holding in specialised experimental zones to enable quality animal-based research.

Australian Cancer Research Foundation (ACRF) Unit for the Molecular Genetics of Cancer houses equipment that can detect and analyse genomic variations such as gene losses, mutations, expression, and methylation on a large scale. Diverse platforms are available for facilitating research within and outside Garvan. The facility strives to achieve high-throughput, sensitivity, accuracy and cost effectiveness. In addition to sequencing and methylation analysis services, there is now a mouse genotyping service available for all researchers in NSW.
Gene Chip Facility contains the Affymetrix Microarray System that is used to compare the levels of gene transcripts in tissue samples. Output helps researchers find potential genes of interest, the subsets of which can then be further analysed in the ACRF Unit that can handle large numbers of samples. Garvan was the first in Australia to establish the system.

Clinical Research Facility is a unique resource dedicated to the conduct of research in people. It provides a vital interface between discoveries in the laboratory and their evaluation in humans. The facility, staffed by highly skilled nurses and clinical investigators, has a range of support services and state-of-the-art equipment to evaluate new therapies.

Peter Wills Bioinformatics Centre applies techniques derived from disciplines such as applied mathematics, statistics and computer science to understand, organise and analyse biological data. This includes the housing of both clinical and microarray data, and the building of computer programs for querying and analysing these datasets. Examples of these programs include Cansto for managing clinical cancer data and Stuart for animal records management. CarSto is used across Australia by the Australian Prostate Cancer Collaboration for all their clinical information management. Garvan’s cDNA array server houses microarray experiment results for researchers across Australia and connects them to the (US) National Cancer Institute’s cancer internet, known as callIG (Cancer Biomedical Informatics Grid). The software tool, GenePattern, enables users to access their data from cDNAarray and analyse it themselves.

MLC Community Foundation Flow Facility provides cell analysis and cell sorting services to members of the St Vincent’s Research Precinct and external users across Sydney. The facility houses two cell sorters and five flow cytometry analysers, and will expand further in size and capability as new facility space opens at the beginning of 2010. Flow Cytometry is a technology that allows simultaneous analysis of the physical, biochemical and molecular characteristics of single cells or particles suspended in a fluid stream. Cell analysis and sorting are frequently used to identify the various cell types present in biological tissues and to determine their developmental or functional relationships. It has wide-ranging applications in immunology, haematology, infectious diseases and cancer. The facility is supported by a generous grant from MLC.

Pieter Huveneers Molecular Imaging Facility consists of a number of state-of-the-art microscopes which, using a variety of fluorescence based techniques, are capable of imaging tissue, cells, intracellular organelles and even multiple individual molecules in live cells. Using techniques such as Total Internal Reflection Fluorescence (TIRF) microscopy we are able to image events occurring on or near the surface of a cell. Using laser scanning confocal microscopy we can precisely image ‘slices’ of samples which can be reconstructed into a 3D representation for analysis. These provide our scientists with the best possible means of identifying where and when molecules of interest are in normal tissue and how this may differ in disease.

Completed the legal, operational and logistical work for The Kinghorn Cancer Centre, our proposed translational cancer research centre (currently under construction).

Integrated the St Vincent’s Hospital Diabetes Centre into the Garvan building.

Completed the first full year of operations at the Australian BioResources (ABR) facility. Within that time ABR reached 50% of total capacity (25,000 mice), completed rededication for lines from partner institutes, introduced DNA preparation and embryo cryopreservation services, and started supplying commonly used inbred strains to Garvan and partner institutes. The facility now holds all major breeding colonies for Garvan and seven partner institutes and constitutes a significant resource for biomedical research in NSW.

Worked closely with Illawarra TAFE to produce the first distance formatted Certificate III Animal Technology course in NSW. This will support the development of technical staff manning the ABR facility.

Completely refurbished laboratories in one of seven levels at Garvan. Air conditioning units were overhauled; automatic doors fitted; gas isolation zones put in place; efficient light fittings and occupancy sensors installed; anti-microbial paint used; and many of the original fittings (such as lab benches and sinks) recycled. The Master Builders Association recognised the excellence of the work with a Merit Award in their category of Interior Fitouts up to $5,000,000.

Provided office facilities at Garvan for Research Australia from July 2009. Research Australia is a member-based advocacy organisation with a mission to make health and medical research a national priority.

Executed Service Level Agreements governing shared essential services for Medical Research Institutes within the St Vincent’s Research Precinct. The Agreements cover stores and dock, waste, medical gases, bulk gases, generators, media prep, glass wash and cryogenics.

Established a Precinct Occupational Health and Safety (OHS) Committee to enable a co-ordinated and aligned approach for OHS management.

Signed an MOU between Garvan and Sydney Water allowing the two businesses to co-operate in water saving initiatives. Water consumption has already been significantly reduced.

Maintained a downward trend in our monthly electricity usage, with a reduction of 20% compared to the corresponding months of 2008.

Installed LED (light emitting diode) lighting in public areas of Garvan, such as the foyer, resulting in energy savings for those areas of around 90%. These findings will have a direct impact on the type of fittings to be installed in any future works and may also be useful in determining the type of fittings to be used in The Kinghorn Cancer Centre.

Received a bioinformatics infrastructure grant from the Cancer Institute NSW to extend our microarray archive, already the biggest in Australia.

This library of information allows us to compare the genes of cancer patients with the genes of healthy people.

Implemented a new $250,000 file server, using the very latest technology as used by medical research facilities around the world. The server stores the huge volume of data collected each day on Garvan’s research-instruments: Microscope images as well as flow cytometry, genomic, mass spectrometry and human genome sequence data.

Delivered a computer solution to implement the Bone Program’s web-based fracture risk calculator.

Won a Computer World Honors award for the Garvan IT Group’s delivery of world-class research information systems.
Overview

The Business Development team engages with the pharmaceutical and biotech sector and partners with other academic organisations to take Garvan’s research discoveries one step closer towards the development of new treatments and diagnostic tests.

Working closely with Garvan scientists, the Business Development team is responsible for all aspects of commercialisation from monitoring research activities to maximising early capture of intellectual property, identifying pharma/biotech market opportunities, and negotiating and managing commercial agreements. Importantly, the Business Development team establishes applied collaborations with organisations who have additional technologies which greatly increase the potential for Garvan’s breakthroughs to be developed for clinical use.

The Garvan patent portfolio comprises 27 patent families covering treatment, diagnostics and screening categories.

G2 Therapies and Novo Nordisk

G2 Therapies is a private company, chaired by Dr John Schubert, which develops and commercialises antibody-based therapeutics for inflammation. Founded at Garvan in 2002, major investors include AMWIN and Baron Nominees.

In early 2006, G2 announced the signing of a major research, development and licensing agreement with Danish healthcare company Novo Nordisk to develop an anti-C5aR antibody. The Anti-C5aR antibody treatment, currently in clinical trials, holds promise for a number of inflammatory conditions including lupus, rheumatoid arthritis and other autoimmune diseases.

Business Development Advisory Council

The Business Development Advisory Council (BDAC) includes several representatives from the biotech and pharmaceutical industries. 2009 members included:

Dr Lisa McIntyre (Chair) Director, LEK Consulting
Professor John Shine AO FAA Executive Director, Garvan
Dr George Moore External Director
Dr Merilyn Sleigh External Director
Peter Carre CEO, Burrill Australia
Christina Hardy Director, Business Development & Legal Affairs, Garvan
John Dakin Chief Operating Officer, Garvan
Garvan Community

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Fennis Family Foundation
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Mrs Margaret Fitzpatrick
Mr Roger Fitzsimmons
Ms Jane Forster & Mr Glenn Eggleton
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Foundation for Prader-Willi Research
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Ms Lynette Gearing
Ms Belinda Gibson
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GlockSmithKline
John Glennie
Chere Glick and family for Joe
Mr Cyril Golding
Mrs Elizabeth Goldsmith
Ms Delta Goodrem
Mr & Mrs William & Jacqueline Goodyear
Bequests

Estate of the Late Gloria M Backhus
Estate of the Late Margaret Benning
Estate of the Late Ella M Bucoz
Estate of the Late Deniz de Ferrars Carrington
Estate of the Late Lynette A Detlor
Estate of the Late Margaret E Kenny
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Estate of the Late Florence A O’Sullivan
Estate of the Late Helen M Poir
Estate of the Late Ronald M Pfeffer
Estate of the Late Elaine E Pope
Estate of the Late Joyce M Proust
Estate of the Late Babette J Ryan
Estate of the Late George W Steed

In Memoriam

Gorakw-Kenewal Lions Club
Gorakw Community

Jill and John Kingston
Garvan Institute Board

Bill Ferris AC
Chairman
Nominated by the Trustees of St Vincent’s Hospital

Mr Bill Ferris is Executive Chairman of the CHAMP Private Equity Group, one of Australia’s leading private capital groups, providing venture capital, expansion capital, and management buyout funding in Australasia. Mr Ferris is Chairman of the Health and Hospitals Fund Advisory Board as part of the Federal Government’s Nation-Building Funds initiative. Former directorships include Chairman, Australian Trade Commission (Austrade), Austra United Communications Limited, and Bradken Resources Pty Ltd. Mr Ferris is also a Director of the Garvan Research Foundation. Mr Ferris was made an Officer in the Order of Australia in 1990 for services to the export industry and in 2008 was made Companion in the Order of Australia for his philanthropic activities and his role in the establishment of the private equity sector in Australia.

Martin Hoffman
Treasurer
Nominated by the Sisters of Charity

Mr Martin Hoffman is a First Assistant Secretary in the Department of the Prime Minister & Cabinet in Canberra. He is Head of the Office of the Coordinator General which is responsible for implementing the Nation Building - Economic Stimulus Plan, and he also coordinates from Prime Minister & Cabinet’s perspective a number of major Government projects including the National Broadband Network. He previously had a lengthy career in digital media and technology, including as CEO of NineMSN, Australia’s largest internet media company. He has also held senior management roles with Fairfax Media and Optus.

Graham J Bradley AM
Nominated by the Garvan Research Foundation

Mr Graham Bradley is a professional company director. Mr Bradley is Chairman of Stockland Corporation Limited, HSBC Bank Australia Limited and Anglo American Australia Limited. From 1995 to 2003 he was Managing Director of Perpetual Limited. He is a former Partner of McKinsey & Company, management consultants, and a former National Managing Partner of Blake Dawson. Mr Bradley was Chairman of the Garvan Research Foundation and a Director of the Garvan Institute Board from 1999–2009.

Nicholas Curtis
Nominated by the Trustees of St Vincent’s Hospital

Mr Nicholas Curtis has a background in investment banking and the resources industry. He is Executive Chairman of Lynas Corporation Limited, an Australian public company specialising in Rare Earths. Mr Curtis served as Chairman of the Board of St Vincent’s & Mater Health Sydney from August 2004 to October 2009 and is a Director of St Vincent’s Health Australia Ltd and St Vincent’s Healthcare Ltd.

Geoff Dixon
Nominated by the Garvan Research Foundation

Mr Geoff Dixon held the position of Managing Director and Chief Executive of Qantas Airways Limited from 2000–2008. After joining Qantas in 1994 he was appointed Deputy Chief Executive in 1998 and then to the Board of Directors in 2000.

Mr Dixon currently sits on the boards of publicly listed Australian companies, Crown Limited and Consolidated Media Holdings Limited. He is Chairman of the Queensland (Australia) Major Events Corporation and Deputy Chairman of Tourism Australia. He also sits on the Board of The Great Barrier Reef Foundation, and the Advisory Board of Seabury Aviation & Aerospace, New York.

John Horvath AO
Nominated by the Federal Minister for Health

Professor John Horvath was the Australian Government Chief Medical Officer from 2003–2009. He is currently continuing to advise the Department of Health & Ageing and the School of Medicine, University of Sydney, and holds the position of Honorary Professor of Medicine. Professor Horvath is currently a member of Council of the NHMRC and Chairman of the Healthcare Committee. He is a Fellow of the Royal Australasian College of Physicians and is a distinguished practitioner, researcher and teacher. Professor Horvath was previously Clinical Professor of Medicine at University of Sydney.
and a specialist renal physician at Royal Prince Alfred Hospital (RPAH), and Area Director of Renal Services for the RPAH and Concord Repatriation General Hospitals. He is also known as a leader in a range of medical training and workforce organisations. He is also a former President of the Australian Medical Council and the NSW Medical Board.

Anne Keating
Nominated by the NSW Minister for Health

Ms Anne Keating is a company director and holds board positions in a range of industries including advertising, banking, and property. She is on the boards of the Goodman Group Limited, Ardent Leisure Group Limited and STW Communications Group Limited. Ms Keating is also a member of the Advisory Council of RBS Group (Australia), Governor of the Cerebral Palsy Foundation and Trustee of the Centennial Parklands and Moore Park Trust. Her former boards include Insurance Australia Group Limited, NRMA Limited, the WorkCover Authority of NSW, the Tourism Task Force and was an inaugural Director at the Victor Chang Cardiac Research Institute. Ms Keating was the General Manager, Australia for United Airlines from 1993–2001.

Lisa McIntyre
Nominated by the Federal Minister for Health

Dr Lisa McIntyre is a partner with the strategy consulting firm LEK Consulting and head of LEK’s Asia Pacific Life Sciences and Health Care practice. She has over 18 years consulting experience for the biotechnology and healthcare sector and has worked with over 100 different biotechnology and life sciences and healthcare clients. Dr McIntyre relocated to Sydney in 2002 after nine years in the United States co-heading LEK’s Life Sciences practice where she advised many of the world’s leading biotechnology and specialty pharmaceutical companies.

Greg Paramor
Nominated by the Garvan Research Foundation

Mr Greg Paramor is a founding Partner of Equity Real Estate Partners. Greg has been involved in the real estate and funds management industry for more than 35 years, and was the co-founder of Growth Equities Mutual, Palaein Australia and the James Fielding Group. Greg was the CEO of Mirvac between 2004 and 2008. Greg is a past President of the Property Council of Australia and past President of Investment Funds Association, a Fellow of the Australian Property Institute and The Royal Institute of Chartered Surveyors. Greg is a director of a number of not-for-profit organisations and is also a board member of the Sydney Swans and LJ Hooker.

Sister Carol Pedersen RSC
Nominated by the Sisters of Charity

Sister Carol Pedersen graduated as a trained nurse at St Vincent’s Sydney in 1963 and is a Sister of Charity. She holds a PhD from UNSW and a BSW (Hons 1) from the same institution. She also holds an Advanced Diploma from the Sydney College of Homoeopathic Medicine, and has completed postgraduate work, obtaining an Associate Diploma in Advanced Homoeopathic Medicine. For over 20 years Sr Carol was a member of various human research ethics committees, and was active at national, state and local levels in the development of Alcohol and Drug Services.

Steven Rubic
Nominated by the Sisters of Charity

Steven Rubic was appointed CEO of St Vincents & Mater Health Sydney (SV&MHS) in April 2008. Prior to this he was Executive Director of St Vincent’s Private Hospital a position he held since 1997. He is currently a Board Member of SV&MHS; the Health Industry (Superannuation) Plan, the Garvan Research Foundation, a member of Australian Commission on Safety and Quality Health Care (Private Hospital Sector Committee) and is a past Chairman of the NSPV Private Hospitals Association. He has completed an MBA and is a Fellow of the Australian Institute of Company Directors.

Warren Scott
Nominated by the NSW Minister for Health

Mr Warren Scott is the General Counsel of the Australian Prudential Regulation Authority and a former Director and the General Counsel of CIGroup in Australia. He was formerly the Chairman of the Woolcock Institute of Medical Research, as well as a delegate to the Australian American Leadership Dialogue. He is a member of the Law Society of New South Wales, the American Bar Association, the New York Bar Association and the California Bar Association. Warren is admitted as a solicitor in New South Wales and as a lawyer in New York and California.

Jillian Segal AM
Nominated by the UNSW

Ms Jillian Segal is a Director of the National Australia Bank and the Australian Securities Exchange Limited. She is also Deputy Chancellor of the UNSW and involved with a number of other community not-for-profit organisations, including the General Sir John Monash Foundation. Ms Segal has had a career in law, regulation, governance and policy development. Formally she was President of the Administrative Review Council and Chair of the Banking and Financial Services Ombudsman Board. From 1997–2002, Ms Segal was a Commissioner of the Australian Securities and Investments Commission (ASIC), being Deputy Chair from 2000–2002. Prior to joining ASIC, Ms Segal was a corporate lawyer specialising in corporate and environmental law, having been a partner at Allen Allen & Hemsley.

John Shine AO FAA
Appointed by the Garvan Institute Board

Professor John Shine is Executive Director of the Garvan Institute of Medical Research and a board member of the Garvan Research Foundation. He is Professor of Molecular Biology and Professor of Medicine at the UNSW, and a director of many scientific, research and medical bodies throughout Australia, including the recent ex-Chairman of the National Health and Medical Research Council (NHMRC) and until 2006 a member of the Prime Minister’s Science, Engineering & Innovation Council (PMSEIC).

Peter Smith
Nominated by the UNSW

Professor Peter Smith is Dean, Faculty of Medicine, UNSW. He specialised in cancer medicine and research following study in Australia, USA and Germany. He has held senior hospital management posts in Brisbane and Melbourne, and senior academic appointments at the Universities of Queensland, Melbourne and Auckland. He has served in a consulting role to Government, including as Chairman of the recent Inquiry into Vietnam Veterans Cancer Incidence and Mortality. Professor Smith is currently a Director of SV&MHS, NewSouth Innovations, and a number of other research centres and institutes.

Bernadette Tobin
Nominated by the Trustees of St Vincent’s Hospital

Associate Professor Bernadette Tobin is Director of the Plunkett Centre for Ethics at St Vincent’s Hospital, Sydney, and Reader in Philosophy at the Australian Catholic University. Dr Tobin is Honorary Ethicist at the Children’s Hospital at Westmead, Honorary Associate Professor in the Faculty of Medicine at the University of Sydney, and Associate Professor in the School of Medicine at UNSW. She served for three triennia on the Australian Health Ethics Committee, a principal committee of the NHMRC. She also chaired the drafting group, which prepared the first Code of Ethics for Catholic Health and Aged Care Services in Australia.

Ronald Trent
Nominated by the Federal Minister for Health

Professor Ronald Trent is Professor of Molecular Genetics, University of Sydney and Head of the Molecular and Cellular Genetics, Royal Prince Alfred Hospital. He is the Chairman of the Advisory Committee for the University’s recently formed Forensic Medicine & Science Network. He was a member of the NHMRC Research Committee from 1997–2009 and has been Chairman of the NHMRC Human Genetics Advisory Committee as well as a member of the NHMRC Council since 2006. Professor Trent discontinued his role as Director in February 2009.
Garvan Research Foundation

Geoff Dixon
Chairman from April 2009

Mr Geoff Dixon held the position of Managing Director and Chief Executive of Qantas Airways Limited from 2000-2008. After joining Qantas in 1994 he was appointed Deputy Chief Executive in 1998 and then to the Board of Directors in 2000.

Mr Dixon currently sits on the boards of publicly listed Australian companies, Crown Limited and Consolidated Media Holdings Limited. He is Chairman of the Queensland (Australia) Major Events Corporation and Deputy Chairman of Tourism Australia. He also sits on the Board of The Great Barrier Reef Foundation, Advisory Board of Seabury Aviation & Aerospace, New York, and the Garvan Institute. He joined the Foundation Board in 2009.

Graham J Bradley AM
Chairman to April 2009

Mr Graham Bradley is a professional company director. Mr Bradley is Chairman of Stockland Corporation Limited, HSBC Bank Australia Limited and Anglo American Australia Limited. From 1995 to 2003 he was Managing Director of Perpetual Limited. He is a former partner of McKinsey & Company, management consultants, and a former national managing partner of Blake Dawson. Mr Bradley was Chairman of the Garvan Research Foundation and a Director of the Garvan Institute Board from 1999-2009.

Jane Allen

Ms Jane Allen is a Partner in Egon Zehnder International’s (EZI) Sydney office, where she focuses on chief executive officer and board appointments. Ms Allen has been at Egon Zehnder International for 10 years and has consulted with corporate boards and companies of all sizes. In addition to a number of speaking engagements, Ms Allen has had a number of articles published on CEO succession and diversity at the executive and board level. She currently leads a number of global strategy initiatives roles for one of the firm’s core client practices. Previously she has been Managing Partner of the Sydney office and co-leader of the Australian Practice as well as Head of the Consumer Products Practice Group for Asia Pacific. She is currently a member of Chief Executive Women, a small active network of Australia’s top women leaders. Prior to joining Egon Zehnder International she worked at Procter & Gamble in sales and then marketing in both the US and Australia. Ms Allen has an MBA from Harvard Business School and a Bachelor of Arts from Smith College. Ms Allen joined the Foundation Board in 2007.

Alec Brennan

Mr Alec Brennan pursues a portfolio of business and not for profit interests. Until March 2007, he was Chief Executive Officer and Managing Director of CSR Limited. He is a Fellow of the Senate of the University of Sydney and Chair of several of its committees. Mr Brennan joined the Foundation Board in 2000.

Melinda Conrad

Ms Melinda Conrad is a consultant and company director for a range of business, health, and community organisations. In addition to the Garvan, she serves as a non-executive director for the Australia New Zealand Breast Cancer Trial Group and the Australian Brandenburg Orchestra. Ms Conrad has extensive experience in strategy, marketing and business development. In her previous executive career, she founded and ran the retail store chain, Conrads Warehouse, and held management roles at Harvard Business School and Colgate-Palmolive. Ms Conrad joined the Foundation Board in September 2003.

Gabriel Farago

Mr Gabriel Farago is a company director and consultant advising corporations on litigation management. Prior to establishing his consultancy, he practised as a solicitor and barrister for over 30 years, specialising in commercial disputes both in Australia and overseas. Mr Farago has extensive business interests, and has been involved in property development for more than 20 years. A passion for philanthropic and charitable causes also reaches back many years, and in 1984 he was made a member of the Knightly Order of Vitez. Mr Farago joined the Foundation Board in 2008.

Bill Ferris AC

Mr Bill Ferris is Executive Chairman of the CHAMP Private Equity Group, one of Australia’s leading private capital groups, providing venture capital, expansion capital and management buyout funding in Australia. Mr Ferris is Chairman of the Garvan Institute of Medical Research and Chairman of the Health and Hospitals Fund Advisory Board as part of the Federal Government’s Nation-Building Funds initiative. Former directorships include: Chairman, Australian Trade Commission (Austrade), Austar United Communications Limited and Bradken Resources Pty Ltd. Mr Ferris was made an Officer in the Order of Australia in 1990 for services to the export industry and in 2008 was made Companion in the Order of Australia for his philanthropic activities and his role in the establishment of the private equity sector in Australia. Mr Ferris joined the Foundation Board in 2001.

Lyn Gearing

Ms Lyn Gearing was appointed to the Garvan Foundation Board as a representative of the Sisters of Charity. Ms Gearing was a Director of Stockland Corporation Limited up until December 2008 and is currently a Director of Queensland Investment Corporation Limited, Hancock Natural Resource Group Australasia Pty Limited, IMB Limited and two other not for profit organisations. Ms Gearing was the Chief Executive Officer of the NSW State Superannuation schemes from 1997 to 2002, and has substantial experience in superannuation, funds management, corporate finance and management consulting. Ms Gearing joined the Foundation Board in 2005.
Mr Loftus Harris AM

Loftus Harris AM

Mr Loftus Harris is a non-executive director on various boards in NSW, Victoria and Queensland, a National Chairman of the Australian Institute of Export, and holds the appointment of Special Trade Representative to the Middle East and India for the Queensland Government. He previously held chief executive positions in the NSW and Queensland public sectors with responsibility for whole-of-Government activities including international trade, investment, innovation, business, and regional development. He also served extensively overseas as an Australian Trade Commissioner. Mr Harris joined the Foundation Board in 2008.

Byram Johnston OAM

Byram Johnston

Mr Byram Johnston is the Chief Executive Officer of MainstreamBPO, a company providing back office processing and administration services to fund managers and superannuation funds. Prior to establishing this business he spent over 30 years as a management consultant. He serves on the board of a number of companies. Mr Johnston joined the Foundation Board in 1997.

John Landerer CBE AM

John Landerer

Mr John Landerer is a solicitor specialising in corporate advisory work and is also a professional company director. He is currently Chairman of Goldsearch Limited and other private companies. He has served as Chairman of the Home Purchase Assistance Authority and is on the Board of Life Education Australia and the Royal Institute for Deaf and Blind Children as well as on the boards of various charitable institutions. Mr Landerer was appointed a Visiting Professor at Macquarie University in Business and Commercial Law and holds an honorary doctorate from that university. He is also a Fellow of University of Sydney. Mr Landerer is a Member of the Order of Australia and a Commander of the Most Excellent Order of the British Empire. He is also a Commander in the Order of the Star of Italian Solidarity. He joined the Board in 2007.

Simon Mordant

Simon Mordant

Mr Simon Mordant is a co-founder and joint Chief Executive of Caliburn Partnership, a leading independent corporate advisory firm specialising in advising major companies on their merger and acquisition and capital markets strategies. He is a chartered accountant and is Chair of the Museum of Contemporary Art Foundation and a director of the Sydney Theatre Company. Mr Mordant joined the Foundation Board in 2009.

Sister Paulina Pilkington RSC AM

Sister Paulina Pilkington

Sister Paulina has a broad background in health policy formation, having been a member of the Hospitals and Health Services Commission (Sax Commission) and Assistant Director General, Nursing Branch, Federal Department of Health. Sister Paulina resigned from the Garvan Institute Board in February 2000 and has been a member of the Foundation Board since 1994.

Brad Rees

Brad Rees

Mr Brad Rees is involved in a number of charitable, arts and educational interests and is a director of a private investment company. Until 2007, he was a Managing Director and Equity Partner of the investment banking firm Goldman Sachs JBWere. Mr Rees was with the firm for 23 years and worked in the Melbourne, Sydney and London offices providing financial and investment banking advice to corporations and governments in Australia and overseas. Mr Rees joined the Foundation Board in 2008.

Steven Rubic

Steven Rubic

Mr Steven Rubic was appointed Chief Executive Officer of St Vincents & Mater Health Sydney (SV&MHS) in April 2008. Prior to this he was Executive Director of St Vincent’s Private Hospital a position he held since 1997. He is currently a Board Member of SV&MHS, the Health Industry (Superannuation) Plan, the Garvan Institute, a member of Australian Commission on Safety and Quality Health Care (Private Hospital Sector Committee) and is a past Chairman of the NSW Private Hospitals Association. He has completed an MBA and is a Fellow of the Australian Institute of Company Directors. Mr Rubic joined the Foundation Board in 2008.

John Shine AO FAA

John Shine

Professor John Shine is Executive Director of the Garvan Institute of Medical Research and a board member of the Garvan Institute Board of Directors. He is Professor of Molecular Biology and Professor of Medicine at the UNSW, and a director of many scientific, research and medical bodies throughout Australia, including the recent ex-Chairman of the National Health and Medical Research Council (NHMRC) and until 2006 a member of the Prime Minister’s Science, Engineering & Innovation Council (PMSEIC).

Karim Temsamani

Karim Temsamani

Mr Karim Temsamani manages Google’s domestic business and strategic partnerships in Australia and New Zealand. Karim joined Google from Fairfax Media, where he was most recently Group Director, Fairfax General Magazines (responsible for growing the profile and advertising revenue of Fairfax’s suite of inserted magazines) and Commercial Director for Newspapers (responsible for agency and group sales, trade marketing and business development).

Prior to this he was the publisher and Vice President of Who Weekly at Time Inc South Pacific from 1999-2002. He has previously served in a variety of senior capacities with Hachette, including the positions of Regional Business Publisher in Hong Kong (1995-96), Associate Publisher for Korea in Seoul (1996-97), and Managing Director for Hachette in Sydney (1997-99). Mr Temsamani joined the Foundation Board in 2008.
A


Protein Eng Des Sel
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Dudgeon K, Famm K, Christ D.

ND. Surgical therapy for gastrointestinal stromal tumours of the upper gastrointestinal tract.

Clin Exp Immunol
Das A, Wilson R, Biankin AV, Merrett ND, Fulcher DA, Avery DT, Fewings NL.

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Primary immune deficiencies affecting lymphocyte differentiation lessons from the spectrum of resulting infections.

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Dudgeon F, Famm K, Christ D.
Sequence determinants of protein aggregation in human VH domains.

E
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Edelsbrunner ME, Panzopp E, Herzog H, Holzer P.
Evidence from knockout mice for distinct implications of neuropeptide-Y Y2 and Y4 receptors in the circadian control of locomotion, exploration, water and food intake.


F
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G
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Evidence of “hat” cells by the orphan G protein-coupled receptor EB12 shapes humoral immune responses.
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Synaptic reporting improves histopathological assessment of pancreatic cancer rejection specimens.

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Alpha-synuclein is part of a diverse and highly conserved interaction network that includes PARK9 and manganese toxicity.

H
Hirshfeld RA, Melki JR, Huschtscha UJ, Paul C, Song JZ, Strizaker C, Reddel RR, Clark SJ.
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Dual ablation of Grb10 and Grb14 in mice reveals their combined role in regulation of insulin signaling and glucose homeostasis.


## Financial Highlights

### Garvan Institute of Medical Research

#### Income Statement

<table>
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<tr>
<th>Year</th>
<th>$'000</th>
<th>$'000</th>
<th>$'000</th>
<th>$'000</th>
<th>$'000</th>
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<tbody>
<tr>
<td>2005</td>
<td>12,080</td>
<td>13,832</td>
<td>16,682</td>
<td>18,695</td>
<td>19,094</td>
</tr>
<tr>
<td>2006</td>
<td>6,865</td>
<td>8,184</td>
<td>8,530</td>
<td>9,159</td>
<td>11,061</td>
</tr>
<tr>
<td>2007</td>
<td>200</td>
<td>655</td>
<td>1,068</td>
<td>4,811</td>
<td>16,524</td>
</tr>
<tr>
<td>2008</td>
<td>3,720</td>
<td>12,174</td>
<td>4,063</td>
<td>4,026</td>
<td>3,797</td>
</tr>
<tr>
<td>2009</td>
<td>-</td>
<td>4,700</td>
<td>1,193</td>
<td>-</td>
<td>-</td>
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<tr>
<td>NHMRC Grants</td>
<td>12,080</td>
<td>13,832</td>
<td>16,682</td>
<td>18,695</td>
<td>19,094</td>
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<tr>
<td>Other Peer Reviewed Grants</td>
<td>6,865</td>
<td>8,184</td>
<td>8,530</td>
<td>9,159</td>
<td>11,061</td>
</tr>
<tr>
<td>Other Grants</td>
<td>200</td>
<td>655</td>
<td>1,068</td>
<td>4,811</td>
<td>16,524</td>
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<tr>
<td>NSW Government Grant</td>
<td>3,720</td>
<td>12,174</td>
<td>4,063</td>
<td>4,026</td>
<td>3,797</td>
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<tr>
<td>Commonwealth Government Grant</td>
<td>-</td>
<td>4,700</td>
<td>1,193</td>
<td>-</td>
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<td>Commercial Collaborations</td>
<td>2,043</td>
<td>4,091</td>
<td>2,714</td>
<td>1,289</td>
<td>737</td>
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<td>Garvan Research Foundation</td>
<td>2,343</td>
<td>2,562</td>
<td>3,817</td>
<td>4,689</td>
<td>5,290</td>
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<td>Other Income</td>
<td>2,774</td>
<td>2,916</td>
<td>3,543</td>
<td>4,050</td>
<td>7,470</td>
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<tr>
<td><strong>Total Operating Income</strong></td>
<td><strong>30,025</strong></td>
<td><strong>49,114</strong></td>
<td><strong>41,610</strong></td>
<td><strong>46,719</strong></td>
<td><strong>63,973</strong></td>
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<tr>
<td>Remuneration Costs</td>
<td>17,377</td>
<td>21,983</td>
<td>23,621</td>
<td>27,337</td>
<td>28,322</td>
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<td>Research Expenditure*</td>
<td>4,571</td>
<td>5,879</td>
<td>7,640</td>
<td>9,377</td>
<td>7,883</td>
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<tr>
<td>Administration and Information Technology</td>
<td>2,931</td>
<td>3,913</td>
<td>3,771</td>
<td>5,331</td>
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<td>Building and Scientific Operations</td>
<td>2,378</td>
<td>2,438</td>
<td>2,461</td>
<td>2,753</td>
<td>3,324</td>
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<td><strong>Total Operating Expenses</strong></td>
<td><strong>27,257</strong></td>
<td><strong>34,213</strong></td>
<td><strong>37,493</strong></td>
<td><strong>44,798</strong></td>
<td><strong>44,351</strong></td>
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<tr>
<td>Building Asset Amortisation</td>
<td>(1,171)</td>
<td>(1,171)</td>
<td>(1,180)</td>
<td>(1,189)</td>
<td>(1,657)</td>
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<td>Property, Plant and Equipment Depreciation</td>
<td>(2,178)</td>
<td>(2,449)</td>
<td>(2,433)</td>
<td>(2,390)</td>
<td>(2,597)</td>
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<td>Transfer from(to) Building Reserve</td>
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<td>1,353</td>
<td>1,047</td>
<td>1,047</td>
<td>1,047</td>
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<td>Endowment Grants</td>
<td>745</td>
<td>10,965</td>
<td>2,210</td>
<td>3,953</td>
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<td>Endowment Earnings</td>
<td>1,011</td>
<td>2,181</td>
<td>2,589</td>
<td>1,700</td>
<td>958</td>
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<tr>
<td>Donations &amp; Requests direct to/(from) Endowment Fund</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>Unrealised gain/(loss) on Endowment Fund Investments</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>(7,407)</td>
<td>1,922</td>
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<tr>
<td><strong>Net Income</strong></td>
<td><strong>2,222</strong></td>
<td><strong>23,074</strong></td>
<td><strong>6,350</strong></td>
<td><strong>3,028</strong></td>
<td><strong>20,683</strong></td>
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<td>Accumulated Surplus Brought Forward</td>
<td>922</td>
<td>308</td>
<td>9,914</td>
<td>11,109</td>
<td>16,571</td>
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<tr>
<td>Transfer from/to Research Program Reserve</td>
<td>(1,110)</td>
<td>(107)</td>
<td>(2,526)</td>
<td>380</td>
<td>(2,189)</td>
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<td>Transfer from/to Endowment Reserve</td>
<td>(1,726)</td>
<td>(11,809)</td>
<td>(3,664)</td>
<td>1,847</td>
<td>(2,530)</td>
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<td>Transfer from/to Infrastructure Expense Reserve</td>
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<td>(1,552)</td>
<td>1,035</td>
<td>207</td>
<td>(23)</td>
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<tr>
<td><strong>Accumulated Surplus Carried Forward</strong></td>
<td><strong>308</strong></td>
<td><strong>9,914</strong></td>
<td><strong>11,109</strong></td>
<td><strong>16,571</strong></td>
<td><strong>32,512</strong></td>
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</tbody>
</table>

*The figures in 2006 and 2007 have been adjusted to improve the comparability with 2008.
Garvan Institute of Medical Research

<table>
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<tr>
<th></th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
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<td><strong>Balance Sheet</strong></td>
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<td>$'000</td>
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<td>Current Assets</td>
<td>5,632</td>
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<td>Property, Plant and Equipment</td>
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<td>40,903</td>
<td>45,160</td>
<td>60,085</td>
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<td>Endowment Fund*</td>
<td>11,630</td>
<td>23,439</td>
<td>27,103</td>
<td>25,255</td>
<td>27,786</td>
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<td>Investment in Associates</td>
<td>84</td>
<td>84</td>
<td>84</td>
<td>84</td>
<td>84</td>
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<tr>
<td><strong>Total Assets</strong></td>
<td>57,284</td>
<td>79,675</td>
<td>90,573</td>
<td>106,538</td>
<td>142,062</td>
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<td>Current Liabilities**</td>
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<td>6,900</td>
<td>8,343</td>
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<td>Provisions</td>
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<td>Borrowings</td>
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<td>18,144</td>
<td>18,078</td>
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<tr>
<td><strong>Total Liabilities</strong></td>
<td>12,004</td>
<td>9,969</td>
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<td>Accumulated Surplus</td>
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<td>9,914</td>
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<td>Reserves</td>
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<td>59,792</td>
<td>63,900</td>
<td>60,419</td>
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<tr>
<td><strong>Total Net Funds</strong></td>
<td>45,280</td>
<td>69,706</td>
<td>75,009</td>
<td>76,990</td>
<td>96,626</td>
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</table>

* Including cash and investments at market value
** The figures in 2006 and 2007 have been adjusted to improve the comparability with 2008.

Garvan Research Foundation

<table>
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<tr>
<th></th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
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<td>1,847</td>
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<td>21</td>
<td>25</td>
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<tr>
<td><strong>Total Income</strong></td>
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<td>(1,018)</td>
<td>(1,184)</td>
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<td>Grants to GSVCC Joint Venture Partner</td>
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<td>129</td>
<td>78</td>
<td>109</td>
<td>507</td>
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<td><strong>Net Assets</strong></td>
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<td>78</td>
<td>109</td>
<td>507</td>
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