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.
The Garvan Institute of Medical Research is a world leader in its field, pioneering study into some of the most widespread diseases affecting our community today. Research at Garvan is focused upon understanding the role of genes in health and disease as the basis for developing future cures.

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.
2011
2011 was a milestone year for Garvan, with the retirement of Professor John Shine after 21 years as Executive Director and announcement of his successor, internationally acclaimed molecular geneticist, Professor John Mattick. I am also very pleased to report that Garvan continued its excellent record of research success in 2011, as measured by grants, publication impacts, national and international awards, and for that we are justly proud of our faculty and staff.

Construction of The Kinghorn Cancer Centre, our exciting joint venture with St Vincent’s Hospital, is on track for formal completion mid 2012. It promises to make a major contribution to Garvan’s vision of translational research and delivery of personalised health care based on detailed knowledge of individual patient genetic makeup.

Financial Performance
Garvan’s operating income grew to approximately $51m in 2011 from $41m the previous year. Philanthropic support through the Garvan Research Foundation, essential for providing critical equipment and facilitating new initiatives, continued to be strong, with over $6.1m in general and specific grants contributed to research programs and almost $3.6m into the long term endowment fund 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. During 2011, our long serving Treasurer, Martin Hoffman, retired from the Board, as did Nicholas Curtis AM, past Chairman of St Vincent’s Hospital. I would like to record the Board’s appreciation for the outstanding contributions made by Martin and Nick. Warren Scott was appointed as the incoming Treasurer and Chair of the Finance and Audit Committee. We welcomed two new Board members — Daniel Petre AO and Annette Pantle, both of whom will bring important new skills and experience to our endeavours.

Many Garvan researchers were distinguished with prizes and awards during 2011, which are listed under each research program. Among these, the Cancer Institute NSW presented the 2011 Premier’s Fellow of the Year Award to Dr Alex Swarbrick and the 2011 Premier’s Scholar of the Year Award to Dr David Chang.

Of special note was the award to Professor John Shine of the inaugural Peter Wills Medal, created by Research Australia “to recognise an outstanding contribution to building Australia’s national and international reputation in the realm of health and medical research”. Given Peter Wills’ contributions to Australian medical research, including his role as Garvan Chairman, it was particularly satisfying that Professor Shine was selected as the inaugural recipient.

Medical Research Reviews
Recognising the importance of health and medical research to a cost effective and world leading health care system, during 2011 both Federal and NSW State governments initiated reviews to examine the structure and funding of medical research. These reviews (on both of which Garvan is represented) provide an important opportunity to address the ever-increasing equipment, resourcing and infrastructure costs that come with the exciting rate of change and amazing possibilities presented by today’s medical research.
Garvan, along with the rest of the medical research sector has been invited to make submissions to these important reviews. Garvan has and will continue to make a strong case for the expansion of the National Health and Medical Research Council funding program and for improvement in State Government support for research.

Looking Ahead

There will be many challenges and exciting opportunities in the year ahead as Garvan continues to grow and as our commitment to translate our research discoveries into meaningful improvements in health care is significantly enhanced with completion of The Kinghorn Cancer Centre.

Our ability to integrate teaching, research and clinical translation on our expanding Darlinghurst campus has never been stronger, and the links with and support from our key stakeholders, St Vincents and Mater Health and University of NSW, will be increasingly important to our ambitions.

With additional government support, as well as community engagement, the Board is confident that Garvan will continue to have a major impact on human health, particularly as we focus on integration with health care delivery.

At last year’s AGM I spoke of the extraordinary contribution made by Professor Shine to medical research worldwide. On behalf of our faculty and staff, our stakeholders and supporters, I thanked John for his outstanding leadership of the Garvan over the last 21 years.

I wish to repeat my appreciation and thanks to John for agreeing to stay at the helm right through 2011 as we completed our worldwide search for his successor.

And this year I enthusiastically welcome Professor John Mattick to his first AGM as Director of the Garvan. Professor Mattick takes over the reins at a most exciting time for the organisation, as well as for medical research. I know that his exceptional research record and interests, combined with his experience and passion, will accelerate Garvan’s delivery of mission... to significantly improve the health care and quality of life for all.

Bill Ferris AC
Chairman
Garvan Institute of Medical Research
An exciting new chapter begins for Garvan with the appointment of the next Director, Professor John Mattick, following an extensive international search. John has pioneered the area of gene structure and regulation, being among the first to demonstrate that the so called “junk” regions of our DNA in fact encode important small RNA genes critical for the ordered regulation of gene expression. This has critical importance for a wide range of life processes — from balanced brain function to orderly development from a fertilised egg to a complex adult.

Professor Mattick’s appointment will also strengthen the Institute’s commitment to translational research initiatives. John’s leadership in this area will ensure that the latest breakthroughs in gene analyses are rapidly applied to development of new specific individualised treatments.

2011 was also 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 over 200 peer reviewed research papers, the top 80% in journals with an average impact factor >8. This remains above internationally accepted benchmark levels and is testament to the excellence and commitment of our researchers. I encourage everyone interested in Garvan’s research and related activities to view the excellent news summaries which are regularly updated on our website www.garvan.org.au.

Research publication productivity was matched by success in applications for competitive grants. Overall peer reviewed grant funding was approximately $29.5m, including $18.5m from the National Health and Medical Research Council (NHMRC). Our Cancer, Immunology and Diabetes and Obesity Programs all have successful NHMRC program grants, which provide the capacity for longer term strategic planning of our research effort. Of particular note this year was the announcement that Dr Greg Neely’s project grant application ranked amongst the top in the country and received the 2011 NHMRC Marshall and Warren Award for most potentially transformative research. This outcome is a strong endorsement of our commitment to support young faculty members, often working on very ambitious and novel projects.

Osteoporosis and Bone Research
The Osteoporosis and Bone Biology Program was restructured and strengthened during 2011 with the appointment of a new leader, Professor Peter Croucher from the UK, as the inaugural Chair in Osteoporosis Research funded by Mrs Janice Gibson and the Ernest Heine Foundation. Professor Croucher, an international leader in osteoporosis, also has a strong interest in the spread of cancer to bone, providing an exciting link to our expanded cancer research in The Kinghorn Cancer Centre.

After 27 years, Professor John Eisman, the founding leader of the Osteoporosis and Bone Biology Program, moves to a new role as Garvan’s Director of Clinical Translation and Advanced Education. This novel development, championed by Professor Eisman, has its initial focus in osteoporosis and is aimed at streamlining the application of new basic and clinical knowledge to clinical care in the community and more efficient and cost-effective health care.

Garvan will be running awareness-raising seminars about ‘bone failure’, with separate sessions for members of the public and general medical practitioners. The program, known as Health Education for Longer Life in Osteoporosis (HELLO) had its inaugural sessions on 26 and 27 November when Her Excellency Ms Quentin Bryce AC, Governor General of Australia, officially launched the initiative.
Our People
Staff numbers across the organisation grew to a total of 575 with significant growth in all our major research programs, reflecting ongoing success in competitive grant applications for new and existing projects. Consistent with its role in international medical research, 65 different countries are represented in Garvan’s research community. During 2011, many Garvan researchers received international recognition for their contributions to medical research, including prestigious awards, fellowships and invitations to present their work at major conferences. These are detailed in each of the research program reports.

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.

With recent agreement between Federal and State Governments to reform the hospital system, Garvan is working even more actively with our campus partners, St Vincent’s and Mater Health and the Victor Chang Cardiac Research Institute, to ensure that the community is well aware of the close integration of research, education, clinical care and regional outreach represented on the St Vincent’s campus.

As this is my final report as Executive Director, I take the opportunity to thank the Board, all the scientific and administrative staff and our many donors for their support, commitment and excellence over the past 21 years. The many achievements of the Institute during this period have only been possible through the teamwork and personal efforts of everyone involved with the Garvan — it has truly been a great privilege to have stewardship of the institute during a time of amazing progress in medical research.

2012
The upcoming years promise much for Garvan, with the addition of approximately 250 new researchers in The Kinghorn 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 2012 under John Mattick’s leadership, I have no doubt that Garvan will remain clearly focused on elucidating the fundamental basis of disease, as well as driving the translation of 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
The Garvan Research Foundation had a very successful year in 2011. In a period that experienced a high degree of international financial uncertainty, it is a tribute to the quality of the research undertaken at Garvan that we continued to receive strong support from a broad section of the community.

In addition to our valued regular givers we received several major gifts, including a commitment from Ms Jane Hemstritch and Team Phil to establish the Philip Hemstritch Pancreatic Cancer Research Fellowship for three years, continued generous support from the Ross Trust for our Type 1 diabetes research and an incredibly generous gift of $2m from the Petre Foundation to support the establishment of an endowed chair in prostate cancer, in partnership with the University of Sydney.

In late 2011 we welcomed Professor Peter Croucher as the new leader of Garvan’s Osteoporosis and Bone Biology Program, thanks to the tremendous support of Mrs Janice Gibson and Ernest Heine Family Foundation.

Importantly, income from bequests grew in 2011, which is vital for the ongoing security of Garvan. These funds are directed to our endowment fund to ensure that Garvan is well positioned to meet increasing demand on infrastructure and to seize unique recruitment opportunities.

Work on supporting The Kinghorn Cancer Centre continued throughout 2011 with a range of events to mark key building milestones. Events were held with our key supporters, including The Kinghorn Cancer Centre patron and cancer survivor, Delta Goodrem, as well as a special rooftop event with Jill and John Kinghorn, and their fellow visionaries, to mark the midpoint of the construction.

A highlight of the year was our inaugural Garvan Gala Dinner. Over 300 people attended a memorable evening at Byron Kennedy Hall, Fox Studios, to acknowledge the almost two decades of outstanding leadership by retiring Garvan Executive Director, Professor John Shine. My sincere thanks to the individuals and organisations that supported this event.

The Young Garvan Committee continued to work tirelessly to raise the profile of Garvan among a younger demographic and to raise funds for the Young Garvan Fellowship. As well as three well-attended forums at Garvan, the Committee co-ordinated its highly successful All Ribbons Ball, attracting more than 400 guests who saw the Young Garvan Fellowship awarded to Dr Ebru Boslem. Dr Boslem is using the award to further her research into Type 2 diabetes, as part of Garvan’s Diabetes and Obesity Research Program.
Garvan was also the beneficiary of a number of community events, including participants in Sydney’s City2Surf and Run Melbourne who chose Garvan as the recipient of the funds they raised. Activities like these achieve two goals for Garvan – raising considerable funds and promoting general awareness about the need and value of medical research.

I would like to take this opportunity to thank my fellow Directors for their support. We were delighted to welcome Dr Jeanne-Claude Strong to the Board in December as she brings to the Board a range and wealth of experience that will be invaluable.

We also welcomed Andrew Giles to the role of Chief Executive Officer of the Foundation. With a long career leading substantial not-for-profit organisations in Australia, Andrew is well-placed to continue to grow the Garvan Research Foundation.

Andrew is ably supported by his small, highly professional team of Gabriella Lang, Dimity Raftos, Janice Lam, Mimy Long, Mona Saade, Carol O’Carroll and Pip Margan. In 2011 Dianne Lavender went on maternity leave and was replaced by Kylie Ironside. Kylie Sherwood-Kelly and Mara-Jean Tilley joined the team, replacing Dr Anita Townsend and Georgie Le Poer Trench respectively.

To all of our wonderful and generous supporters – thank you for your ongoing commitment to Garvan’s work.

Geoff Dixon
Chairman
Garvan Research Foundation
Garvan welcomed incoming Executive Director, Professor John Mattick AO FAA FRCPA, in early January 2012. Prior to his appointment, Professor Mattick was based at the University of Queensland for 23 years, where he was the foundation director of the world-renowned Institute for Molecular Bioscience and the Australian Genome Research Facility.

A visionary in his field, Professor Mattick has changed our view of the function of the majority of the human genome, which had previously been regarded as "junk DNA". He challenged the scientific establishment in the mid-1990s with his then-radical theories about the vast tracts of DNA which do not code for proteins, but which are copied into RNA.

Until questioned, the so-called central dogma of molecular biology had been that 'DNA makes RNA makes protein' and therefore that genes specified proteins through the intermediate of RNA. That assumption reflected the highly mechanical view of the world that existed in the 1950s and 1960s, and while it was largely true for bacteria and other simple organisms, it was not true for people. As it turned out, only a tiny fraction - around 1.5% - of the human genome encodes proteins. Much of the rest produces RNA that does not code for proteins. Professor Mattick's breakthrough came when he realised that another layer of information was being expressed by the genome, and that the non-coding RNAs form a massive and previously unrecognised regulatory network that controls human growth and differentiation, from a single fertilised cell to the hundred trillion cells that form the myriad of organs, muscles and bones in the adult.

The science community now realises that the genome is extraordinarily complex, and the deeper we drill down, the more surprises we find. Indeed, what was dismissed as junk because it was not understood almost certainly holds the secret to understanding human development and cognition. It is also likely to hold the secret to understanding many complex diseases.

Professor Mattick studied at the University of Sydney and Monash University, and subsequently undertook postdoctoral training at Baylor College of Medicine in Houston. He then spent seven years with the CSIRO Division of Molecular Biology in Sydney, before moving to the University of Queensland in 1988 to take up the Foundation Chair of Molecular Biology. He has also spent sabbatical periods at the Universities of Cambridge, Oxford, Cologne and Strasbourg. His honours and awards include the Biotechnology Medal of the Australian Biochemical Society, Honorary Fellowship of the Royal College of Pathologists of Australasia, the Australian Government Centenary Medal, the inaugural University of Strasbourg Gutenberg Professorship, the IUBMB (International Union of Biochemistry and Molecular Biology) Medal and most recently the Chen Award 2012 for Distinguished Academic Achievement in Human Genetic and Genomic Research (awarded by the Human Genome Organisation). He is an Associate Member of EMBO (European Molecular Biology Organisation) and a Fellow of the Australian Academy of Science. Professor Mattick was appointed an Officer in the Order of Australia in 2001.
GARVAN AT A GLANCE
**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 2011 Garvan achieved an “average impact factor” of 8 for the top 80% of its publications. This is a very respectable tally, well above the international benchmark.

**Philanthropic Support**

**Total Income**

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

*Excluding bequests and contributions to the construction cost of The Kinghorn Cancer Centre.*
### Staff Profile

Staff Breakdown

<table>
<thead>
<tr>
<th>Year</th>
<th>Researchers</th>
<th>Students</th>
<th>Scientific Facility Staff</th>
<th>Secretarial &amp; Admin</th>
<th>Foundation</th>
<th>DVDC</th>
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<td>14</td>
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<td>575</td>
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</table>

Demographics

- Average age 36 years 11 months
- Researchers from over 65 countries
- Research staff 44% male, 56% female

### Operating Income

2011 $51 Million*

- Peer reviewed grants 58%
- Donations 12%
- NSW Government 8%
- Industry partners 1%
- Other income 21%

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.

* Excludes donations for construction of The Kinghorn Cancer Centre

### Peer Reviewed Grant Income

<table>
<thead>
<tr>
<th>Year</th>
<th>NHMRC $000</th>
<th>Other $000</th>
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<tr>
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<td>2010</td>
<td>16,637</td>
<td>10,232</td>
</tr>
<tr>
<td>2011</td>
<td>18,574</td>
<td>10,896</td>
</tr>
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</table>
Research Collaborations
_ Identified the cytokine (chemical messenger) IL-21 as the main driver of successful antibody responses in people.

_ Determined the genetic defect in the cytotoxic immune cells (killer T cells) of patients with a particular immunodeficiency that renders them defenceless when infected with the Epstein-Barr virus.

_ Showed that the EBI2 receptor was responsible for previously unexplained movements of B cells during an immune response.

_ Identified a new subset of T cells that home to the gut and are involved in the induction of autoimmunity.

_ Discovered a new pain receptor required for thermal pain sensation, conserved from flies to humans, further highlighting pain perception as an ancient process conserved through evolution.

_ Detailed the skeletal actions of the major circulating member of the neuropeptide Y (NPY) family, PYY. These studies may shed new light on our understanding of anorexia nervosa.

_ Conducted the first study of long-term oral treatment to alter NPY signalling in living animals. The drug BIBO2234 inhibits an NPY receptor, leading to a significant increase in bone mass, without adverse side effects.

_ Demonstrated significant biochemical change (hyperphosphorylation) of a GSK3 target, a protein called CRMP2, specifically in the brains of Alzheimer’s disease patients, but not in other forms of dementia. This appears to occur early in the disease process and has the potential to be a biomarker for early and specific detection of Alzheimer’s disease.

_ Demonstrated that a molecule known as ‘hedgehog’ helps breast cancer cells survive by communicating their needs to the healthy cells that surround them. Hedgehog-blocking drugs (in trial for other cancers) offer a potential therapy for breast cancer.

_ In collaboration with the University of Auckland, identified potential new cancer therapeutics that inhibit the metabolism of glucose and so target the abnormal energy metabolism that fuels tumour growth.

_ Identified a panel of genes, from ovarian cancer patients, which may be suitable candidates for the development of a new blood-based diagnostic test for ovarian cancer.

_ Developed novel epigenetic sequencing technologies and bioinformatics tools to unravel the layers of chemical change that affect the ways in which genes behave, and demonstrated which sections of the genome are commonly ‘activated’, or ‘switched on’, in prostate cancer. This work provides new diagnostic markers for prostate cancer and provides a new mechanism for cancer-specific gene activation.

_ Sequenced the genomes of >100 pancreatic cancers as part of the International Cancer Genome Consortium and developed the most detailed landscape of mutations and genomic rearrangements yet available for pancreatic cancer.

_ Demonstrated that fat accumulation in the liver, in response to a high fat diet, depends on the action of an enzyme, which can be targeted to improve insulin action.

_ Identified Id1 as a novel inhibitor of insulin secretion and beta cell differentiation.

_ Demonstrated that increasing the amount of a transcriptional co-activator can up-regulate mitochondrial metabolism and alleviate fat-induced insulin resistance.

_ Noted an extraordinary and unexpected benefit of osteoporosis treatment – that people taking bisphosphonates are not only surviving well, better than people without osteoporosis, they appear to be gaining an extra five years of life.

_ Identified novel chromosomal regions that harbor osteoporosis genes as part of international collaborations using genome-wide analysis advanced technology.
Program Summary

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 genomics/epigenomics 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.

Research Highlights

- Demonstrated that a molecule known as ‘hedgehog’ helps breast cancer cells survive by communicating their needs to the healthy cells that surround them. Hedgehog-blocking drugs (in trial for other cancers) offer a potential therapy for breast cancer.

- Discovered that although breast cancer cells which overexpress cell cycle gene cyclin E2 are resistant to endocrine therapy and drugs inhibiting cell cycle kinase CDK4, cyclin E2 can be targeted with other cell cycle inhibitors (CDK2). This suggests the alternative cell cycle inhibitors should be studied further as potential therapies in endocrine-resistant breast cancer.

- Identified two potential drug targets, the proteins Lyn and SgK269, which promote proliferation and migration of cancer cells in the particularly aggressive basal-like breast cancer.

- In collaboration with the University of Auckland, identified potential new cancer therapeutics that inhibit the metabolism of glucose and so target the abnormal energy metabolism that fuels tumour growth.

- Identified a panel of genes, from ovarian cancer patients, which may be suitable candidates for the development of a new blood-based diagnostic test for ovarian cancer.

- Developed novel epigenetic sequencing technologies and bioinformatics tools to unravel the layers of chemical change that affect the ways in which genes behave, and demonstrated which sections of the genome are commonly ‘activated’, or ‘switched on’, in prostate cancer. This work provides new diagnostic markers for prostate cancer and provides a new mechanism for cancer-specific gene activation.

- Showed that lower-than-normal expression of the MCC gene, as observed in a subset of colorectal cancers, may underlie the development of cancer because it is required for cells to migrate. Healthy cells in the gut need migration capacity in order to move to the colon surface and heal damage caused by harmful dietary agents or drugs.

- Developed a database of “network modules”, groups of densely interconnected proteins with functional associations, which help us understand how cellular processes are perturbed in cancer.

- Sequenced the genomes of >100 pancreatic cancers as part of the International Cancer Genome Consortium and developed the most detailed landscape of mutations and genomic rearrangements yet available for pancreatic cancer.

- Demonstrated that a simple histopathology test, Gleason grade at a positive surgical margin, identifies prostate cancer patients who are likely to benefit from adjuvant radiotherapy.
People Highlights

Professor Andrew Blankin and Clinical Associate Professor Sandra O'Toole were made Founding Fellows of the Faculty of Science of The Royal College of Pathologists of Australasia.

Dr David Chang was awarded the NSW Premier’s Award for Outstanding Research Scholar 2011, the Pfizer Oncology International Studentship Award 2011, the ASCO Cancer Foundation Merit Award 2011 and an Early Career Development Award from NHMRC.

Dr Alex Swarbrick and Professor Andrew Blankin were promoted to the Garvan Faculty.

Professor Liz Musgrove had her Career Convened the 5th Pacific Rim Breast and Human Epigenome Consortium.

Drs Goli Samimi and Ilse Rooman were appointed to the Steering Group Committee of the International Alliance, and appointed to the Steering Representative of the Asian Epigenome Alliance, the Australian Member and President of the Australian Epigenome Faculty.

New recruits Drs Andrew Burgess, James Rae and Eric Collison were awarded Future Research Leader grants from the Cancer Institute NSW renewed for a further three years.

Professor Susan Clark was elected President of the Australian Epigenome Alliance, the Australian Member and Representative of the Asian Epigenome Alliance, and appointed to the Steering Group Committee of the International Human Epigenome Consortium.

Members of the Program were awarded >$15M of new research grants for 2012–2015.

Several senior members of the Program convened the 5th PacRim Breast and Prostate Cancer Conference from 3–7 May, 2011 and served on national grant review panels including NHMRC, Cancer Australia, the Cancer Council NSW, the National Breast Cancer Foundation and the Prostate Cancer Foundation of Australia.

Drs Goli Samimi and Ilse Rooman were given conjoint senior lecturer appointments in St Vincent’s Hospital Clinical School, University of NSW, and Maia Kohonen–Corish was appointed a Conjoint Associate Professor at the University of Western Sydney.

Basic Cancer Research

Apoptosis Research Group
Group Leader: Dr Alison Butt
Apoptosis (cell death) is a physiological process of cell removal that plays a critical role in the development of cancers and how they respond to treatment. Oestrogen not only causes breast cancer cells to proliferate but it also protects them from apoptosis. We are investigating how this occurs and are identifying the genes that might regulate this process. We are also using new technologies to determine the differences between breast cancer cells that are sensitive, and those that are resistant, to tamoxifen at the protein level. Such studies will enable us to understand how these proteins may influence the way anti–oestrogens such as tamoxifen can effectively kill breast cancer cells. Together with the Breast Cancer Group, we are also examining whether these proteins are aberrantly expressed in breast cancers, and if they can predict how patients will respond to tamoxifen treatment. Such work could, ultimately, lead to the development of more effective and ‘tailored’ therapies for breast cancer patients.

Cancer Bioinformatics Group
Group Leader: Dr Jianmin Wu
High-throughput technologies accelerate the screening of potential biomarkers and therapeutic targets for cancer and other diseases, however, how to detect signals from the high dimension of screening data poses a significant challenge. Our group focuses on developing and applying different computational and statistical methods to solve these problems. Recently, in collaboration with the Pancreatic Cancer and Signal Transduction Groups, we are undertaking integrative analysis of multidimensional “-omics” datasets generated by deep sequencing of the cancer genome and profiling of the transcriptome, epigenome and proteome, with the aim of identifying candidate driver mutations and pathway aberrations in pancreatic cancer. We have also developed a database and numerous tools to study how potential candidates cooperate in a network context, utilizing publicly available protein interaction data.

Cell Cycle Group
Group Leader: Professor Liz Musgrove
Female steroid hormones like oestrogen strongly influence cell reproduction in the breast. We are particularly interested in how these hormones act on the cell cycle machinery and how control over the cell cycle is lost in breast cancer cells. Our current work concentrates on the cell cycle genes c-Myc, cyclin D1 and cyclin E2, all of which are targeted by oestrogen and are overexpressed in breast cancer. In collaboration with the Steroid Hormone Action and Breast Cancer groups we are searching for new genes that might link oestrogen action with the cell cycle and that could be involved in resistance of certain breast cancers to the anti-oestrogen tamoxifen. We have recently found that cyclin E2 is one such gene. We are continuing this work using transcriptome and epigenome data from experimental models and clinical samples together with functional genomics. We are also using functional genomics to find genetic events specific to particular cancer subtypes that can be targeted therapeutically.

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 Elf5 controls the development of the mammary gland during pregnancy and also regulates the proliferation and function of breast cancer cells. We are investigating how Elf5 exerts these effects to provide a way to therapeutically target this mechanism. We have placed Elf5 downstream of progestin signalling via regulation by RankL. This year four papers in Nature, including one to which we contributed, established the RankL mechanism as the key to understanding the role of exogenous progesterin use in the promotion of breast cancer.

Epigenetics Group
Group Leader: Professor Susan Clark
Cancer cells can modify the expression of critical cancer genes independently of the DNA sequence, using epigenetic biochemical processes including DNA methylation, histone modification and aberrant expression of non-coding RNA. Our research focuses on understanding the mechanism that triggers epigenetic change between normal and cancer cells. We have developed state of the art genome-wide sequencing methods to map epigenomic changes during early
cancer development and have discovered that epigenetic changes can take place not only in single genes, but also occur across very large regions of DNA during the spread of cancer. These changes include both regional gains and loss of epigenetic marks associated with regional changes in gene and non-decoding RNA expression. Using epigenome sequencing technology we have discovered novel tumour “signatures” for cancer diagnosis as well as potential targets for cancer therapy. We are now trying to determine which epigenetic 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 cancer epigenome.

**Pancreatic Carcinogenesis Group**

**Group Leader: Dr Ilse Rooman**

Our team is focused on identifying key drivers and biomarkers of pancreatic cancer through studying the earliest changes in the exocrine tissue (how a normal pancreas cell is turned into a cancer precursor). We focus on the role of genes identified as aberrantly expressed by the Pancreatic Cancer Group, and through previous discoveries. Mouse models are being set up to define the functional consequences and molecular mechanisms by which these genes and their mutations contribute to alterations in exocrine pancreas cell differentiation, proliferation and carcinogenesis. Potential applications extend to early detection, screening and chemoprevention.

**Signal Transduction Group**

**Group Leader: Professor Roger Daly**

Our research focuses on how signals regulating biological processes such as cell proliferation, survival and motility are transmitted within the cell, and how these signals are altered in cancer cells. We are using a technique termed mass spectrometry to identify the signalling networks associated with particular cancer subsets. This has: identified a novel signalling pathway that drives cell proliferation in an aggressive breast cancer subtype, basal-like breast cancer; subclassified pancreatic cancer into 3 different subgroups, each characterized by particular signalling events; and identified signal transduction processes that contribute to resistance to the drug docetaxel in prostate cancer. In addition, we have developed a new affinity reagent for purification of the ‘kinase’ class of signalling protein from cells, and are using this to comprehensively define which kinases are expressed and activated in specific cancer cells. These projects have important clinical ramifications, because they identify potential drug targets in specific cancer subsets, a key prerequisite for personalised cancer therapy.

**Steroid Hormone Action Group**

**Group Leader: Professor Rob Sutherland AO FAA**

Our research aims to determine and characterise the genes that mediate the actions of the sex steroid hormones oestrogen, progesterone, and androgens in steroid-responsive cancers (breast, prostate and ovarian). These constitute a third of all newly diagnosed cancers. In collaboration with the Cell Cycle and Apoptosis Groups we have identified and are characterising a number of steroid-regulated genes involved in the control of cell proliferation, cell differentiation and cell death in breast cancer. Several of these genes and their cognate gene networks contribute to the development of resistance to common endocrine therapies (tamoxifen and aromatase inhibitors) for breast cancer. In partnership with the Breast and Prostate Cancer Groups and the Cancer Therapeutics Development Laboratory we have demonstrated that some of these genes are new markers of cancer progression and response to therapy and novel targets for the development of new cancer therapies.

**Tumour Progression Group**

**Group Leader: Dr Alex Swarbrick**

Aggressive cancers have two features in common: they proliferate endlessly (a property known as 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 several genes that are key controllers of the growth and metastasis of poorly differentiated cancers. These include the Inhibitor of Differentiation transcriptional regulators, the Hedgehog signalling pathway and microRNAs. Understanding the contribution of these genes to cancer progression, and the ways in which they interact, will help us predict the behaviour of aggressive metastatic cancers and will lead to the development of new drugs to stop their growth.

**Ubiquitin Signalling Group**

**Group Leader: Dr Darren Saunders**

Our research is focused on mechanisms of cancer development and progression, using the emerging technology of functional genomics – a powerful, cutting-edge approach to understand gene function and define biological networks involved in cancer. By integrating a number of methods, including high-throughput gain/loss of function genetic screens with novel fluorescent assays and high-content imaging, we are working to identify targets of various components in the ubiquitin/proteasome system, a cellular recycling and garbage disposal system. Using this approach, we are able to scan the human genome/proteome to see which proteins are tagged by ubiquitin in tumour and normal cells. This will help us to understand how normal cells become cancerous through changes in their protein content, and also identify new molecules that might be targeted by anti-cancer drugs.
Breast Cancer Group
Group Leader: Professor Rob Sutherland AO 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 and validate new biomarkers of disease subtype, disease progression and response to particular therapies. These studies assist in the implementation of a biomarker guided personal medicine approach to breast cancer treatment. 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.

Colon and Lung Cancer Group
Group Leader: Associate Professor Maija Kohonen-Corish
Colon and lung cancers are among the most common malignancies. In lung cancer we are characterising new biomarkers of prognosis and therapeutic responsiveness, in order to improve the clinical management of cancer. Our research in colon cancer is focused on understanding how and why cancer develops and how it should be best treated. This work involves three main approaches, study of cancer specimens from patients, analysis of cancer cells grown in cell culture and study of tumours in mice. We have made the unexpected discovery that an arthritis drug sulindac, used in humans, can actually cause cancer in the mouse. This is being pursued as a new model of colon cancer and the susceptibility genes that increase the risk of carcinogenesis. Another major area of recent work involves the rediscovery of ‘Mutated in Colorectal Cancer’ (MCC) as a candidate tumour suppressor protein, including a role in the DNA damage response and lamellipodia formation. 

Ovarian Cancer Group
Group Leader: Dr Goli Samimi
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, in collaboration with the Epigenetics Group, 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.

Pancreatic Cancer Group
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 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. The group co-leads the Australian Pancreatic Cancer Genome Initiative with the Queensland Centre of Medical Genomics at the Institute for Medical Bioscience in Brisbane. The Initiative is part of the International Cancer Genome Consortium (www.icgc.org) and aims to use the latest technology to sequence 400 pancreatic cancers and use that information to inform personalised therapy trials.

Prostate Cancer Group
Group Leader: Professor Rob Sutherland AO FAA
Prostate cancer is the most frequently diagnosed cancer in men. Our group is concerned with the identification of biomarkers for early prostate disease, disease prognosis i.e. distinguishing indolent from potentially fatal disease, and response to therapy. 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 currently 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.

Cancer Therapeutics Development Laboratory
Group Leader: Dr Charlie Watts
The Cancer Therapeutics Development Laboratory is developing novel cancer drugs against molecular targets expressed by cancer cells. Our current project aims to block the activity of a regulatory enzyme that allows cancer cells to produce energy for their growth. Following identification of candidate inhibitor compounds from a chemical library, we have worked with medicinal chemists at the University of Auckland to identify and structurally optimize those compounds which are most active and inhibit the proliferation of cancer cells. These will be further modified to produce potent compounds for pre-clinical development.
The Kinghorn Cancer Centre is a joint venture between Garvan and St Vincent’s Hospital that will provide around 11,000m² of research and clinical space and bring together the scientific and medical expertise of the two partners to provide a personalised medicine approach to the treatment and care of cancer patients.

The 250-plus researchers and clinicians working in this purpose-built cancer centre will ensure that clinical challenges drive laboratory research, and that research findings are applied quickly to clinical care. As well as state-of-the-art clinical and consulting rooms and laboratories, the centre will provide workspaces and meeting rooms so that researchers and clinicians can come together into multidisciplinary teams to exchange information and ideas about the diagnosis, treatment and care of cancers.

In 2011, the bulk of construction was completed, with the building ‘topping out’ in November. This allowed the installation of the facade and internal fit-out to commence. A number of events and site visits were arranged throughout the year to enable donors and supporters of the project an opportunity to see first-hand the technical, engineering and design complexity that will underpin this state-of-the-art facility. Thanks to the unflagging work of all involved in the construction phase, the centre remains on track to begin operations in mid-2012.

The vision and concept of The Kinghorn Cancer Centre is one that many people have found engaging and appealing. Thanks to the support of a key group of visionaries, the project has secured close to $40,000,000 in philanthropic support.

These visionaries include:
Mr John and Mrs Jill Kinghorn
The Ferris Family Foundation
Mr Roy and Mrs Cindy Manassen
Mr Greg and Mrs Kerry Paramor
The Petersen Family Foundation
Mr Laurie Sutton
Mr Nicholas and Mrs Angela Curtis
Mr Cyril Golding
Mr John Porter and Ms Susan Mougey
Mr Tony and Mrs Coleen De Saxe
Mr Simon and Mrs Catriona Mordant

In addition, the Australian Cancer Research Foundation (ACRF) committed significant funds in memory of Lady Sonia McMahon, a founding member of the ACRF. The Nelune Foundation, a long time benefactor of cancer services at St Vincent’s Hospital, has also provided a leadership gift towards the fit-out of a new outpatient chemotherapy suite, putting the comfort and amenity of patients at the heart of the design.
Program Summary

Obesity has emerged as a major risk factor for a series of diseases. Aside from the obvious - diabetes, heart disease and stroke - a number of less intuitive candidates include cancer of the breast, bowel, kidney and oesophagus as well as Alzheimer’s disease. This strengthens the notion that modern living, probably food, has increased our predisposition to many diseases that are linked mechanistically and biologically. This provides a firm basis for convergent thinking in research of non-communicable disease and in intervention. Because many of these diseases take years to develop with a tremendous heterogeneity throughout the population it would seem that it is a gradual long term accumulation of damage that ultimately compromises health and there is some kind of genetic influence on the likelihood that this will occur. Due to the immense time delay in disease onset in humans it is difficult to pinpoint those factors that cause the damage and then which kinds of damage cause disease. In a perfect world we would follow the progression of all of these parameters in different individuals throughout the course of their lives and try to dissect cause from effect. Unfortunately this cannot be done and so we are forced to use simpler more tractable model systems to recapitulate these complex processes and then strategically use this information to determine its relevance to human disease. This is the approach that our program has begun to carve out and will represent our major focus for the next 5 years.

Research Highlights

- Demonstrated that fat accumulation in the liver, in response to a high fat diet, depends on the action of an enzyme, which can be targeted to improve insulin action.

- Identified a previously unappreciated link between ceramide metabolism, disrupted protein trafficking and ER stress in beta cell death in Type 2 diabetes.


- Comprehensive analysis of the insulin-regulated phosphoproteome provides the first glimpse of the extent of insulin action and the many molecules it invokes to get the job done.

- Discovery of two new insulin regulated Akt substrates that demarcate novel actions of insulin on cell motility and on autophagy.

- The proteins comprising the cell surface of the adipocyte were sequenced using mass spectrometry revealing the repertoire of receptors, channels, transporters and other molecules expressed in this important organelle.

- Established that eradication of the Hepatitis C virus in infected humans results in correction of insulin resistance; we have previously shown this insulin resistance is in muscle, rather than liver.

- Identified Id1 as a novel inhibitor of insulin secretion and beta cell differentiation.

- Demonstrated that increasing the amount of a transcriptional co-activator can up-regulate mitochondrial metabolism and alleviate fat-induced insulin resistance.

People Highlights

- Ross Laybutt was awarded an NHMRC Project Grant and Michael Swarbrick, Samantha Hocking and Amanda Brandon were also Chief Investigators on a successful NHMRC Project Grant application.

- Ted Kraegen, David James and their United States colleague Neil Ruderman, were awarded a National Institutes of Health (NIH) grant to investigate regulation of glucose metabolism in muscle.

- David James, together with Jiming Ye from RMIT, was successful in obtaining an ARC grant to study drug discovery in diabetes.

- Will Hughes was successful on an NHMRC Project grant “Regulation of glucose uptake by tropomysins and myosins” with Peter Gunning and Edna Hardeman at UNSW.

- Katherine Samaras and Susan Clark were successful in a cross-Garvan collaboration in obtaining funding from the CSIRO’s Science and Industry Endowment Fund for “Early Nutrition, the Epigenome and the Prevention of Disease”. The project will examine the role of nutrition in the epigenetics of obesity, in collaboration with researchers from the University of Adelaide, CSIRO Sydney and CSIRO Adelaide.
mechanism involving C/EBa and PPARg. Islet 1 may
fat and modulates fat cell differentiation, by a
factor, Islet 1, which is uniquely expressed in visceral
reversed when the virus is eradicated by antiviral
muscle - not, as previously believed, in liver and is
conjunction with the Storr Liver Unit at Westmead
Hepatitis C, which is known to increase insulin
We have now completed studies of patients with
Group Leader: Professor Don Chisholm AO
Fat, Infection and Insulin Resistance
are characterising the accompanying lipidomic
profiles in muscle and plasma.
are significantly more weight than those without such
relatives, we have been able to identify the early
changes associated with development of insulin
resistance in healthy humans with weight gain and
are characterising the accompanying lipidomic
profiles in muscle and plasma.
were awarded PhD degrees.
Recruitment of Daniel Hesselson from University
of California (UCSF). Dan is an expert in the use of
zebra fish to study insulin secretion.
was awarded the Australian Diabetes Society Young Investigator of the Year award.
Dorit Samocha-Bonet won the ADS Skip Martin
Early Career Fellowship.

Research Groups

Appetite and Adiposity in Pre-diabetes and Prader Willi Syndrome (PWS)
Group Leader: Professor Lesley Campbell AM
Our group focuses on the underlying defects in metabolism and appetite control in prediabetes and in the commonest genetic obesity disorder, Prader Willi Syndrome (PWS). The latter is associated with relentless weight gain after childhood and is distressing to manage. In collaboration with Royal Prince Alfred Hospital PWS Clinic, we have shown a resistance to common satiety hormones but high levels of a “hunger” hormone ghrelin in these individuals. We have conducted a pilot study in PWS, which shows that available diabetes/weight control drugs have efficacy without obvious side-effects. We have shown that individuals predisposed to Type 2 diabetes co-inherit obesity genes with type 2 diabetes genes. From an overfeeding study, where relatives of people with diabetes gained significantly more weight than those without such relatives, we have been able to identify the early changes associated with development of insulin resistance in healthy humans with weight gain and are characterising the accompanying lipidomic profiles in muscle and plasma.

Fat, Infection and Insulin Resistance
Group Leader: Professor Don Chisholm AO
We have now completed studies of patients with Hepatitis C, which is known to increase insulin resistance and risk of Type 2 Diabetes. This work, in conjunction with the Storr Liver Unit at Westmead Hospital, has shown that the insulin resistance is in muscle – not, as previously believed, in liver and is reversed when the virus is eradicated by antiviral treatment. Work continues on the transcription factor, Islet 1, which is uniquely expressed in visceral fat and modulates fat cell differentiation, by a mechanism involving C/EBa and PPARg. Islet 1 may be important in restraining the adverse effects of this “noxious” fat.

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, environmental and hormonal) 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 burned to produce energy. We are studying the regulation of glucose and fat metabolism and how tissue metabolism changes at different times of the day. These studies will help explain how increased food availability and altered eating habits have contributed 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 mechanism 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.

Clinical Diabetes and Metabolism
Group Leader: Dr Jerry Greenfield
We have completed a major clinical study in a cohort of individuals with a broad range of metabolic defects to dissect molecular defects that cause muscle insulin resistance. Inclusion of an unusual group of ‘healthy obese’ individuals enabled us to uncouple the contributions of obesity and insulin resistance to disease risk. These studies have led to a major breakthrough in our understanding of metabolic disease in that insulin resistance was found to be ‘selective’ for carbohydrate metabolism while other actions of insulin were normal. This led us to propose a model whereby the defect in carbohydrate metabolism triggers the pancreas to over secrete insulin which hyper stimulates those insulin resistant individuals. This would have the effect of reducing the insulin resistance per se.

Studies have also been established examining the effects of the amino acid glutamine on metabolism, 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.
Phospholipid Biology
Group Leader: Dr Will Hughes
Our goal is to apply cutting edge live cell microscopy techniques to understand complex processes in individual mammalian cells. We have developed state of the art fluorescent probes to study the insulin dependent movement of the glucose transporter to the surface of muscle and adipocytes. This system mimics the situation that occurs in our muscle and fat cells each time we eat a meal. Using this approach we can watch these molecules moving toward the membrane and then deciding whether to merge with the membrane or return to the cellular interior. Importantly we are beginning to use molecular approaches to dissect how this process becomes disrupted in disease.

Cellular Systems Biology
Group Leader: Professor David James FAA
We are using ‘omics approaches to deconvolute the complexity of metabolic disease. This involves the measurement of thousands of parameters in cells or animals as they transition between different metabolic states. Then by using mathematics, engineering and physics our goal is to construct an in silico model for metabolic disease. Such a model can be used to provide novel insights into complex diseases and as a vehicle for in silico drug discovery.

Diabetes and Metabolism
Group Leader: Professor Edward Kraegen
Understanding how too much fat causes insulin resistance in muscle and liver is the major thrust of our work. Various experimental models and state-of-the-art techniques are being used to identify and manipulate key proteins in muscle that link fat metabolism to insulin action. These continue to play a role investigating various physiological consequences of basic findings in the Program (e.g. oxidative stress and insulin action). We are investigating important signalling pathways, particularly involving the hormone adiponectin and enzyme AMP-kinase, a major intracellular regulator of cellular energy status, and how they influence potency of insulin action in cells. Further work with Boston University, partly funded by the US funding agency NIH, is opening up new ways of looking at the early stages of muscle insulin resistance in response to increased nutrient availability. Lastly studies using traditional Chinese medicines aim to help identify new insulin-sensitising agents that could be more useful than current therapeutics.

Adipose tissue biology in diabetes
Group Leader: Associate Professor Katherine Samaras
Obesity is the major factor accelerating development of Type 2 diabetes. Dysregulation of adipose tissue biology impacts upon metabolism and inflammation. We have found modest weight reduction improves immune function in morbidly obese people with Type 2 diabetes, associated with reductions in arterial stiffness. Our results show these improvements are not explained by weight loss. We have also shown that obese people with diabetes have greater levels of genes regulating inflammation in abdominal fat. We are currently investigating the role of circulatory and tissue-based inflammation in the reversal of diabetes with weight reduction, which will provide insights into how diabetes develops and identify potential targets for treating the commonest form of diabetes.

Mitochondrial Bioenergetics
Group leader: Dr Nigel Turner
Mitochondria are the primary site of energy production within cells. Mitochondrial dysfunction has been linked with a number of inherited and acquired human diseases and has also been implicated in the aging process. A major focus of our studies is to examine how alterations in mitochondrial function in different tissues influence insulin action in obesity and type 2 diabetes. We are interested in how certain drugs and different types of dietary fats affect mitochondrial content and metabolism. We are also examining the role of post-translational modification in the function of mitochondrial proteins. Another area of research is the importance of alterations in mitochondrial bioenergetics in certain types of cancers.

Insulin Signalling
Group Leader: Dr Carsten Schmitz-Peiffer
My group has previously shown that the protein kinase C (PKC) family of enzymes plays an important role in metabolic disease. We are currently using proteomic approaches to identify downstream targets of specific PKC members, which will provide insights into the molecular mechanisms by which they control glucose and lipid metabolism in the liver. We have identified novel candidates, which may mediate these effects and which we are now pursuing, to determine whether they may be new targets for intervention. We have also studied the role of different lipid species in insulin action in muscle and have discovered distinct effects of lipid modifying enzymes, which play positive or negative roles in insulin action and glucose disposal. In combination with high throughput lipid analysis, we are testing the actions of these enzymes in cell, tissue and animal models of fat-induced insulin resistance to determine those that can be modulated to improve whole body glucose metabolism.

Beta Cell Signalling
Group Leader: Professor Trevor Biden
Increased beta cell death and disruption of beta cell function are characteristics of Type 1 and Type 2 diabetes. We have discovered that the enzyme protein kinase C delta (PKCδ) contributes to disease onset in models of Type 1 diabetes and have shown that the mechanism involves stabilisation of gene transcripts encoding inflammatory proteins. Another major project is examining the molecular links between fatty acids and beta cell death, with particular emphasis on ER stress. We have employed systems biology approaches to screen lipid metabolites that change in beta cells undergoing ER stress and identified sphingolipids as potential causative agents. Our ongoing work is focused on delineating how and where these lipid metabolites exert their effects.

Islet Biology
Group Leader: Dr Ross Laybutt
Our goal is to identify mechanisms responsible for pancreatic beta cell dysfunction and destruction in type 1 and type 2 diabetes. We have discovered a previously unrecognised role in beta cell biology of a transcriptional regulator, Id1. We identified Id1 as a novel inhibitor of insulin secretion. Id1 expression plays a crucial role in the abnormalities in beta cell gene expression and glucose homeostasis induced by excess fat. Studies have also made important contributions to understanding how cytokines produced by the immune system lead to beta cell killing. We investigated the role of stress within the endoplasmic reticulum cellular compartment in cytokine-mediated beta cell death. Studies identified the signalling molecules that control the decision of beta cells to undergo cell death rather than adapt to endoplasmic reticulum stress and survive a cytokine attack.

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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 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.

The Centre's mission is to provide a platform to translate Type 1 diabetes research into improved clinical outcomes - prevention and therapy.

With substantial in-house expertise for the conduct of clinical trials, DVDC currently manages a portfolio of preclinical and clinical research projects (see below), and coordinates a network of eleven trial sites across Australia and New Zealand. The Network has focused on children and young adults, and is now expanding to include more of the adult Type 1 diabetic population.

Highlights
- Opened new trial sites in Monash, Victoria, and Munich, Germany, for the INIT II Study
- Executed a Co-operation Deed with the Australasian Paediatric Endocrine Group (APEG) to work together to enhance the management and coordination of Type 1 diabetes trials in Australia and New Zealand.
- Entered into a Consultancy Agreement with Cell Care Australia for the provision of consulting services by DVDC.

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.

Study of Proinsulin Peptide Immunotherapy in New-onset Type 1 Diabetes (MonoPepT1De Study)
Peptide immunotherapy represents a novel approach to preventing loss of insulin production from the pancreas in Type 1 diabetes. The MonoPepT1De Study, which is being conducted in the UK, aims to address the safety of P1 peptide administration in newly-diagnosed T1D preparatory to a larger study to determine whether this intervention promotes the survival of residual insulin-producing beta cells.

Use of BAFF Blockers to Prevent Type 1 Diabetes in Man
DVDC has supported Associate Professor Shane Grey at Garvan to undertake pre-clinical studies aimed at testing a therapy targeting the B cell arm of the immune system. Using non-obese diabetic (NOD) mice, this study aimed to test the hypothesis that B-cell depletion, by way of BAFF-blockade, will restore tolerance to islets and prevent diabetes occurrence. Complete prevention of diabetes in NOD mice was achieved. DVDC has been liaising with Associate Professor Grey in relation to the design of a project that moves this work from the lab to a clinical application.

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DVDC Limited
Membership of the DVDC Board
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Senior Principal Research Fellow
Diabetes and Obesity Research Program
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Professor John Shine AO FAA
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Mr Mike Wilson
Chief Executive Officer
JDRF Australia

Professor Don Chisholm
Chair
DVDC Board

Ms Rowena Tucker
Chief Executive Officer
DVDC

Mr Ron McNeilly
A/g Director Research Administration
National Health and Medical Research Council
Program Summary
The 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 malignant 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 how this 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. The latest technologies in manipulating and analysing immune cell behaviour are employed. These include sophisticated gene manipulation and analysis techniques, precise and detailed approaches for analysing the rare cell populations that initiate immune responses, and the new capability to microscopically visualise individual cells as they function within the body.

Research Highlights
- Identified the cytokine (chemical messenger) IL-21 as the main driver of successful antibody responses in people.
- Determined the genetic defect in the cytotoxic immune cells (killer T cells) of patients with a particular immunodeficiency that renders them defenceless when infected with the Epstein-Barr virus.
- Identified an important role for the signalling protein DOCK8 in the development and differentiation of killer T cells.
- Collaborated with the Cancer Program to characterise the role of the hedgehog protein in breast cancer.
- Identified the cIAP proteins to be fundamental regulators of antibody production as well as potential tumour suppressors in B cells.
- Showed that the EBI2 receptor was responsible for previously unexplained movements of B cells during an immune response.
- Identified a new subset of T cells that home to the gut and are involved in the induction of autoimmunity.
- Showed that if offspring have a mother with diabetes in pregnancy, they get fat, and if they also inherit the risk for diabetes, they get even fatter – suggesting that control of blood sugar levels in pregnant women is important in preventing their babies growing up to be fat adults.
- Showed that 41% of a cohort of pregnant women with gestational diabetes in Sydney had low Vitamin D levels and that this was associated with higher blood sugar levels in pregnancy.
- Revealed that the CD94/NKG2A inhibitory molecule is downregulated during immune responses to promote the activity of anti-viral killer T cells.

People Highlights
- Associate Professor Shane Grey was an invited plenary speaker at several international meetings: the International Transplant Society’s Basic Science Symposium Boston USA 2011; the 5th Asian Autoimmunity Congress 2011, Singapore; and the 41st meeting of the Australasian Society for Immunology. He was also invited to write a review for Trends in Immunology.
- Jeanette Villanueva was awarded the Kidney Health Australia Award by the Transplantation Society of Australia and New Zealand.
- Nathan Zammit was awarded a Travel Award by the Transplantation Society of Australia and New Zealand to present his work at the Cell Transplant Meeting in Miami USA.
Dr Daniel Christ was awarded an NHMRC development grant to further advance his collaboration with St Vincent’s Hospital on the development of antibody-based therapeutics.

Romain Rouet won the 2011 Castle-Harlan Award as the most outstanding second year PhD student for his work on antibody therapeutics.

Dr Kendle Maslowski won the 2011 Garvan thesis prize for the Institute’s most outstanding PhD thesis of the year.

Stuart Tangye was promoted to Associate Professor at the University of NSW. He was also awarded the Gottschalk Medal by the Australian Academy of Sciences, which recognises “outstanding research in the medical sciences by scientists under 40 years”; was an organiser of, and invited plenary speaker at, the Keystone Symposia on New Insights into Normal versus Dysregulated B Cell Function, held in Whistler, Canada; was an invited plenary speaker at the Swiss Society of Immunology and Allergy annual meeting, held in Lugano, Switzerland; and was invited to be an Advisory Editor with the Journal of Experimental Medicine and an Associate Editor for the Journal of Immunology.

Dr Elissa Deenick was an invited speaker at the annual meeting of the Japanese Society of Immunology, held in Chiba, Japan; was selected to present her work as an oral presentation at the Keystone Symposia on New Insights into Normal versus Dysregulated B Cell Function, held in Whistler, Canada; was awarded an NHMRC Project grant to continue her studies into the function of STAT3 in the function of immune cells; and was appointed as co-editor of the News & Commentary section for the journal Immunology & Cell Biology.

Dr Cindy Ma was awarded a travel bursary to attend the Keystone Symposia on New Insights into Normal versus Dysregulated B Cell Function, held in Whistler, Canada.

Dr Mainthan Palendira was awarded a travel bursary to attend the FOCIS meeting held in Washington DC.

Helen McGuire was the 2011 winner of the first quarter prize for best PhD thesis in the School of Biotechnology and Biomolecular Sciences, UNSW.

Emeritus Professor Tony Basten attended the Cambridge Immunology Forum.

Dr Marcel Batten received an NHMRC CDA Fellowship.

Dr Cecile King won the 2012 Diabetes Australia Research Trust (DART) Millennium award; was invited to write reviews for Immunity and Trends in Immunology; was an invited speaker at the 2011 International Conference of Diabetes and Metabolism in Seoul, Korea and the 2011 International congress for Mucosal Immunology in Paris; and was elected to the board of councillors for the Society of Mucosal Immunology.

PhD students Tyani Chan, Eliana Marino, Kenneth Ho and Helen McGuire all had their doctoral theses formally accepted by the University of NSW.

Dr Jenny Gunton was promoted to Associate Professor at University of NSW and at University of Sydney.

Dr Jenny Gunton was invited to speak at the 2012 Keystone Advances in Hypoxic Signalling meeting.

Associate Professor Robert Brink was invited to work with an international team of scientists to prepare a special issue of Immunological Reviews focusing on the Germinal Centre response; and was invited to be a plenary speaker at the Keystone Symposium on B Cell Biology in January, 2013.

Dr Tyani Chan was awarded a bursary to attend the annual conference of the Australasian Society of Immunology and participate in the finals of the New Investigator of the Year competition. She was also selected to present her work as an oral presentation at the Keystone Symposia on New Insights into Normal versus Dysregulated B Cell Function, held in Whistler, Canada.

Research Groups

Cellular Immunity

Group Leader: Professor Jonathan Sprent FAA FRS

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 while 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 Biology**

**Group Leader:** Associate Professor Robert Brink and Emeritus Professor Antony Basten

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 hemolytic anemia 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:** Associate Professor 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.

**Immunology & Immunodeficiency**

**Group Leader:** Associate Professor Stuart Tangye

Our focus is on understanding the development and effector function of B cells – the population of white blood cells responsible for the production of protective antibodies – and the mechanisms underlying 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 that controls the behaviour of B cells. Thus, a major focus of our work is to understand exactly how helper T cells instruct B cells to produce antibodies. We also investigate the requirements for the immune system to generate protective responses against viruses, such as Epstein Barr virus which is also known to cause cancer. Our approach to these questions involves studying several genetic conditions of the immune system, and corresponding mouse models, that result in immunodeficiencies – which are often life-threatening disorders where affected individuals are unable to mount appropriate immune responses following exposure to some infections or pathogens. These diseases include X-linked lymphoproliferative disease, the autosomal dominant and autosomal recessive hyper-IgE syndromes, and X-linked severe combined immunodeficiency. 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.

**Immunobiology of Cancer**

**Group leader:** Dr Tatyana Chtanova

Our group is interested in understanding how the immune system responds to cancer and how these responses can be manipulated to produce better anti-cancer therapeutics. We have developed an innovative system to visualise immune cells in vivo in intact tumours and to ‘tag’ tumour-infiltrating cells. With the aid of 2-photon microscopy, a cutting edge technique that allows us to ‘see’ cells hundreds of microns below the surface of intact organs, we are monitoring the interactions between the tumour and immune cells taking place below the tumour surface. Using this system together with a novel reporter to mark tumour-infiltrating cells, we can determine whether these cells participate in anti-tumour immune responses or whether they aid tumour metastasis, one of the most fearsome aspects of cancer.

**Mucosal Autoimmunity**

**Group leader:** Dr Cecile King

Our laboratory is interested in how T lymphocytes drive autoimmune responses that cause destruction of tissues at the mucosal interface between the body’s own tissues and the environment. We focus on the chemokine and cytokine networks that direct the regional specification of immunity and autoimmunity. Broad-based immunosuppression is commonly used to treat 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 T 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
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 B cells recognising beta cell proteins to persist and thus activate 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.

Diabetes and Transcription Factors
Group leader: Associate Professor 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 diabetes and diabetes in pregnancy. We are currently focusing on a two main factors: HIF-1, and the vitamin D receptor (VDR), both of which are decreased in the beta cell containing islets of people with Type 2 diabetes. Recently we have been working on a drug which improves diabetes in mice, and are in the process of starting a human clinical trial.

Translational Immunology
Group leader: Professor Charles Mackay FAA
Professor Mackay continues to run a small group of students and postdoctoral researchers at Garvan after taking up a Chair at Monash University in 2009. Their research is studying the link between diet, fatty acid binding proteins and asthma, as well as looking more broadly at the links between inflammatory and metabolic diseases.

Cooperative Research Centre for Asthma and Airways
Head: Professor Charles Mackay FAA
Group leader: Dr. David Zahra
A node of the CRC for Asthma and Airways, our group has focused on the G-protein coupled receptors, GPR43 and GPR18. Knockout animals have demonstrated that these two molecules are important in inflammatory disease. The natural ligand for GPR43 is acetate and animal models have demonstrated that agonists of GPR43, such as acetate, have beneficial therapeutic efficacy. Hence, one major aim is to isolate a novel small molecule ligand that could act as an agonist of GPR43. To facilitate the isolation of a small molecule agonist, a collaboration with the WEHI Biotechnology research centre has been initiated to screen their library of small molecules. Another main aim is to isolate antibodies to GPR43 and GPR18, which would be used for diagnostic and potentially therapeutic purposes. Our work has also developed 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 neutralises this cytokine. Three patents protect the potential therapeutic and a feasibility study has been conducted in collaboration with a major pharmaceutical company. Negotiations are on going to complete this licensing agreement.

Immunobiology of Cytokines
Group leader: Dr. Marcel Batten
Immune responses, be they beneficial responses to infection or harmful autoimmune responses, require highly coordinated interactions between various immune cells. One cell type that is very important for orchestrating the response is called a “T cell”. These cells do their work by producing chemical signals called cytokines. My group is interested in how T cells control immune responses, with a particular interest in how things go wrong during autoimmune disease and whether we can identify points of intervention. In particular, we are interested in the autoimmune diseases multiple sclerosis (MS) and lupus. We are closely studying a recently identified cytokine, called IL27, which we have now shown to be important in these disease processes. We are also working to understand the function of a number of new proteins with links to MS. We hope our work will inform us as to whether these cytokines and other proteins could form the basis for new therapeutics.
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. The program has recently been expanding its interest in other research areas with several new groups joining including a group focusing on brain control of bone formation, a group investigating neuronal cell activity in Alzheimer's disease, and a group focusing on pain research. We aim to identify new therapeutic approaches in these areas, with a special interest in regenerating the nervous system for therapeutic purposes as well as achieving a better understanding of the brain's control of body functions including the regulation of energy balance (intake and expenditure), which affects fertility, mood, weight gain and physical fitness.

Research Highlights
- Discovered a new pain receptor required for thermal pain sensation, conserved from flies to humans, further highlighting pain perception as an ancient process conserved through evolution.

- Identified that the satiety hormone peptide YY (PYY), in addition to being released into the gut after a meal is also released into saliva from glands in the tongue, helping to reduce food intake.

- Detailed the skeletal actions of the major circulating member of the neuropeptide Y (NPY) family, PYY. These studies may shed new light on our understanding of anorexia nervosa.

- Initiated studies to investigate the role of NPY in controlling osteoclasts, the bone removing cells responsible for the major early post-menopausal bone loss.

- Demonstrated that male sex hormones are critical for the positive actions of NPY in bone cells.

- Conducted the first study of long-term oral treatment to alter NPY signalling in living animals. The drug BIBO3304 inhibits an NPY receptor, leading to a significant increase in bone mass, without adverse side effects.

- Showed that NPY and PYY have different roles in regulating olfactory stem cells during neurogenesis.

- Discovered a novel target of the enzyme GSK3 in the brain, a protein called 'beta-adducin', which is important for new synapse formation in learning and memory.

- Demonstrated significant biochemical change (hyperphosphorylation) of a GSK3 target, a protein called CRMP2, specifically in the brains of Alzheimer's disease patients, but not in other forms of dementia. This appears to occur early in the disease process and has the potential to be a biomarker for early and specific detection of Alzheimer's disease.

- Demonstrated the rescue of dopamine nerve cells in a Parkinson's disease model, which opens up a potential new therapeutic strategy for the disease.

People Highlights
- Professor Herbert Herzog was invited to give the plenary lecture at the 15th Japan Society for Eating Disorder Conference in Kagoshima, Japan and was also an invited speaker at the 6th International Cachexia Conference, Milan, Italy. He was awarded two NHMRC project grants, one being ranked in the top 3 out of 3500 applications, and was renewed as an NHMRC Principal Research Fellow.

- Associate Professor Amanda Sainsbury-Salis received an NHMRC Project Grant.

- Dr Greg Neely was invited to speak at the Drosophila Neurobiology meeting in Cold Spring Harbor, as well as at the 61st Annual American Society for Human Genetics meeting. He also received the 2011 NHMRC Marshall and Warren Award for most potentially transformative research, as well as 3 NHMRC project grants and an NHMRC Career Development fellowship.

- Dr Kevin Wang received an NHMRC Early Career Fellowship.
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. Defects in the brain pathways that regulate these processes may be responsible for causing excess weight gain leading to obesity but also 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

Hearing loss due to noise trauma is one of the most common sensory disabilities in humans, particularly in industrialised countries. The Hearing Research Group is investigating whether stem cell therapy can reduce hearing loss caused by acute noise trauma. Our research is focused on whether stem cells can replace damaged cells or secrete factors that enhance the survival and/or proliferation of cells remaining in the inner ear. We have recently discovered that transplanted stem cells can integrate into the host tissue and can improve hearing levels after noise trauma. Our research in the ear is strengthened by investigations in the brain, where we explore how nerve cell connections are changed by deafness. Our goal is to develop new initiatives to provide benefits to the young and ageing community suffering from noise-induced hearing loss.

Neurodegenerative Disorders – Repair and Regeneration

Group leader: Dr Bryce Vissel

The Neurodegeneration Research Group is working to identify approaches to understand and treat Parkinson’s disease, Alzheimer’s disease and spinal disorders. These are devastating neurodegenerative diseases. Our goal is to harness the nervous system’s own repair systems, in order to stimulate the formation of new nerve cells and their connections. We also investigate approaches to block nerve cell loss. Our team have identified new mechanisms to stimulate brain repair and have discovered potential approaches to block neurodegeneration. We aim to develop new therapeutic approaches with a goal of generating outcomes for clinical trials in people. Our research outcomes have significant theoretical and clinical implications for impacting the lives of people who confront devastating neurodegenerative diseases.

Skeletal Neurobiology

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.
Research Assistant Silas Sugiharto applies a probe to fly larvae to measure their sensitivity to heat.

Neurosignalling Research Group
Group leader: Dr Adam Cole
GSK3 and Cdk5 are important brain enzymes that control neuroplasticity, which is the ability of the brain to change and refine itself in response to different experiences and circumstances. This is especially important for higher order functions, such as learning and memory. Defects in GSK3 and Cdk5 function are implicated in the development of several neurological disorders, including Alzheimer’s disease, Bipolar disorder and schizophrenia. In order to understand how GSK3 and Cdk5 regulate neuroplasticity in healthy and diseased brains, the Neurosignalling Group focuses on discovering novel targets of these enzymes. So far, we have discovered 10 targets involved in important brain functions, such as synapse formation, neurotransmission and neuronal survival. This information will not only inform us of the mechanisms that control neuroplasticity and cognitive function, but will also help to identify new therapeutic targets for the treatment of age-related cognitive decline, dementias and mood disorders.

Neuro-Pain Research Group
Group leader: Dr Greg Neely
One of the Neuro-Pain Research Group’s major goals is to identify and characterise new genes that participate in chronic pain, with the goal of developing a next generation of therapeutics for this debilitating condition.

Fifty percent of the population will experience some form of chronic pain within their life, especially patients that suffer from arthritis, cancer, diabetes, migraine, or nerve injuries. Despite the astonishing prevalence, there are few effective therapeutic options for these patients.

To this end, we have developed a novel, systematic strategy for identifying new components of the pain pathway using the fruit fly *Drosophila melanogaster*. Using this system we have identified ~600 new pain genes in *Drosophila*. Most of these have mammalian counterparts, and we are currently prioritising and confirming these genes one by one. For example, we have identified a component of a calcium channel (A2D3) as a component of the pain relay system in the brain. This work also led to identification of the first gene ever shown to play a role in sensory cross activation or synesthesia.
Professor Peter Croucher joined Garvan in December 2011 to take up a new Chair in Osteoporosis funded by Mrs Janice Gibson and Ernest Heine Family Foundation. He succeeded Professor John Eisman as Leader of the Osteoporosis and Bone Biology Program.

Professor Croucher established himself as an international authority in the bone field over the last two decades. After completing post-doctoral training in the Department of Medicine at the University of Cambridge and later in the Department of Human Metabolism and Clinical Biochemistry at the University of Sheffield (UK), he was awarded a prestigious five year Bennett Senior Fellowship by the Leukaemia Research Fund. After a period at Oxford University as a Senior Research Fellow, he returned to the University of Sheffield as Professor of Bone Biology in 2003, before becoming Head of the Department of Human Metabolism. While in Sheffield Peter founded the Mellanby Centre for Bone Research, an interdisciplinary centre focused upon addressing key questions in skeletal medicine.

With his current research focused upon osteoporosis, one of Peter’s key interests is identifying the genes responsible for regulating the skeleton. An ongoing collaboration with colleagues at Imperial College, London and The Wellcome Trust Sangar Institute in the UK has identified a series of new genes that regulate the amount of bone in the skeleton. Importantly, a number of these genes increase the amount of bone in the skeleton and the strength of bone. These discoveries are playing an important role in developing new approaches to stimulating bone repair. Peter will expand this work at Garvan.

In addition to his research on osteoporosis Peter also has a long-standing interest in cancers that cause bone destruction. In particular, the blood cancer known as multiple myeloma is a long-standing research interest. In his words, “this is a particularly devastating haematological malignancy that only grows in the skeleton and causes devastating bone destruction”. Using various animal models, his group, while in the UK, developed a number of ways of stopping the bone destruction caused by these cancer cells. Several of these discoveries have now been through clinical trials and are being translated into the clinic. They are also being applied to other cancers that grow in bone, such as metastatic breast and prostate cancers. The next challenge will be to stop these cancers growing in bone, an area which Peter will explore at Garvan.

As Bone Program Leader, Professor Croucher aims to expand the program by recruiting world-class researchers and a creating high-quality infrastructure to support the research that will have an impact on common skeletal diseases.
Program Summary
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; improve our understanding of bone biology; and help identify new treatment possibilities. To this end, we have been working on several translational projects, including the ongoing development and refinement of our Garvan prognostic models for predicting fracture-associated adverse outcomes. We have collaborated with colleagues around the world, including the US, Canada, Norway and the Netherlands to validate our predictive tools for absolute fragility fracture risk. Similar collaborations are underway with the Geelong Osteoporosis Study (Melbourne), CAIFOS study (Perth) and other major cohorts in Norway, Holland, UK and New Zealand. The model has been implemented in a web-based tool, www.fractureriskcalculator.com, that is widely used by doctors and patients worldwide.

Research Highlights
- Noted an extraordinary and unexpected benefit of osteoporosis treatment – that people taking bisphosphonates are not only surviving well, better than people without osteoporosis, they appear to be gaining an extra five years of life.
- Continued to recruit all major epidemiological studies worldwide to participate in our analyses of refining prediction of fracture risk and adverse outcomes from osteoporotic fractures.
- In collaboration with colleagues at Vietnam National University in Ho Chi Minh City, conducted a study on ASEAN countries as a group, providing a useful snapshot of the scientific landscapes and capabilities of our regional neighbours, and how those attributes are likely to drive their economies.
- Reported findings of initial clinical studies of a novel treatment, developed by Merck Sharp and Dohme, that reduces bone breakdown and which has major potential in osteoporosis treatment.
- Expanded our work on the genetics of osteoporosis (including linkage analysis to identify novel loci that may be associated with bone phenotypes) to assess genetic roles in other major body compositions including muscle mass and fat mass.
- 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 that genetic profiling could enhance the prognosis of fracture.
- In collaboration with Westmead Children’s Hospital, developed a unique treatment regime for children with neurofibromatosis type 1 (NF1), a bone disease that frequently results in limb amputation.
- Revealed that osteoclasts (bone removing cells) play a role in the actions of PTH (parathyroid hormone), the only clear-cut anabolic treatment available for osteoporosis.
- Detailed the actions of neuropeptide Y in control of bone stem cell function.

People Highlights
- The Program has been strengthened with the appointment of a new Leader, Professor Peter Croucher, as the inaugural Chair in Osteoporosis, funded by Mrs Janice Gibson and Ernest Heine Family Foundation. We extend our thanks for this generous support.
- After 27 years Professor John Eisman, the founding director of the Osteoporosis and Bone Biology Program moves to a new role as Director of Clinical Translation and Advanced Education. This novel Garvan development has its initial focus in osteoporosis and is aimed at streamlining the application of new basic and clinical knowledge to clinical care in the community and more efficient and cost-effective health care.
Professor John Eisman has been appointed as a visiting Professor at the University of Maastricht. This role, planned over several years, is key to our international epidemiology data analyses. He was an invited speaker at the 16th Congress of the ASEAN Federation of Endocrine Societies, at the US Endocrine Society and chaired the Symposium on Secondary Fracture Prevention at the American Society for Bone and Mineral Research.

Professor Tuan Nguyen was invited by the Osteoporosis Society in Vietnam to chair and lecture at its 6th Annual Scientific Meeting in Ho An, July 2011. He chaired the scientific committee of the 16th Congress of the ASEAN Federation of Endocrine Societies in Ho Chi Minh City in November 2011. The meeting attracted more than 1500 participants from Asia and around the world.

Dr Paul Baldock received an NHMRC project grant. He and was invited to present a Meet the Professor Session at the 2011 American Society for Bone and Mineral Society meeting in San Diego. He was also invited to join the Scientific Advisory Committee of the Australian and New Zealand Bone and Mineral Society, as well as the organising committee for the joint meeting of the International Bone and Mineral Society and the Japanese Society of Bone and Mineral Research in Kobe in 2013.

Associate Professor Jackie Center was invited to speak in a plenary session at the IOF Regionals ANZBMS (Australian and New Zealand Bone and Mineral Society) Annual Scientific Meeting in 2011 and invited to write a book chapter for Osteoporosis and the Primer in Metabolic Bone Diseases and Disorders of Mineral Metabolism.

Ms Iris Wong’s PhD thesis was accepted.

Ms Ayse Zengin received a Young Investigator Award from the International Bone and Mineral Society. Ayse also won the AMGEN Best Presentation Award at the International Osteoporosis Foundation Asia-Pacific Regional Meeting.

Dr. Nguyen D. Nguyen passed his AMC medical qualification with the absolute mark of 100%.

Garvan bone researchers were awarded 6 orals presentations at the 33rd Annual Scientific Meeting of the American Society of Bone and Mineral Research in San Diego and 2011 IOF Regionals - 2nd Asia-Pacific Osteoporosis and Bone Meeting in the Gold Coast.

Bone Program students had the following successes: Bich Tran graduated with a PhD and was appointed as a postdoc researcher at the Queensland Institute of Medical Research. PhD student Shuman Yang was awarded a young investigator prize at the 2011 IOF Regionals - 2nd Asia-Pacific Osteoporosis and Bone Meeting held in conjunction with the Australian and New Zealand Bone Mineral Society Annual Scientific Meeting and Japanese Society of Bone and Mineral Research, Mei Chan (PhD student) and Dr. Nguyen D. Nguyen were awarded travel grants for presenting “hot topic research” at the 33rd Annual Scientific Meeting of the American Society of Bone and Mineral Research in San Diego.

### 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 have allowed us to develop powerful predictive models to identify men and women at high risk of fracture, and so who would benefit most from preventative interventions. We have formed international collaborations to explore in more detail predictors for adverse outcomes following fracture including re-fracture and mortality following our initial Dubbo findings.

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.

**Fracture Prevention – Clinical Studies**

**Group Leader: Professor John Eisman**

Our clinical studies group continues to participate in Phase III international clinical trials evaluating potential novel osteoporosis treatments. Most recently we have gained a role in testing of ‘anabolic’ treatments that lead to new bone production. Involvement in these studies helps ensure we remain at the cutting edge of knowledge of novel therapies. These connections facilitate access to major pharmaceutical clinical database sets in which we can expand our Dubbo findings.

Professor Eisman’s major focus on Clinical Translation has led to the development of the HELLO (Health Education for Longer Life – Osteoporosis) educational series. Through these series the Garvan Institute is partnering with the premier scientific (Australia and New Zealand Bone and Mineral Research Society) and patient organisations (Osteoporosis Australia) as well as the Australian Women’s Coalition and the Rural Health Education Foundation (RHEF). This series, which is planned to rollout across Australia, combines up-to-date information for primary health care (GPs) as well as Public education to set up an environment in which more appropriate health care can be achieved. The linkage with the RHEF will facilitate the most efficient delivery of this reliable information to rural and remote doctors and the public.

**Bone Biology**

**Group Leader: Dr Paul Baldock**

This group’s research continues to be focused upon understanding how the brain controls bone formation and strength. This work continues its close collaborations with researchers in the Neuroscience Program using unique transgenic mouse models. These investigations have expanded from an initial focus on neurotransmitter Neuropeptide Y (NPY) to other integrated neurotransmitters that regulate the production of bone and its strength and the tightly linked control of body composition, including fat and lean mass, and clinically important responses to stress. This work is leading to novel targets and new approaches to treatment.

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Professor John Eisman and Associate Professor Jackie Center (standing) with visiting Norwegians, Professor Haakon E. Meyer and PhD student Helene Devold. Professor Haakon and Ms. Devold (from the University of Oslo) are doing collaborative work with Garvan on behalf of NOREPOS (Norwegian Epidemiological Osteoporosis Studies), a research collaboration network from five different scientific institutions across Norway.
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.

**Antibody Development (ADL)** facility focuses on the generation of monoclonal antibodies against targets from the Garvan research programs. Monoclonal antibodies represent almost half of all drugs entering clinical studies, with more than $30 billion sales worldwide in 2010. The ADL provides an essential platform for translational research at Garvan and is developing new antibody-based drug candidates. It also provides support for academic research within all Garvan programs.

**Australian BioResources (ABR)** facility, based in Moss Vale, breeds genetically modified mice under clean conditions for Garvan and 10 partner institutes, all involved in medical research. Additional services provided include the import and export of mice, recreation, embryo and sperm freezing, DNA preparation interfacing with Garvan’s mouse genotyping service, and microinjection to produce novel transgenic lines.

**The Biological Testing Facility (BTF),** located at Garvan Darlinghurst, receives mice from ABR for holding during experimentation. The BTF contains both standard and specialised holding facilities to enable a range of research activity under clean containment conditions. The BTF is being refurbished in 2011 and 2012 to allow effective logistics support and integration with The Kinghorn Cancer Centre’s animal imaging facilities. BTF staff provide training and support for research staff in the use and care of animals during research.

**Australian Cancer Research Foundation (ACRF)** facility houses equipment that can detect and analyse genomic and epigenomic variations on a large scale. Diverse platforms and robotics are available for facilitating research within and outside Garvan. The facility strives to achieve high-throughput, sensitivity, accuracy and cost effectiveness. In addition to capillary sequencing, the facility offers an SNP genotyping and methylation quantification service. In collaboration with the ABR DNA extraction service in Moss Vale, the ACRF facility also offers a mouse genotyping service that is available for all researchers in NSW.

**Clinical Research Facility (CRF)** 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 people. 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.

**The MLC Community Foundation Flow Facility** is a world-class cytometry facility that provides cell sorting and analysis services to Garvan and the St Vincent’s Research Precinct as well as the wider research community. While the facility can visualise, identify and localise a wide variety of particles (including cells, bacteria, algae, microparticles and even marine microorganisms) the bulk of its work lies in identifying and sorting mammalian cells for the understanding and treatment of diseases such as cancer, diabetes and a range of immunological disorders. Modern flow cytometers can assess the physical and functional characteristics of cells at up to 200,000 events per second and can rapidly identify and sort populations that could be easily missed by other techniques. The facility is currently one of Australia’s largest core cytometry facilities and provides access to some of the most technologically advanced instrumentation in the world.

**Molecular Imaging Facility** consists of a number of state-of-the-art microscopes, which are capable of imaging tissue, cells, organelles inside cells and even individual molecules in live cells. Using techniques such as total internal reflection fluorescence (TIRF) microscopy, it is possible to image events occurring on or near the surface of a cell. Laser scanning confocal microscopy can precisely image ‘slices’ of samples, which can then be reconstructed into a 3D representation for analysis. The recently acquired multiphoton microscope captures images deep within living tissue and the electron microscope can resolve structures way beyond the limits of conventional light microscopy. With these tools, Garvan scientists have the best possible means of identifying where and when molecules of interest are in normal tissue and how this may differ in disease.

**Peter Wills Bioinformatics Centre** applies techniques from fields like physics, chemistry, applied mathematics, statistics and computer science to achieve a genome-wide understanding of biology and disease. During 2011 we added 20 analytical tools to our GenePattern analysis environment and continued to grow our microarray archive, caArray.

As high-throughput sequencing costs have continued to fall we saw large sequence-driven projects like 1000 genomes and The Cancer Genome Atlas rapidly expand, and had more Garvan researchers embracing high-throughput sequencing for their own projects and begin using data from these large sequence-driven projects. A large equipment grant from Cancer Institute NSW will see the establishment of a 1000 core computer cluster with expanded storage on a very fast computer network. The cluster will empower users to do their own high-throughput sequencing analyses and analyse data from these large sequencing studies using a software system called Galaxy.
_ Undertook joint OHS and HR initiatives to promote health and wellbeing activities, services and information to staff, including free influenza vaccinations.

_ Ran an in-house management course for developing leadership skills among promising research and administrative staff.

_ Increased resourcing for research and grants administration to ensure that Garvan’s researchers are provided with high levels of support and assistance in managing their grant funds, and that the Institute complies with its obligations under funding agreements and other regulatory aspects of conducting research.

_ Undertook the complete re-membraning of levels 11 and 12 to prevent water leaking to level 10 laboratories.

_ Converted several rooms on level 4 to accommodate the establishment of a next-generation sequencing facility.

_ Carried out controller upgrades to all 17 fume cupboards in the building - providing more accurate user information, greater efficiency in operation and future expandability.

_ Completed major works that significantly increase Garvan’s computing capability. Two large upgrades to the main file server saw dramatic increases in Garvan’s ability to store and manage the huge volumes of scientific data pouring out of high-end scientific tools (see graph).

_ Installed additional uninterruptable power supply (required to keep the computer servers safe in the event of fluctuations in power supply) as well as additional cooling capacity. Much of this work was funded by a $1m CINSW grant successfully proposed by Dr Warren Kaplan of the Peter Wills Bioinformatics Centre. The final component of this grant will be the installation of a 1000-core high performance computer (HPC) server due to be installed in early 2012. This computing capability will now allow Garvan’s researchers to ask and answer the complex research questions posed by modern genome-based medical research.

_ Developed and released additional capability in information management tools such as CanSto for research in pancreatic, breast, prostate and lung cancer, as well as mesothelioma (for the Asbestos Disease Research Institute) and pituitary disease. A new Mass Spectrometry information management solution was deployed that, for the first time, allows Garvan researchers to answer questions about how their proteins behave across multiple experiments.

_ Enhanced ‘Stuart’, the application developed in-house for management of animal breeding and research.

_ Increased the number of cages held at the Australian BioResources facility (ABR) from 8,000 in January to 9,500 by the end of 2011, moving the facility to 65% capacity.

_ Increased ABR partners from 7 to 10, with ANZAC Institute, researchers at Monash University and one researcher at University of Wollongong signing partnership agreements.

_ Appointed a Scientific Services Manager at ABR to introduce new services including sperm freezing and microinjection.

_ Renovated several rooms in the former breeding area of the Biological Testing Facility (BTF). This has provided additional procedures rooms, an expanded immunodeficient suite and specialised labs for hearing studies. Further renovation of this facility will take place in 2012.
Overview

The Business Development team works with the biotech and pharmaceutical sector and other organisations to translate Garvan’s research discoveries to clinical use.

Engaging with Garvan’s researchers, the Business Development team is responsible for all aspects of commercialisation from capturing intellectual property and identifying development opportunities through to negotiation of industry agreements. Importantly, it establishes collaborations with organisations and companies who have additional technologies which greatly increase the potential for Garvan’s breakthroughs to be developed for clinical use.

The Garvan patent portfolio comprises 21 patent families covering treatment, diagnostics and screening categories.

G2 Therapies

Garvan’s most clinically advanced program is through G2 Therapies, a private company chaired by Dr John Schubert AO.

G2 has an exclusive licensing agreement with Danish healthcare company Novo Nordisk to develop an anti-C5aR antibody. 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

Business Development Advisory Council (BDAC) provides strategic advice to Business Development. BDAC has several representatives from the biotech and pharmaceutical industries.

Dr Lisa McIntyre (Chair)
Director, L.E.K. Consulting

Professor John Shine AO FAA, Executive Director, Garvan

Dr George Moore, External Director

Dr Merilyn Sleigh, External Director

Dr Mike Hirshorn (deceased November 2011), Director, Four Hats Capital

Mr Manoj Santiago, Partner, PricewaterhouseCoopers

Mr John Dakin, Chief Operating Officer, Garvan

Ms Christina Hardy, Director, Business Development & Legal Affairs, Garvan

Professor Trevor Biden, Diabetes & Obesity Research Program, Garvan
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Garvan Institute Board

William D 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 and in October 2011 joined the expert panel for the Federal Government’s Strategic Review of Medical Research in Australia. Former directorships include: Chairman, Australian Trade Commission (Austrade), Austar United Communications Limited, and Bradken Resources Pty Ltd. Mr Ferris is also a director of the Garvan Research Foundation and member of the Harvard Business School Asia Pacific Advisory Board. 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.

Warren Scott
Treasurer (from August)
Nominated by the NSW Minister for Health
Mr Warren Scott is the General Counsel of the Australian Prudential Regulation Authority and former Managing Director and the General Counsel of Citigroup 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, the Australian Law Council, and the California Bar Association. Mr Scott is admitted as a solicitor in New South Wales and as a lawyer in New York and California.

Martin Hoffman
Treasurer (until August)
Nominated by the Sisters of Charity
Mr Martin Hoffman is currently the Deputy Secretary of the Commonwealth Department of Resources, Energy and Tourism. He joined the Australian Public Service in March 2009 as First Assistant Secretary in the Department of the Prime Minister & Cabinet. Mr Hoffman previously had a lengthy private sector career primarily in digital media and technology, including as CEO of NineMSN, Australia’s largest internet media company, and as a venture capital investor and executive to smaller companies. He also held senior management roles with Fairfax Media and Optus.

Annette Cunliffe RSC
Nominated by the Sisters of Charity
Sister Annette attended St Vincent’s College Potts Point before becoming a Sister of Charity. She completed a Bsc (UNSW), Diploma of Education (UNE), Master of Education (Hons) (UNSW) and PhD (Griffith), meanwhile teaching in secondary colleges in various states, then holding the position of Senior Lecturer at Australian Catholic University. From 1996–2002 and since 2002 Sister Annette has been Leader of the Sisters of Charity of Australia. She has held the positions of President of Conference of Leaders of Religious Institutes (CLRI; NSW) and Inaugural Chair of the Stewardship Board of Catholic Health Australia and served on a number of incorporated boards.

Nicholas Curtis AM
(unchanged)
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 is the Chairman of Forge Resources Limited and of the corporate advisory firm, Riverstone Advisory Pty Limited. He served as a non-executive director of Conquest Mining Limited from 12 May 2010 to 18 October 2011 prior to the company’s restructure to become Evolution Mining. Mr Curtis also serves as Chairman of Faces in the Street Urban Mental Health Research Institute at St Vincent’s Hospital Sydney. He previously served as Chairman of the Board of St Vincents & Mater Health Sydney from 2004–2009 and as a director of St Vincent’s Health Australia Ltd and St Vincent’s Healthcare Ltd from 2004–2010.
Geoff Dixon  
Nominated by the Garvan Research Foundation  
Mr Geoff Dixon was Managing Director and Chief Executive Officer of Qantas Airways Limited from 2001–2008. He joined Qantas in 1994 and was also Chief Commercial Officer and, for two years, Deputy Chief Executive. He has also worked in the media, mining and government sectors. Mr Dixon is currently Chairman of the Australian Government’s major tourism marketing organisation, Tourism Australia, and Chairman of the Garvan Research Foundation and Queensland Events. He sits on the boards of publicly listed Australian companies Crown Limited, Consolidated Media Holdings and Facilitate Digital. He is on the boards of Voyages Indigenous Tourism Australia, the Museum of Contemporary Art and the Great Barrier Reef Foundation, and is an Ambassador for the Australian Indigenous Education Foundation.

Annette Pantle  
Nominated by the NSW Minister for Health  
Dr Annette Pantle completed her MBBS at the University of Sydney before pursuing a career in rural general practice and then metropolitan medical administration. Dr Pantle also holds a Masters of Public Health, a Graduate Diploma from the University of Sydney, and holds the position of Honorary Professor of Medicine. She is currently a member of Council of the NHMRC, Chairman of the Healthcare Committee and of the Prosthesis Listing Advisory Committee of the Australian Government. Professor Horvath is an independent non-executive director of Crown Ltd Crown Ltd and Crown Melbourne Ltd. Professor Horvath is a fellow of the Royal Australasian College of Physicians and is a distinguished practitioner, researcher and teacher. Professor Horvath was previously a clinical professor of medicine at University of Sydney, a specialist renal physician at Royal Prince Alfred Hospital (RPA), and Area Director of Renal Services for the RPA 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 directorships of companies in a range of industries including financial services, property and life sciences. She is on the boards of the Goodman Group Limited, Ardent Leisure Group Limited, Reva Medical Inc, GI Dynamics Inc and Clearview Wealth Limited. Ms Keating is also a member of the RBS Group (Australia) Advisory Council, a governor of the Cerebral Palsy Foundation and a trustee of the Centennial Parklands and Moore Park Trust. Her former boards include Insurance Australia Group Limited, NRMA Limited, STW Group, 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 non-executive director of the HCF Group, and I-MED Australia. She is also a member of the Commercial Executive Committee of CSIRO. Dr McIntyre was formally a senior partner with LEK Consulting in Boston and Sydney where she led the firm’s Asia Pacific Life Science and Health Care practice. She has spent the majority of her career as a strategy consultant advising companies and organisations in the health and life sciences sector on growth strategies and performance improvement. Dr McIntyre continues to serve as a Senior Advisor to LEK Consulting in Australia.

Annette Pantle  
(from October)  
Nominated by the Sisters of Charity  
Dr Annette Pantle completed her MBBS at the University of Sydney before pursuing a career in rural general practice and then metropolitan medical administration. Dr Pantle also holds a Masters of Public Health, a Graduate Diploma from the Australian Institute of Company Directors and Fellowship of the Royal Australasian College of Medical Administrators. She also holds a Fellowship of the Australasian Association for Quality in Health Care and is the current president of that organisation. Dr Pantle most recently served as the Director Clinical Practice Improvement for the NSW Clinical Excellence Commission – a statutory health corporation with responsibility for building capacity for quality and safety improvement and reporting to the NSW Minister for Health. Dr Pantle was responsible for the development and implementation of clinical quality improvement projects and programs across NSW Health, incorporating evidence into practice and instituting change management and project management processes. Dr Pantle joined St Vincent’s Health Australia in 2010 as Group General Manager Clinical Governance and Chief Medical Officer.

Greg Paramor  
Nominated by the Garvan Research Foundation  
Mr Greg Paramor is CEO of Folkestone Limited. Mr Paramor 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, Paladin Australia and the James Fielding Group. He was the CEO of Mirvac between 2004 and 2008. Mr Paramor is a past president of the Property Council of Australia and a past president of Investment Funds Association, a fellow of the Australian Property Institute and The Royal Institute of Chartered Surveyors. Mr Paramor is a director of a number of not-for-profit organisations and is also a board member of the Sydney Swans and LJ Hooker.
Daniel Petre AO
(from October)
Nominated by the Trustees of St Vincent's Hospital
Mr Daniel Petre has been at the forefront of the technology industry in Australia for more than 25 years. Currently he is Chairman of netus (a technology investment joint venture with News Ltd) and prior to this role he founded Australia’s largest internet investment company, ecorp, (a subsidiary of PBL, Publishing and Broadcasting Limited). Mr Petre spent nine years with Microsoft where he held a range of roles both in Australia and the US. He was Managing Director of the Australia subsidiary for three years before moving to the US as Vice President in the Development Group then returning to run the Asia-Pacific region for Microsoft. Mr Petre has served in many corporate and not-for-profit boards and currently serves on the Board of the Sydney Children’s Hospitals Network and the advisory boards for the Private Ancillary Fund Service at SVA (Social Ventures Australia), CSI (Centre for Social Impact) and the University of NSW.

Steven Rubic
Nominated by the Sisters of Charity
Mr Steven Rubic was appointed CEO of St Vincents & Mater Health Sydney 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 Health Industry Superannuation, Macquarie University Council, a member of the Department of Health & Ageing Second Tier Default Health Insurance Committee and is a past chairman of the NSW Private Hospitals Association. Mr Rubic is a fellow of AICD and AIST.

Jillian Segal AM
Nominated by the University of NSW
Ms Jillian Segal is a director of the National Australia Bank and ASX Limited. She is also Deputy Chancellor of the University of NSW and involved with a number of other community not-for-profit organisations, including as Chairman of the General Sir John Monash Foundation. Ms Segal is also a member of the Federal Government’s Remuneration Tribunal. 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
(until December)
Appointed by the Garvan Institute Board
Professor John Shine was Executive Director of the Garvan Institute of Medical Research until 31 December. He is Professor of Molecular Biology, Professor of Medicine at the University of NSW and President of the Museum of Applied Arts and Science. As well as Chairman of CSL Ltd, Professor Shine is a director or member of many scientific, research and medical bodies throughout Australia, including the Prime Minister’s Science, Engineering & Innovation Council (PMSEIC), and is the recent ex-Chairman of the National Health and Medical Research Council (NHMRC).

Peter Smith
Nominated by the University of NSW
Professor Peter Smith is Dean of Medicine at the University of NSW. He specialised in cancer medicine and research following study in Australia, USA and Germany. Peter has held senior hospital management posts in Brisbane and Melbourne and senior academic appointments at the universities of Queensland, Melbourne and Auckland. He is a Group Captain, RAAF and Director, Air Force Health Reserves (NSW/ACT), Directorate of Health Reserves, Air Force and has served as a consultant to governments in Australia and New Zealand. Professor Smith is currently a board director of St Vincent’s Health Australia, Neuroscience Research Australia, Ingham Medical Research Institute, the Sax institute for Health Research and the Arts and Health Foundation.

Bernadette Tobin
Nominated by the Trustees of St Vincent’s Hospital
Dr Bernadette Tobin is the 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, an honorary associate professor in the Faculty of Medicine at the University of Sydney, and a conjoint associate professor in the School of Medicine at the University of NSW. 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.
Garvan Research Foundation

Geoff Dixon
Chairman
Mr Geoff Dixon was the Managing Director and Chief Executive Officer of Qantas Airways Limited from 2001-2008. He joined Qantas in 1994 and was also Chief Commercial Officer and, for two years, Deputy Chief Executive. He has also worked in the media, mining and government sectors. Mr Dixon is currently Chairman of the Australian Government’s major tourism marketing organisation, Tourism Australia, and Queensland Events. He sits on the boards of publicly listed Australian companies Crown Limited, Consolidated Media Holdings and Facilitate Digital. He is on the boards of the Garvan Institute, Voyages Indigenous Tourism Australia, the Museum of Contemporary Art and the Great Barrier Reef Foundation, and is an Ambassador for the Australian Indigenous Education Foundation. He joined the Foundation Board as Chair in 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 EZI for 13 years and has consulted with corporate boards and companies of all sizes. She often attends speaking engagements and has published many articles on CEO succession and diversity at the executive and board level. She also leads a number of global strategy initiatives roles for one of the firm’s core client practices. She has been the 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 a member of Chief Executive Women, a network of Australia’s top women leaders. Prior to joining EZI she worked at Procter & Gamble in 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.

Bruce Baird
AM
The Hon Bruce Baird has an impressive career spanning the Australian Trade Commission and the parliaments of NSW and the Commonwealth. Mr Baird currently serves on several national boards including as Chair of Tourism & Transport Forum and the Commonwealth’s Refugee Resettlement Advisory Council. Among his positions with the NSW Parliament, he was a member of the NSW Legislative Assembly from 1984-1995, serving as Shadow Minister for Finance, then for Transport and Aboriginal Affairs, as Minister for Transport and Regional Services, Minister for Sydney’s Olympic Bid, and Minister for Tourism and Roads. He was the Deputy Leader of the Liberal Party in NSW from 1992-1995. From 1995 he served as Managing Director of the Tourism Council Australia and as Chair of National Rail Corporation and a director of ABN AMRO Hoare Govett, Tourism Training Australia and Tourism Education Services. He served in Federal Parliament, House of Representatives, from October 1998 until his retirement at the 2007 election. Mr Baird joined the Foundation Board in 2010.

Melinda Conrad
Ms Melinda Conrad is currently a non-executive director of APN News & Media, The Reject Shop Limited, the NSW Government’s Clinical Excellence Commission and Agency for Clinical Innovation, and the Australian Brandenburg Orchestra. Ms Conrad is the former founder and CEO of a retail chain of stores and was previously an executive at Colgate Palmolive. She has extensive expertise in strategy, retail, marketing and business development. She holds an MBA from Harvard Business School and is a member of the Australian Institute of Company Directors. 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.

William D 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 Australasia. Mr Ferris is Chairman of the Health and Hospitals Fund Advisory Board as part of the Federal Government’s Nation-building Funds initiative and in October 2011 joined the expert panel for the Federal Government’s Strategic Review of Medical Research in Australia. Former directorships include: Chairman, Australian Trade Commission (Austrade), Austar United Communications Limited, and Bradken Resources Pty Ltd. Mr Ferris is the Chairman of the Garvan Institute and a member of the Harvard Business School Asia Pacific Advisory Board. 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 is currently a director of Queensland Investment Corporation Limited, IMB Limited, Global Mining Investments Limited, and Commonwealth Superannuation Corporation. Ms Gearing was the Chief Executive Officer of the NSW State Superannuation schemes from 1997-2002, and has substantial experience in superannuation, funds management, corporate finance and management consulting. Ms Gearing joined the Foundation Board in 2005.
Mr Loftus Harris is a non-executive director on various boards, the immediate past National Chair 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.

Mr Wal King has worked in the construction industry for over 40 years and was the Chief Executive Officer of Leighton Holdings Limited, a company with substantial operations in Australia, Asia and the Middle East, from 1987 until his retirement on 31 December 2010. He remains as a consultant. Mr King is Deputy Chairman of Ausdrill Limited, a director of Coca-Cola Amatil Limited, the University of NSW Foundation Limited and Kimberley Foundation Australia Limited, and a council member of the University of NSW. Mr King is an honorary fellow of the Institution of Engineers Australia; a foundation fellow of the Australian Institute of Company Directors, and a fellow of the Australian Institute of Management, the Australian Academy of Technological Sciences and the Australian Academy of Technological Sciences and Engineering. Mr King joined the Foundation Board in 2010.

Mr John Landerer is a solicitor specialising in corporate advisory work and is also a professional company director. He is currently Chair of Goldsearch Limited and other private companies. He has served as the Chair 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 holds an honorary doctorate from Macquarie University in business and commercial law. 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 Foundation Board in 2007.

Mr Simon Mordant is Co-Chief Executive of Greenhill Caliburn, a leading independent corporate advisory firm specialising in advising major corporates on their merger and acquisition and capital markets strategies. He is a chartered accountant and is Chair of the Museum of Contemporary Art, a director of the Sydney Theatre Company and Commissioner for Australia at the 2013 Venice Biennale. He is a member of the International Council of the Tate, the Leadership Council of the New Museum, the International Council of the Museum of Modern Art and a member of the Executive Board of Wharton Asia. Mr Mordant joined the Foundation Board in 2009.

Sister Clare entered the Sisters of Charity following nurse training at the Mater Hospital in Brisbane. She has over 43 years experience in health and research services. Her ministry experience includes health, welfare, governance and administration, serving on boards within the Sisters of Charity Health Service and other Church bodies. Her present Ministry is one of hospitality. Hospitality to women who have loved ones in hospital within the St Vincent's campus, to patients who come from the Solomon Islands for health care within the St Vincent's campus, to women and men who suffer with mental health issues. Sister Clare joined the Foundation Board in 2010.

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.

Professor John Shine was Executive Director of the Garvan Institute of Medical Research until 31 December. He is Professor of Molecular Biology, Professor of Medicine at the University of NSW and President of the Museum of Applied Arts and Science. As well as Chairman of CSL Ltd, Professor Shine is a director or member of many scientific, research and medical bodies throughout Australia, including the Prime Minister's Science, Engineering & Innovation Council (PMSEIC), and is the recent ex-Chairman of the National Health and Medical Research Council (NHMRC).

Dr Jeanne-Claude Strong is a qualified medical practitioner with a post-graduate diploma in applied finance and investment and a Bachelor of Arts in Literature and Philosophy. Dr Strong established and ran three medical clinics in Melbourne and Sydney, focusing on occupational, sports and preventative medicine and stressing the importance of lifestyle management. She was a member of the Advisory Board of Bluearth for ten years, a not for profit organisation which promotes greater physical activity to reduce the incidence of disease and increase well-being. She is a pilot with a command multi engine instrument rating and has flown her own plane from California to Australia. Dr Strong has a passion for yacht racing with an occasional foray in international regattas. She illustrates that a successful life must be balanced, and the success of her full professional and personal life is testimony to her principles. Dr Strong joined the Foundation Board in 2011.


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Akerfeldt MC, Laybutt DR. Inhibition of Id1 augments insulin secretion and protects against high-fat diet-induced glucose intolerance. *Diabetes* 2011; 60:2506-14.


Akerfeldt MC, Laybutt DR. Inhibition of Id1 augments insulin secretion and protects against high-fat diet-induced glucose intolerance. *Diabetes* 2011; 60:2506-14.


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Deenick EK, Ma CS. The regulation and role of T follicular helper cells in immunity. *Immunology* 2011; 134:361-7.


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Shi YC, Baldock PA. Central and peripheral mechanisms of the NPY system in the regulation of bone and adipose tissue. *Bone* Epub 2011/10/20.


Valdes-Mora F, Song JZ, Statham AL, Strbenac D, Robinson MD, Nair SS, Patterson KI, Tremethick DJ, Strzaker C, Clark SJ. Acetylation of H2A.Z is a key epigenetic modification associated with gene deregulation and epigenetic remodeling in cancer. *Genome Res* Epub 2011/07/27.
### Garvan Institute of Medical Research

#### Income Statement

<table>
<thead>
<tr>
<th></th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
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<tbody>
<tr>
<td>NHMRC Grants</td>
<td>16,682</td>
<td>18,695</td>
<td>19,094</td>
<td>16,637</td>
<td>18,574</td>
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<td>Other Peer Reviewed Grants</td>
<td>8,530</td>
<td>9,159</td>
<td>11,061</td>
<td>10,232</td>
<td>10,896</td>
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<tr>
<td>Other Grants</td>
<td>1,068</td>
<td>4,811</td>
<td>1,624</td>
<td>-</td>
<td>1,869</td>
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<tr>
<td>NSW Government Grant</td>
<td>4,063</td>
<td>4,026</td>
<td>3,797</td>
<td>2,600</td>
<td>4,135</td>
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<tr>
<td>Commonwealth Government Grant</td>
<td>1,193</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Commercial Collaborations</td>
<td>2,714</td>
<td>1,289</td>
<td>737</td>
<td>202</td>
<td>347</td>
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<tr>
<td>Garvan Research Foundation</td>
<td>3,817</td>
<td>4,689</td>
<td>4,120</td>
<td>5,174</td>
<td>6,113</td>
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<tr>
<td>Other Income</td>
<td>3,543</td>
<td>4,050</td>
<td>7,470</td>
<td>6,872</td>
<td>9,167</td>
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<tr>
<td>Other Income (Insurance Claim Facade)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2,750</td>
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<tr>
<td><strong>Total Operating Income</strong></td>
<td>41,610</td>
<td>46,719</td>
<td>47,903</td>
<td>44,467</td>
<td>51,101</td>
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#### Remuneration Costs

<table>
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<tr>
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<tr>
<td>Remuneration Costs</td>
<td>23,621</td>
<td>27,337</td>
<td>28,322</td>
<td>29,196</td>
<td>32,215</td>
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<td>Research Expenditure</td>
<td>7,640</td>
<td>9,377</td>
<td>7,883</td>
<td>7,517</td>
<td>6,828</td>
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<tr>
<td>Administration and Information Technology</td>
<td>3,771</td>
<td>5,331</td>
<td>4,822</td>
<td>3,989</td>
<td>5,115</td>
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<tr>
<td>Building and Scientific Operations</td>
<td>2,461</td>
<td>2,753</td>
<td>3,324</td>
<td>6,272</td>
<td>4,743</td>
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<tr>
<td><strong>Total Operating Expenses</strong></td>
<td>37,493</td>
<td>44,798</td>
<td>44,351</td>
<td>46,974</td>
<td>48,901</td>
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#### Building Asset Amortisation

<table>
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<tr>
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<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
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</thead>
<tbody>
<tr>
<td>Building Asset Amortisation</td>
<td>(1,180)</td>
<td>(1,189)</td>
<td>(1,657)</td>
<td>(1,659)</td>
<td>(1,723)</td>
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<tr>
<td>Property, Plant and Equipment Depreciation</td>
<td>(2,433)</td>
<td>(2,390)</td>
<td>(2,597)</td>
<td>(2,670)</td>
<td>(3,939)</td>
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<tr>
<td>Transfer from Building Reserve</td>
<td>1,047</td>
<td>1,047</td>
<td>1,047</td>
<td>1,047</td>
<td>1,047</td>
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<tr>
<td>Endowment Grants from Garvan Research Foundation</td>
<td>2,210</td>
<td>3,953</td>
<td>6,388</td>
<td>1,604</td>
<td>3,586</td>
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<tr>
<td>Endowment Earnings</td>
<td>2,589</td>
<td>1,700</td>
<td>958</td>
<td>1,192</td>
<td>1,665</td>
</tr>
<tr>
<td>Donations &amp; Bequests direct to/(from) Endowment Fund</td>
<td>-</td>
<td>5,393</td>
<td>(5,000)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Unrealised gain/(loss) on investment</td>
<td>-</td>
<td>(7,407)</td>
<td>1,922</td>
<td>(142)</td>
<td>(2,504)</td>
</tr>
<tr>
<td><strong>Net Income</strong></td>
<td>6,350</td>
<td>3,028</td>
<td>20,683</td>
<td>7,960</td>
<td>17,978</td>
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</table>

#### Accumulated Surplus Brought Forward

<table>
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<tr>
<th></th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accumulated Surplus Brought Forward</td>
<td>9,914</td>
<td>11,109</td>
<td>16,571</td>
<td>32,512</td>
<td>43,128</td>
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</table>

#### Transfer from/(to) Research Program Reserve

<table>
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<tr>
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<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
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<tbody>
<tr>
<td>Transfer from/(to) Research Program Reserve</td>
<td>(2,526)</td>
<td>380</td>
<td>(2,189)</td>
<td>1,133</td>
<td>(2,090)</td>
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#### Transfer from/(to) Endowment Reserve

<table>
<thead>
<tr>
<th></th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfer from/(to) Endowment Reserve</td>
<td>(3,664)</td>
<td>1,847</td>
<td>(2,530)</td>
<td>1,190</td>
<td>3,493</td>
</tr>
</tbody>
</table>

#### Transfer from/(to) Infrastructure Expense Reserve

<table>
<thead>
<tr>
<th></th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfer from/(to) Infrastructure Expense Reserve</td>
<td>1,035</td>
<td>207</td>
<td>(23)</td>
<td>333</td>
<td>-</td>
</tr>
</tbody>
</table>

#### Accumulated Surplus Carried Forward***

<table>
<thead>
<tr>
<th></th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accumulated Surplus Carried Forward***</td>
<td>11,109</td>
<td>16,571</td>
<td>32,512</td>
<td>43,128</td>
<td>62,509</td>
</tr>
</tbody>
</table>

* The Kinghorn Cancer Centre (TKCC).
** Garvan’s share of TKCC construction costs to date are capitalised (refer balance sheet - Asset Under Construction (TKCC)).
*** Includes funds for the construction of TKCC.
## Garvan Institute of Medical Research

### Balance Sheet

<table>
<thead>
<tr>
<th></th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current Assets</td>
<td>18,226</td>
<td>21,114</td>
<td>52,136</td>
<td>59,765</td>
<td>62,379</td>
</tr>
<tr>
<td>Property, Plant and Equipment</td>
<td>45,160</td>
<td>60,085</td>
<td>60,325</td>
<td>57,060</td>
<td>58,369</td>
</tr>
<tr>
<td>Asset Under Construction (TKCC*)</td>
<td>-</td>
<td>-</td>
<td>1,731</td>
<td>8,399</td>
<td>29,660</td>
</tr>
<tr>
<td>Endowment Fund**</td>
<td>27,103</td>
<td>25,255</td>
<td>27,786</td>
<td>26,597</td>
<td>23,103</td>
</tr>
<tr>
<td>Investment in associates</td>
<td>84</td>
<td>84</td>
<td>84</td>
<td>84</td>
<td>84</td>
</tr>
<tr>
<td><strong>Total Assets</strong></td>
<td>90,573</td>
<td>106,538</td>
<td>142,062</td>
<td>151,905</td>
<td>173,595</td>
</tr>
</tbody>
</table>

| Current Liabilities    | 8,343 | 7,860 | 23,372 | 26,187 | 29,995 |
| Provisions             | 3,042 | 3,545 | 3,986  | 4,125  | 5,102  |
| Borrowings             | 4,179 | 18,144| 18,078 | 18,054 | 18,028 |
| **Total Liabilities**  | 15,564| 29,549| 45,436 | 48,366 | 53,125 |

| Accumulated Surplus    | 11,109| 16,571| 32,512 | 43,128 | 62,509 |
| Reserves               | 63,900| 60,419| 64,114 | 60,411 | 57,961 |
| **Total Net Funds**    | 75,009| 76,990| 96,626 | 103,539| 120,470|

* The Kinghorn Cancer Centre (TKCC)

** Including cash and investments at market value.
## Garvan Research Foundation

### Statement of Funds

<table>
<thead>
<tr>
<th></th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statement of Funds</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Donations &amp; Pledges</td>
<td>4,961</td>
<td>6,277</td>
<td>4,026</td>
<td>5,231</td>
<td>4,696</td>
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<tr>
<td>Donations &amp; Pledges (for TKCC*)</td>
<td>-</td>
<td>584</td>
<td>1,742</td>
<td>7,126</td>
<td>9,390</td>
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<tr>
<td>Events</td>
<td>409</td>
<td>105</td>
<td>38</td>
<td>215</td>
<td>1,273</td>
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<tr>
<td>Bequests</td>
<td>1,847</td>
<td>3,132</td>
<td>7,764</td>
<td>2,981</td>
<td>6,356</td>
</tr>
<tr>
<td>Interest and Other Income</td>
<td>25</td>
<td>55</td>
<td>19</td>
<td>44</td>
<td>37</td>
</tr>
<tr>
<td><strong>Total Income</strong></td>
<td>7,242</td>
<td>10,153</td>
<td>13,589</td>
<td>15,597</td>
<td>21,752</td>
</tr>
<tr>
<td><strong>Fundraising Expenses</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1,184)</td>
<td>(1,114)</td>
<td>(1,268)</td>
<td>(1,496)</td>
<td>(2,152)</td>
<td></td>
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<tr>
<td>Grants to TKCC Joint Venture Partner</td>
<td>-</td>
<td>-</td>
<td>(1,170)</td>
<td>(3,528)</td>
<td>(4,723)</td>
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<tr>
<td><strong>Net Funds Raised</strong></td>
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<td>9,039</td>
<td>11,151</td>
<td>10,573</td>
<td>14,877</td>
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<td>Accumulated Funds Prior Years</td>
<td>78</td>
<td>109</td>
<td>507</td>
<td>(20)</td>
<td>248</td>
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<td><strong>Funds Available for Grants to Institute:</strong></td>
<td>6,136</td>
<td>9,148</td>
<td>11,658</td>
<td>10,553</td>
<td>15,125</td>
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<td>General Research</td>
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<td>926</td>
<td>1,010</td>
<td>1,200</td>
<td>1,200</td>
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<tr>
<td>Specific Research</td>
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<td>3,762</td>
<td>4,280</td>
<td>7,501</td>
<td>9,638</td>
</tr>
<tr>
<td>Endowment Funds</td>
<td>2,210</td>
<td>3,953</td>
<td>6,388</td>
<td>1,604</td>
<td>3,586</td>
</tr>
<tr>
<td><strong>Total Grants</strong></td>
<td>6,027</td>
<td>8,641</td>
<td>11,678</td>
<td>10,305</td>
<td>14,424</td>
</tr>
<tr>
<td>Accumulated Funds Carried Forward</td>
<td>109</td>
<td>507</td>
<td>(20)</td>
<td>248</td>
<td>701</td>
</tr>
<tr>
<td>Represented By:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assets</td>
<td>311</td>
<td>1,391</td>
<td>164</td>
<td>401</td>
<td>907</td>
</tr>
<tr>
<td>Liabilities</td>
<td>(202)</td>
<td>(884)</td>
<td>(184)</td>
<td>(153)</td>
<td>(206)</td>
</tr>
<tr>
<td><strong>Net Assets</strong></td>
<td>109</td>
<td>507</td>
<td>(20)</td>
<td>248</td>
<td>701</td>
</tr>
</tbody>
</table>

* The Kinghorn Cancer Centre (TKCC)