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.
"Human beings are incredibly complex organisms, made up of around 75 trillion cells that interact with each other in a very specific programmed way. Each cell has a complete complement of our genes, and so in a way is independent, although it needs the environment of the body, and the interaction with other cells, to survive.

You could think of the body as an orchestra, with cell types as instruments. Just as the violins or cellos have to come in at a certain point and adapt their performances to the other instruments, so our cells have to work together in concert.

We stay healthy if each cell type knows when to play and when to keep quiet – when to ‘switch on’ and when to ‘switch off’. By understanding this body-wide molecular and cellular interplay, we hope one day to understand and prevent disease."

Professor John Shine AO FAA
Executive Director
Garvan Institute of Medical Research

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.
I am pleased to report that Garvan continued its excellent record of research success in 2010, as measured by grants, publication impacts, national and international awards, and for that we are justly proud of our faculty and staff.

Several important strategic initiatives progressed during the year, including:
- The Kinghorn Cancer Centre, an exciting joint venture with St Vincent’s Hospital, moved to the early construction phase.
- The Institute’s International Scientific Advisory Council held its inaugural meeting and strongly endorsed the quality and direction of Garvan research, and
- Australian BioResources, our major breeding and holding facility for experimental mouse models in the Southern Highlands, expanded to 65% capacity and increased its partners from 7 to 10.

Financial Performance

Garvan's operating income was a pleasing $41m in 2010, a direct measure of the quality of Garvan research. Philanthropic support through the Garvan Research Foundation, essential for providing critical equipment and facilitating new initiatives, continued to be strong, with over $5.1m in general and specific grants contributed to research programs and almost $1.6m into the long term endowment fund of the Institute.

Our People

Garvan has been very well served for many years by the board and its counsel and an outstanding board of directors. During 2010 Sister Carol Pedersen completed her term on the board and I take the opportunity to express our gratitude for her commitment and insights over the past 5 years. Replacing Sister Carol, we welcomed Sister Annette Cunliffe, Congregational Leader of the Sisters of Charity in Australia. The Institute is particularly grateful for the additional contributions made by members of the major board committees – Finance and Audit, Business Development, and Remuneration.

Many Garvan researchers were distinguished with prizes and awards during 2010. Among them, Professor Rob Sutherland received the Cancer Institute NSW Premier’s Award for Outstanding Cancer Researcher and Dr Stuart Tange received the Academy of Science Gottschalk Medal, the most prestigious award in the field for early career researchers.

Of special note was the award of the 2010 Prime Minister’s Prize for Science to Professor John Shine. This is the nation’s top science award and recognised John Shine’s breakthrough discoveries in genetics and molecular biology. While too complex to summarise here, John’s achievements include the cloning of human hormone genes (insulin and growth hormone among others) and the demystification of fundamental genetic processes. It is my privilege to record in this report the Garvan community’s congratulations and gratitude to John for his outstanding contribution to medical advances worldwide.

Business Development

2010 saw excellent progress in several collaborations with the biotechnology and pharmaceutical industries. Of particular note, Garvan spin-out company, G2 Therapies, collaborated with the Danish pharmaceutical group, Novo Nordisk, to progress a potential treatment for inflammatory disorders through clinical development.

Internally, Garvan’s own Antibody Development Laboratory (ADL) sought to identify new antibody-based drug candidates, while the Cancer Development Laboratory focused on finding compounds that might inhibit the proliferation of cancer cells. Both initiatives aim to close the gap between early research and clinical development.

Looking Ahead

There will be many challenges in the year ahead as Garvan continues to grow. As we embrace the many new technologies that come with the current exciting rate of change, we are faced with ever-increasing equipment, resourcing and infrastructure costs.

Garvan, along with the rest of the medical research sector, must 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.

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.

With continued sound project management, and a modicum of good fortune, we can look forward to the opening of the $110m The Kinghorn Cancer Centre by June next year.

In the immediate months ahead much needs to be prepared and finalised for the appropriate resourcing of the Centre, in terms of Garvan and St Vincent’s faculty and staff, equipment for labs and patient care, and the on-going operational funding.

In all of this, it will be essential that the work of the Centre be fully understood by and integrated with Garvan as a whole. Only in this way can we hope to optimise the opportunities for moving more of our knowledge into improved clinical outcomes for patients.

There will be a later occasion when I, along with others, will be able to acknowledge the extraordinary achievements and contributions of Professor John Shine to Garvan and medical research. But on this day, his last formal delivery of a Garvan annual report, I wish to record on behalf of all Garvan supporters past and present, our deep admiration and gratitude for John’s energetic and inspiring leadership of this great institute over the past 20 years.

Bill Ferris AC
Chairman
Garvan Institute of Medical Research
2010 was another very productive year for Garvan in terms of significant research findings, success in obtaining competitive grants and growth in the number of papers accepted for publication in prestigious international journals. We published 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.

Research publication productivity was matched by success in applications for competitive grants. Overall peer reviewed grant funding was approximately $27m, including $16.6m from the National Health and Medical Research Council (NHMRC). Garvan’s Immunology Program was a successful partner in the renewal of a major NHMRC Program Grant. Similar recent success with ongoing program grants in our Cancer and Diabetes and Obesity Programs provides the capacity for longer term strategic planning of our research effort.

The 2010 review by our International Scientific Advisory Council was extremely gratifying, finding overall that the performance of our researchers... is excellent to outstanding and the research is performed at a very high level by international standards”. The council suggested several specific initiatives in bioinformatics, proteomics and clinical research that could bolster Garvan research in the future. These recommendations were fully supported by the Institute’s executive and Board, although their implementation will depend on obtaining additional resources.

Of particular importance in 2010 was support from Garvan donors in helping us upgrade critical research facilities. Our sincerest appreciation goes to Christina and Trevor Kennedy and to Val and Peter Duncan, whose respective contributions allowed us to purchase an electron microscope and two-photon microscope. Other significant donations enabled the acquisition of two new cell sorters and mass spectrometry equipment.

Translational Research Initiatives

Construction of The Kinghorn Cancer Centre (TKCC) began in earnest during 2010 and was paralleled by intensive planning between Garvan and St Vincent's Hospital to ensure that the research and clinical programs were ready for the opening of the Centre in early 2012. At this stage it is agreed that the initial focus will be on breast, prostate, pancreatic and blood cancers – important cancers where the two institutions have particular strengths.

The St Vincent’s Diabetes Centre was relocated to Garvan during 2010 as part of the construction program for TKCC, providing Garvan and St Vincent’s with an opportunity to extend their already close collaborative relationship in diabetes research and care.

Ongoing findings from our important long-running Dubbo Osteoporosis Epidemiology Study confirmed the benefits of effective treatment of osteoporosis, not only for improved quality of life, but also for actual length of life.

Our People

Staff numbers across the organisation grew to a total of 505. Growth was particularly strong in our Cancer, Immunology and Diabetes and Obesity Programs, reflecting ongoing success in competitive grant applications for new and existing projects.

Consistent with its role in international medical research, 55 different countries are represented in Garvan’s research community. During 2010, 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.

Australian BioResources (ABR)

The state-of-the-art holding and breeding facility for experimental mouse lines at Moss Vale provides critical infrastructure for Australian innovation. The facility completed another highly successful year of operation in 2010, holding over 30,000 mice. This is rapidly approaching total capacity for stage 1 of the facility which now holds all major breeding colonies for Garvan and 10 partner institutes.

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.

2011

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 2011 we will remain clearly focused on elucidating the fundamental basis of disease. We will also drive the translation of our research discoveries into new and improved ways to prevent and treat the major diseases that challenge our society.

John Shine AO FAA
Executive Director
Garvan Institute of Medical Research
I am very pleased to report that the Foundation’s results have surpassed budgeted expectations for 2010 with gift and bequest income of $8.5m. An additional $7.1m was donated specifically to The Kinghorn Cancer Centre, bringing total income to $15.6m.

Gift Income

The relationships the Foundation team helps to forge between researchers and philanthropic supporters are absolutely critical to the ongoing success of an organisation like Garvan. Gift income excluding bequests totalled $5.5m this year.

We are blessed in having a community of support that includes incredibly generous individuals such as Peter and Valerie Duncan, who together gifted over $600,000 to purchase a two-photon microscope for the Institute. The Ernest Heine Family Foundation and Mrs Janice Gibson have committed $3m over five years for the establishment of a named Chair in Osteoporosis Research. Mr James Packer has supported a Fellowship to enable recruitment of a new group leader in diabetes.

Requests increasingly form a most important part of our gift income, and we have been fortunate this year to receive just under $3m income of this nature. Gifts such as the bequest made by George Quigg, who was one of our most faithful Partners for the Future, can make such a difference to the Institute. George enjoyed attending our events in his trademark Akubra hat and agreed to be featured in our bequest promotional materials. We were incredibly grateful to learn that he had also personally bequeathed over $1m to Garvan.

The Kinghorn Cancer Centre

The Foundation successfully completed its part in the $110m capital campaign to build The Kinghorn Cancer Centre. Around $40m was raised in philanthropic funding, largely facilitated by the $25m commitment by the Kinghorn Foundation, an exceptionally generous gift and the largest private donation we have ever received.

The second phase of fundraising for positions and equipment got underway in late 2010. Mr Daniel Petre made a commitment to establish a Petre Chair in Prostate Cancer Research in the Centre - a commitment which is all the more generous given that in 2003 he had already established the Petre Chair in Breast Cancer Research. The Australian Cancer Research Foundation also made a most significant commitment with a grant of $5m in honour of Lady (Sonia) McMahon, one of their Founding Trustees.

Events

The Young Garvan Committee is to be congratulated on a most successful launch of their concept event, the All Ribbons Ball. Held in August at the Sofitel with Pfizer as the major sponsor, the Ball attracted over 400 guests and netted $70,000. This enabled two Young Garvan Fellowships to be awarded to outstanding young scientists. The recipients were Dr Liz Caldon, for her work on breast cancer, and Dr Matt Prior, for his work on Type 2 diabetes.

MS Dianne Lavender, Public Relations Manager, instigated and carried through an audacious concept this year – challenging the official Guinness World Record for building the longest DNA model. The previous record, held by a university in Japan, was 22.5m. Bringing together 150 students from six different high schools, Garvan smashed the record by building a DNA model of the neuropeptide Y gene which was 25.66m long.

The Foundation team also successfully ran our second Open Day, attracting nearly 900 guests to listen to our expert panel on ‘What will it take to cure cancer?’ and chat with our scientists at booths dedicated to everything from hearing loss to prostate cancer.

Board and Staff Movements

I wish to take this opportunity to thank my fellow directors for the support they offer to the Foundation.

I would like to acknowledge the major contribution and long service of Mr Byram Johnston, a director from 1997 to 2010. Mr Johnston was instrumental in the establishment of our bequest program, a testament to his far-sightedness. We also farewelled Sister Paulina Pilkington, who represented the Sisters of Charity on the board from 1994. Her wisdom and encouragement was particularly appreciated. Mr Karim Temsamani left the board this year after two years of service to relocate to the US. In his leadership capacity at Google, Mr Temsamani assisted the Foundation team in the online space.

It has been my pleasure to welcome to the board, in the course of 2010, Mr Wal King AO and the Hon Bruce Baird AM. The skill sets of both these incredibly experienced new directors will be invaluable to the board.

Dr Anita Hoskins, Ms Carol O’Carroll and Ms Pip Margan joined the Foundation team as Public Engagement Coordinator, Bequests Officer and Events Manager respectively.

We close 2010 with the departure of our CEO, Carole Renouf, after five exemplary years of service at the helm of the Foundation. During her tenure, Carole and her team have dramatically increased fundraising for Garvan research. My fellow directors and I trust we can maintain the upward trend masterfully initiated by Carole, as philanthropic support of this scale and scope is so essential to the Institute’s ability to transform our health future.

I hope, and look forward to, the continued company of our supporters on this journey.

Geoff Dixon
Chairman
Garvan Research Foundation
After serving as Executive Director of Garvan for 20 years, Professor John Shine announced last year that he would be retiring in 2011, making 2010 his last full year at Garvan. All who know John will be sad to see him leave, and will wish him well in the years to come. What follows is a brief personal account of his years at Garvan.

When I started at Garvan in 1990, the organisation was fairly small and limited in its research scope. While respected in Australian medical research circles, it was representative of the scattered expertise around Sydney as opposed to the large, more integrated institutes of Melbourne.

An Act of Parliament had established Garvan’s independence in 1984, but its make up still revealed its origins within the endocrine department of St Vincent’s Hospital. The Founding Director, Les Lazarus, was an endocrinologist – as were several group leaders when I took over his role: John Eisman (head of bone research), Don Chosholm (head of diabetes research) and Ken Ho (head of pituitary research). Only Rob Sutherland (head of cancer research) was a cell biologist, recently recruited from the University of Sydney.

The Garvan Institute was in fact an amalgam of NHMRC funded research groups and researchers working for the NSW Endocrine Assay Service. In effect, hormone assays required for patients from around the State were sent to our labs for analysis and processing.

Unfortunately, the two streams of research confused our vision and divided our purpose. So one of my very first tasks when I became Director in 1990 was to transfer the assay service to SydPath – the pathology service of St Vincent’s Hospital.

The transfer allowed us to lift our research game and develop our critical mass, although it meant we lost the income from the assay service, an important source of infrastructure funding. While to this day we battle to meet our infrastructure costs, letting go of the assay service was ultimately a reasonable price to pay.

The 1990s saw a move away from observational research and measurement by assay towards research that focused on targeted hypotheses. By 1990, recombinant DNA and gene cloning were starting to make a big impact across all fields of research, with scientists mutating genes to see what would happen in specific disease models.

I had been immersed in gene cloning and recombinant DNA research for years, and when I arrived I was interested in gene families, especially receptor genes. In particular, I was looking at neuropeptide receptor families, with the aim of determining whether or not they held the key to the functional diversity of the nervous system. In other words, did structurally similar receptors achieve incredible diversity of function by binding the same neuropeptide but elicit very different cellular responses. This research interest helped spawn Garvan’s Neuroscience Program, which is now headed by Herbert Herzog who joined the lab as a young postdoctoral fellow in 1991.

Garvan’s success throughout the 90s was evident not only by the strength of its publications tally, but also by its impressive and diverse research outcomes. Scientists here were the first to pinpoint a gene involved in susceptibility to osteoporosis, the first to clone several neuropeptide receptor genes, including NPY, adenosine and galanin, the first to decipher important signalling pathways underlying insulin resistance, and the first to recognise the role of different cell cycle genes in the development of breast cancer.

After the molecular biology changes of the 90s came the ‘big’ science of our current century. The launch in 2000 of the first draft of the human genome led to huge sequence databases and gene arrays – no more single genes and painstaking testing of specific hypotheses. Gene chips now allowed us to look at 40,000 genes at once – to determine how gene expression is changed in disease. Fortunately we were able to embrace this new research paradigm quickly and were the first in Australia to install the new Affymetrix arrays. In a similar way, we have recently embraced proteomics, epigenetics and bioinformatics.

While technologies are undoubtedly important to research success, the human mind is obviously the essential factor. One of my favourite quotes is “imagination, based on knowledge, is the key to discovery”. As Director of Garvan, my core responsibility has been to develop our internal talent and at the same time recruit exceptional creative researchers. In 2000, we started to grow what has become an outstanding Immunology Program – by attracting Charles and Fabienne Mackay from the United States, and then other leading immunologists from the Centenary Institute. These distinguished researchers formed a critical mass in the discipline, which permeates all other Garvan research areas.

Today the gap between research discovery and its clinical application is smaller than ever. Garvan is developing a state-of-the-art translational cancer research centre described later in this report, our Osteoporosis Epidemiology Study is informing treatment decisions the world over, and our diabetes research is being seamlessly integrated with the St Vincent’s Diabetes Centre.

It has been an enormous privilege to be a part of Garvan’s journey from a small endocrine research unit to a major multi-disciplinary research institute.

John Shine
Organisation Chart

**Garvan Institute of Medical Research**
Board of Directors
- **Chairman**: Mr Bill Ferris AC
- **Executive Director**: Prof John Shine ACFAA

**Garvan Research Foundation**
Board of Directors
- **Chairman**: Mr Geoff O’ adjective

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

**Institute Committees**
- Executive Research
- Appointments & Promotions
- Scientific Advisory Council
- OH&S Consultation
- Operations Advisory
- Seminar Program
- Common Users of Building Equipment (CUBE)

**St Vincent’s Research Precinct (SVRP)**
Committees
- Animal Ethics
- Human Research Ethics
- Institutional Biosafety
- SVRP Management
- SVRP OH&S

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

Patent Portfolio by Category

<table>
<thead>
<tr>
<th>Portfolio</th>
<th>Percentage</th>
<th>Number of Patents</th>
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</thead>
<tbody>
<tr>
<td>Therapeutics</td>
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<td>1</td>
</tr>
<tr>
<td>Drug discovery tools</td>
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</tr>
<tr>
<td>New treatments</td>
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<td>6</td>
</tr>
<tr>
<td>Diagnostics</td>
<td>32%</td>
<td>7</td>
</tr>
<tr>
<td>Therapeutic target</td>
<td>32%</td>
<td>7</td>
</tr>
</tbody>
</table>

Scientific Publications

Impact factor of scientific publications

Each paper published constitutes a new piece of knowledge, and scientists aim to publish in the most highly regarded journal in their area of research. Each journal has an “impact factor” which is a common measure of its relative importance within a specific discipline. Research organisations use “average impact factor” measurements to determine the overall significance of their research output. For example, in 2010 Garvan achieved an “average impact factor” of 8.2 for the top 80% of its publications. This is a very respectable tally, well above the international benchmark.

Philanthropic Support

Total Income

(excluding bequests and contributions to the construction cost of The Kinghorn Cancer Centre)

- $2,790,000
- $4,158,000
- $5,370,000
- $6,521,000
- $3,485,000
- $5,561,000

Donations are particularly important in two respects:

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

Operating Income

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 and proceeds from a one-off insurance claim.

Staff Profile

<table>
<thead>
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<th>Staff Breakdown</th>
<th>2009</th>
<th>2010</th>
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<tbody>
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<td>290</td>
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<tr>
<td>Students</td>
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<tr>
<td>Scientific Facility Staff</td>
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<tr>
<td>Secretarial &amp; Admin</td>
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<td>10</td>
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<tr>
<td>DVOC</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>504</td>
<td>505</td>
</tr>
</tbody>
</table>

Demographics

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

Peer Reviewed Grant Income

<table>
<thead>
<tr>
<th>Year</th>
<th>$ Mil NHMRC</th>
<th>$ Mil Other</th>
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<tbody>
<tr>
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</tr>
<tr>
<td>2010</td>
<td>16,637</td>
<td>10,232</td>
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</table>
Research Collaborations
Tissue sample showing late stage breast cancer. Cancer cells (dark purple) can be seen invading milk ducts and surrounding tissue. Cancer cell photographs by Dr David Gallego Ortega.

RESEARCH HIGHLIGHTS

- Identified a new group of immune cells (a subset of T cells) that for the first time directly link two autoimmune diseases, Type 1 diabetes and Sjogren’s syndrome.
- Demonstrated that increasing the amount of a gene regulatory protein (nur77) in muscle had the same positive effect on glucose metabolism as exercise.
- Extended our prognostic models for predicting fracture risk for men and women implemented in www.fractureriskcalculator.com, widely used by doctors and patients worldwide.
- Showed why certain childhood cancers (sarcomas) are resistant to new therapies that target the cell surface receptor, insulin-like growth factor-1. These insights may lead to therapies that help overcome drug resistance in these patients.
- Showed in mice that tongue stem cells injected into the inner ear are incorporated into the cochlear tissue and have the potential to reverse noise-induced hearing loss.
- Showed that administration of a drug to block IL-21 (a key regulatory molecule of the immune system) protects transplanted insulin-producing pancreatic cells and reverses Type 1 diabetes in mice.
- Identified a new range of biomarkers that better define different subtypes of breast cancer. In particular they appear to distinguish between good and poor prognosis in hormone-responsive cancers.
- Demonstrated which sections of the genome are commonly ‘silenced’, or ‘switched off’, in prostate cancer. This work not only provides new diagnostic markers for prostate cancer, it suggests that all cancers show similarly widespread and specific silencing.
- Showed that a gut hormone released after we eat determines the speed at which we digest food and absorb nutrients across the gut into our blood. This makes it very influential in disorders such as Type 2 diabetes, and a promising therapeutic target.
- Showed that the cell cycle genes cyclins E1 and E2 are expressed in different phases of the cell cycle and that cyclin E2 overactivity in cancer causes more genomic aberrations than E1, helping explain why the two genes contribute to different patient outcomes.
- Showed for the first time that a primary tumour can be shrunk by inhibiting a particular class of gene known as a microRNA, a finding that provides hope for new microRNA-based therapeutics for cancer.
- Clarified how a pivotal class of immune cells known as ‘T follicular helper cells’ are generated. These cells play a critical role in helping the white blood cells known as ‘B cells’ make long-lived high-potency antibodies.
- Demonstrated the frequency of vitamin D insufficiency in general populations and in severely ill individuals in hospital. These findings suggest that vitamin D deficiency contributes to in-hospital mortality in the intensive care setting.
- Discovered that the SATB1 gene is silenced in lung and colorectal cancer, and that this is associated with poorer prognosis in both cancers.
- Demonstrated that a molecule on bone beta-blocker use and reduced fracture risk in elderly men and women.
- Demonstrated that the level and balance of gut bacteria can affect whether or not mice predisposed to developing Type 1 diabetes succumb to the illness – and that the same mice without any bacteria always become diabetic.
- Found an existing anti-inflammatory drug may combat insulin resistance in muscle by reducing the toxic by-products of fat metabolism.
- Co-led the Australian arm of the International Cancer Genome Consortium, which is cataloguing the genetic changes of the 50 most common cancers – and making them freely available to the broader scientific community. Australia’s focus is pancreatic cancer, and Garvan drove the clinical aspect of this research.
- Found a potential therapeutic target for preventing the loss of nerve cells that occurs in diseases such as Parkinson’s and Alzheimer’s.
- Found that an existing anti-inflammatory drug may combat insulin resistance in muscle by reducing the toxic by-products of fat metabolism.
- Discovered that the level and balance of gut bacteria can affect whether or not mice predisposed to developing Type 1 diabetes succumb to the illness – and that the same mice without any bacteria always become diabetic.
- Used cutting-edge protein technology to characterise new cellular signalling networks of breast and pancreatic cancer, as well as drug-resistant prostate cancer. This will assist in the design of targeted therapies for these different cancers.
“Cancer cells actually create an environment for themselves that allows them to thrive – a self-made kind of Darwinian selection. They stimulate the growth of new blood vessels to get more nutrients to the tumour, they de-activate genes that would kill them, and they encourage neighbouring cells to produce chemicals that will help them grow.

In breast cancers, for example, cancer cells often feed off the stromal cells that make up the breast’s connective tissue. The cancer cells effectively ask the stromal cells to send back signals that make them proliferate – and the stromal cells oblige.”

Professor Rob Sutherland AO FAA
Leader Cancer Program

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

Research Highlights

- Identified the protein PUMA as a new marker of tamoxifen sensitivity in hormone-responsive breast cancers.
- Used cutting-edge protein technology to characterise new cellular signalling networks of breast and pancreatic cancer, as well as drug-resistant prostate cancer. This will assist in the design of targeted therapies for these different cancers.
- Identified a range of biomarkers that better define different subtypes of breast cancer. In particular they appear to distinguish between good and poor prognostic in hormone-responsive cancers.
- Established a collaborative partnership with QUT/Diamantina Institute to identify genes that alter the response of breast cancer cells to anti-oestrogens, and so potentially develop treatments for the 25% of oestrogen receptor-positive breast cancer patients who do not respond to current hormone therapies.
- In collaboration with Monash University, identified that loss of the cell-signalling regulator, INPP4B phosphatase, is a common feature of basal breast cancer, a particularly aggressive subtype of breast cancer.
- Showed why elevated expression of the SerpinB2 protein in tumours is a marker of good prognosis in some breast cancer patients.
- Helped define the mechanism that underlies progesterin-promotion of breast cancer.
- Demonstrated that the cell cycle genes cyclins E1 and E2 are expressed in different phases of the cell cycle and that cyclin E2 overactivity in cancer causes more genomic aberrations than E1, helping explain why the two genes contribute to different patient outcomes.
- Detailed exactly how the two cancer proteins, cortactin and Gab2, use the same intermediate (RhoA) to communicate with other proteins in the cell, leading to increased cell proliferation or cell migration, respectively.
- Described a new role for the important cell surface receptor (beta1 integrin), which tells cells how to interact with their environment. This finding is significant for better understanding of the development of the urogenital tract, as well as prostate cancer.
- Showed why certain childhood cancers (sarcomas) are resistant to new therapies that target the cell surface receptor, insulin-like growth factor-1. These insights may lead to therapies that help overcome drug resistance in these patients.
- Discovered a new mutation in the SerpinA1 gene that causes alpha-1 antitrypsin deficiency, an inherited disorder characterised by chronic lung and liver disease.
- Identified a new mechanism for the control of tumour cell metabolism that might help in the development of cancer therapies. Tumour cells grow more quickly than normal cells because they change the way they burn fuel and oxygen.
- Demonstrated for the first time that a primary tumour can be shrunk by inhibiting a particular class of gene known as a microRNA, a finding that provides hope for new microRNA-based therapeutics for cancer.
- Together with collaborators in the USA and Queensland, discovered how tumours grow new blood vessels by recruiting cells from the bone marrow, and showed that blocking this process dramatically slows tumour growth.
- Co-led the Australian arm of the International Cancer Genome Consortium, which is cataloguing the genetic changes of the 50 most common cancers – and making them freely available to the broader scientific community. Australia’s focus is pancreatic cancer, and Garvan drove the clinical aspect of this research.
- Developed novel sequencing technologies and bioinformatics tools to unravel the layers of chemical change (chromatin modification and DNA methylation) that affect the ways in which genes behave without altering their sequence or structure.
- Demonstrated which sections of the genome are commonly ‘silenced’, or ‘switched off’, in prostate cancer. This work not only provides new diagnostic markers for prostate cancer, it suggests that all cancers show similarly widespread and specific silencing.
- Developed a new gene-based predictive tool that can identify those clinically localised prostate cancers that are likely to progress and require more aggressive therapy.
- In collaboration with the University of Adelaide, identified changes in histones which predict prostate cancer progression. Histones are the ‘beads on a string’ which help DNA coil into a tight structure.
- Discovered that the SATB1 gene is silenced in lung and colorectal cancer, and that this is associated with poorer prognosis in both cancers.

CANCER PROGRAM
_ Showed that the MCC gene, often expressed at low levels in the tumours of people with colorectal cancers, has an important role to play in how our cells cope with DNA damage. This helps explain why benign colon polyps develop into cancer and why some patients are more responsive to certain cancer treatments.

_ Developed a novel mouse model of colon cancer using a drug treatment that initially only causes irritation and surface tissue damage in the colon, but subsequently leads to cancer development. This model provides new insights into how colon cancer is triggered.

_ In collaboration with The Children’s Hospital at Westmead, identified two new proteins that are frequently over-expressed in ovarian cancer and are associated with different subtypes of this cancer, as well as different patient outcomes.

**People Highlights**

_ Professor Rob Sutherland was made an Officer of the Order of Australia (AO) for distinguished service to medicine as an international contributor to the research of cancer, the development of Australia’s research capacity and through leadership roles in ‘duty bodies’ and also won the NSW Premier’s Award for Outstanding Cancer Researcher 2010.

_ Professor Andrew Bainkin and the Pancreatic Cancer Research Group were awarded the Landon Foundation - American Association for Cancer Research INNOVATOR Award for International Research to establish the Johns Hopkins – Garvan Institute Pancreatic Cancer Alliance for a collaborative project with Ralph Hruban at Johns Hopkins.

_ Dr Alison Butt served as President of the American Association for Cancer Research Inovator Award for 2010 and wrote an Invited Report on the Human Variome Project.

_ Dr Falko Hochgrafé was awarded a Human Proteome Organization ‘Young Guns’ prize for his research characterising cellular signalling pathways in an aggressive type of breast cancer.

_ Wee Siang Teo was awarded the University Medal in Molecular Biology from the University of NSW for his Honours thesis and has been selected to attend the prestigious 2011 Nobel Laureates meeting in Lindau, Germany.

_ Dr Toby Holf was awarded a travelling prize to attend the EMBL Symposium Non Coding Genome, Germany, October, 2010.

_ Members of the Cancer Program were awarded over $9m in new competitive peer reviewed research grants for 2011 – 2015.

_ David Chang was awarded the 2011 American Society of Clinical Oncology Cancer Foundation Merit Award for developing a Biomarker Prognostic Nomogram for Pancreatic Cancer. The work was presented as an oral presentation at ASCO GI in San Francisco in January 2011.

_ Dr Falko Hochgrafé was awarded a Human Proteome Organization ‘Young Guns’ prize for his research characterising cellular signalling pathways in an aggressive type of breast cancer.

_ Emily Stoddart and Carole Tactacan received Cancer Institute NSW Research Scholar Awards. Venessa Chen was awarded the McCaughey Research Entry Scholarship from the Royal Australasian College of Physicians to commence her PhD in 2011.

_ Dr Liz Caldon was awarded a National Breast Cancer Foundation and a Young Garvan Fellowship.

_ Dr Darren Saunders and Dr Alex Swarbrick were given Conjoint Senior Lecturer appointments in St Vincent’s Hospital Clinical School, University of NSW.

_ Cancer Institute NSW awarded Career Development Fellowships to Dr Maja Kohonen-Corish and Dr Georgia Holloway, an Early Career Development Fellowship to Dr Marina Pajic, a Future Research Leader Fellowship to Dr Ilse Rooman and Clinical Research Fellowships to Professor Andrew Bainkin and Dr Sandra O’Toole.

_ The Cancer Institute NSW Cancer Program senior scientists are members of several major national and international networks: Professor Susan Ormandy on the NHMRC Project Grant Review and Program Grant Review panels; Professor Rob Sutherland on the NHMRC Project Grant Review panel and the NBCF Novel Concept Award Committee, Associate Professor Chris Ormandy on the NHMRC Project Grant Review panel and the NBCF Scientific Advisory Board, and Dr Alex Swarbrick has been selected to serve on the Health Research Council of New Zealand Biomedical Science Assessing Committee for 2011.

_ The Cancer Program received prizes for their conference presentations. The Inaugural Biomarker Discovery Conference in Shool Bay awarded Dr Kristina Warton (Early Cancer Researcher First Prize), Brian Gloss (Runners-Up Student Prize) and Dr Tina Selinger (Best MasterClass Hot Topics). Dr Clare Strizaker and Aaron Statham won a joint first place Poster Prize at the illumina User Symposium in Phuket, Thailand, Aaron Statham presented the Best Student Poster at AMARA, Hobart, Dr Chris Scarle was the joint winner of the Cancer Research Network Innovation Award at the Sydney Cancer Conference, The St Vincent’s and Mater Health Annual Research Symposium awarded Alex Shaw (Best Oral Presentation) and Warwick Lodge (Millennium Biotech Poster Prize).

_ Professor Roger Daly continued to serve on the Cancer Institute NSW Research Advisory Committee.

_ Several members of the Cancer Program served on grant review panels. Professor Liz Musgrove on NHMRC Project Grant Review and Program Grant Review panels; Professor Rob Sutherland on the NHMRC Project Grant Review panel and the NBCF Novel Concept Award Committee, Associate Professor Chris Ormandy on the NHMRC Project Grant Review panel and the NBCF Scientific Advisory Board, and Dr Alex Swarbrick has been selected to serve on the Health Research Council of New Zealand Biomedical Science Assessing Committee for 2011.

_ Cancer Program senior scientists are members of several major national and international networks. Professor Susan Clark is President of the Australian Epigenome Alliance, the Australian Member and Representative of the Asian Epigenome Alliance, and a Steering Group Committee Member of the International Human Epigenome Consortium; Professor Andrew Bainkin and Professor Rob Sutherland are members of the International Cancer Genomics Consortium; Dr Maja Kohonen-Corish is a member of an expert international Working Group to collect and classify data on inherited cancer gene variants in association with the Human Variome Project.

_ Dr Alison Butt is a member of the ASMR and Women in Science Enquiry Network, Inc, Dr Darren Saunders is a member of the Novara Health and Medical Research Institute Network; and Professor Rob Sutherland is a member of the International Breast Cancer Study Group and TransHERA.

_ Several members of the Cancer Program were involved in conference organisation: Associate Professor Chris Ormandy was the organiser and Chair of the Cancro Research Conference on Mammary Gland Development held in Italy 6-11 June, Professor Roger Daly convened the 5th Garvan Signalling Symposium 18-19 October, which was co-sponsored by the American Society for Biochemistry and Molecular Biology.

_ Professor Liz Musgrove convened the Cell Cycle Workshop held in Katoomba 7-9 November; Professor Andrew Bainkin organised the Translational Genomics Symposium held at the Garvan Institute on 30 November; Dr Maja Kohonen-Corish helped organise the Human Variome Project-InSiGHT Workshop at UNESCO in Paris 10 May 2010 and wrote an invited Report on the Human Variome Project Integration and Implementation Meeting in Paris 10–14 May 2010.

_ Dr Alex Swarbrick served as Facilitator, ASMR Career Development Day 2010.

_ Three new Junior Group Leaders have been recruited Dr Ise Rooman in pancreatic cancer cell biology, Dr Jarmm Wu in cancer bioinformatics, and Dr Goli Sammi in ovarian cancer, from Brussels, Helsinki and the USA respectively.
Basic Cancer Research

Apoptosis Research
Group Leader: Dr Alison Butt
Apoptosis (cell death) is a physiological process of cell removal that plays a critical role in both the development of cancers, and how they respond to treatment. Oestrogens not only cause 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 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.

Cell Cycle
Group Leader: Professor Liz Musgrove
Female steroid hormones like oestrogen and progesterone 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 Translational Groups we are searching for new genes that might link oestrogen action with the cell cycle and so could be involved in resistance of certain breast cancers to the anti-oestrogen tamoxifen. We are collaborating with the Peter MacCallum Cancer Institute in Melbourne and the University of Queensland’s Diamantina Institute in Brisbane to undertake functional screens to identify genes involved in endocrine resistance.

Development
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 EPI controls the development of the mammary gland during pregnancy, and also regulates the proliferation and function of breast cancer cells. We are investigating how EPI exerts these effects to provide a way to therapeutically target this mechanism. We have placed EPI downstream of progesterin 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 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 mechanisms that trigger epigenetic change between normal and cancer cells. We have developed state of the art genome-wide profiling sequencing methods to map epigenetic 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.

Integrin and Cell Biology
Group Leader: Dr Matthew Naylor
Our research aims to understand the mechanisms that regulate cell fate decisions during the progression of cancer to metastatic disease. Integrins mediate the adhesion of cells to the extracellular matrix and provide cells with a positional identity in addition to coordinating growth factor and hormone signalling to control cell function. Modulation of integrin expression and function can alter the cancer phenotype. We are currently investigating integrin function during mammary and prostate gland development and in experimental models of carcinogenesis and metastasis. We are also investigating the role of several cell fate transcriptional regulators during mammary gland development, cancer and metastasis.

Signal Transduction
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. Until recently, our approach has been to characterise the detailed signalling mechanism and function of individual signalling molecules, such as Gab2 and cortactin, that are dysregulated in human cancers. However, over the last few years we have also undertaken a ‘global approach’ where we use a technique termed mass spectrometry to identify the signalling networks associated with particular cancer subsets. This has revealed that a class of signalling proteins termed Src family kinases play a prominent role in an aggressive breast cancer subtype, basal breast cancer. In addition, it has allowed subclassification of pancreatic cancer into three different subgroups, each characterised by particular signalling events. We have identified signal transduction processes that contribute to resistance to the drug docetaxel in prostate cancer. These findings 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 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. In partnership with the Breast and Prostate Cancer Groups and the Cancer 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 Leader: Dr Alex Swarbrick

Most aggressive cancers have two features in common: they proliferate endlessly (have high self-renewal) and contain mostly unspecialised, poorly differentiated cells. We are investigating genes that control self-renewal and differentiation in cancer, with a particular focus on breast cancer. Together with the Breast Cancer Group and external collaborators we have discovered 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 will help us predict the behaviour of aggressive metastatic cancers and may ultimately lead to the development of new drugs to stop their growth.

Ubiquitin Signalling
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. A second major focus of our work is investigating structure-function relationships in serpin molecules, and we are working to understand the role of novel mutations in serpins.

Translational Cancer Research

Breast Cancer
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 markers of disease subtype, disease progression and response to particular therapies. A major joint project with the Cell Cycle, Apoptosis and Steroid Hormone Action Groups is identifying molecular markers of tamoxifen resistance, since loss of response to tamoxifen is a major reason for treatment failure. We are also conducting collaborative studies in-house and with other institutions to define the role of newly-discovered breast cancer genes in the disease process.

Colorectal and Lung Cancer
Group Leader: Dr Maja Kohonen-Corish

Our area of expertise is cancer genetics and epigenetics and mouse models of cancer. The challenge is to work out which key biomarkers are the most useful for determining prognosis and treatment outcomes, in order to improve the clinical management of patients. In the mouse, we have made the unexpected discovery that the same drug treatment (sulindac) can prevent cancers in one region of the colon but cause new tumours in another part of the colon. This model has given new insights to the factors that trigger and promote colon malignancy. Our work in patients has produced new candidate cancer genes, which are currently being characterised in functional assays in vitro and in the mouse, including the emerging tumour suppressor genes MCC and SATB1. We have identified a new function for the MCC gene in the DNA damage response. This provides a potential mechanism whereby loss of MCC expression can promote carcinogenesis and may help explain how benign colon polyps develop into cancer.

Ovarian Cancer
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 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 Leader: Professor Andrew Blainkin

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 Australasian 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 Leader: Professor Rob Sutherland AO FAA

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

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 continued the screening process to identify the compounds which are most active and inhibit the proliferation of cancer cells. These will be modified in collaboration with medicinal chemists 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 over 10,000m² 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 the 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.

During 2010, the complex task of demolishing existing buildings and excavating the site was completed. The first stage of the construction phase, pouring concrete footings, commenced in January 2011. The coming year will see the completion of construction and the building should be ready for occupation in early 2012.

Developing a world-class clinical and research facility requires considerable capital expenditure, and further generous donations were made to The Kinghorn Cancer Centre during 2010. The Australian Cancer Research Foundation (ACRF) announced a contribution of $5m, given in memory of Lady Sonia McMahon, a founding member of the ACRF. The Nekane Foundation, a long time benefactor of cancer services at St Vincent’s Hospital, also provided a donation of $2.5m towards the fit-out of a new outpatients chemotherapy suite, putting the comfort and amenity of patients at the heart of the design.
“We’ve created a bizarre situation in the western world over the last fifty years or so — very few people go hungry, and most people eat too much of the wrong foods. So what happens? Our cells send out distress signals to one another, and we start to become sick. It’s almost as if we’ve caught evolution with its pants down.

Diabetes is a direct consequence of our cells trying to protect themselves, doing what’s worked for thousands of years. Our fat cells evolved to help us survive, expanding during feast, shrinking during famine. At this point in time, they’re sending out a constant red alert, telling us to stop eating. It just so happens we’re ignoring their message.”

Professor David James FAA
Leader Diabetes & Obesity Program

Program Summary

Obesity is one of the greatest risk factors for a range of diseases including diabetes, cardiovascular disease and cancer. However, many obese people do not acquire these diseases. To decipher this puzzle we must understand the complex interaction between the environment, especially increased food intake, and genetics.

Much effort in the past has involved reductionist approaches, focusing on the role of individual molecules or processes. ‘Big picture’ science has introduced new possibilities, however, that might help us understand how simple changes in the environment, such as increased availability of food, contribute to disease.

The genomes of most key organisms are now sequenced, genetic linkage studies are revealing dozens (soon hundreds) of metabolic disease candidate genes in people and there is a proliferation of information about changes in gene expression, molecular interactions and post-translational modifications in different cells and animals treated in a variety of ways. This revolution of methodology and explosion of new data provides opportunities and challenges both of which have invigorated our research capacity and efforts.

Research Highlights

- Showed that healthy people who have diabetic relatives tend to gain more weight by overeating than their non-genetically-prone counterparts.
- Revealed a novel action of insulin to regulate mRNA levels (the copies of genes from which cells make functional proteins), independently of gene transcription. This provides major insights into a previously unexplored layer of cellular regulation.
- Demonstrated that increasing the amount of a gene regulatory protein (nur77) in muscle had the same positive effect on glucose metabolism as exercise.
- Identified that insulin itself can initiate insulin resistance, indicating that this mechanism is likely a normal adaptation of cells to avoid hyperstimulation with the hormone.
- Demonstrated that a modest weight loss of 6kg in very obese people with diabetes reduces the inflammatory state of immune cells, which have been implicated in the disease.
- Found that an existing anti-inflammatory drug may combat insulin resistance in muscle by reducing the toxic by-products of fat metabolism.
- Established that the insulin resistance of Hepatitis C is in muscle, rather than liver (as previously thought), and is not influenced by liver fat accumulation.
- Revealed that a commonly-used drug to treat HIV-infection causes elevations in circulating fats, helping to explain why HIV treatment is associated with increased risk of cardiovascular disease.
- Showed that resistance to insulin in the short-term can be a good thing, as it protects muscle from the damaging effect of eating too much.

People Highlights

- Professor Trevor Biden, Associate Professors Greg Cooney, Antony Cooper and Katherine Samaras, and Dr Carsten Schmitz-Pfeiffer were each awarded NHMRC project grants.
- The Juvenile Diabetes Research Foundation presented Professor Don Chisholm with a Lifetime Achievement Award.
- Trevor Biden was appointed Professor by the Faculty of Medicine, University of New South Wales.
- Greg Cooney was Visiting Professor at the Department of Biochemistry and Biophysics at the University of Sao Paulo in Brazil.
- Dr. Jerry Greenfield was appointed as the new Head of Endocrinology at St Vincent’s Hospital.
- Associate Professor Katherine Samaras was appointed the Don Chisholm–GSK Clinical Fellow for 2010.
- Drs. Jerry Greenfield and James Cantley were appointed Don Chisholm Fellows in Diabetes Research for 2011.
- Dr. James Cantley received a Viertel fellowship from the Australian Diabetes Society.
- Dr Matt Prior was awarded the Young Garvan fellowship.
- Alex Rowland, Jonathan Davey and Lindsay Wu were all awarded their PhDs.
- David Pedersen was awarded the Australian Diabetes Society Young Investigator of the Year award.
- Sean Humphrey was awarded the Castel Hafan award for the best second year PhD student.
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 useless 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

In collaboration with the Cellular Systems Biology group, we have completed a major study to identify defects in insulin signal transduction in skeletal muscle from at-risk individuals. We have also examined the characteristics of a group of obese people who seem to be protected from developing insulin resistance and diabetes. In addition, studies have been established examining the effects of 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. In another study, we are examining the possible role of the autonomic nervous system in the development of diabetes and obesity.

Phospholipid Biology
Group Leader: Dr Will Hughes

Phospholipids are the basic building blocks of cell membranes but, as is becoming clearer, some are also dynamically regulated to enable control of many of the major functions of cells. One example is the process of regulated exocytosis – the mechanism by which insulin is secreted from pancreatic beta cells or glucose transporter (GLUT4) is translocated to the surface of muscle or fat cells. We continue to use state-of-the-art live cell microscopy to image this process. We are characterising the role phospholipids play in specific steps of exocytotic vesicles are transported to the cell surface before they attach and fuse to deliver their cargo. A better understanding of insulin and GLUT4 exocytosis is essential as the process is central to glucose homeostasis.
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.

Diabetes Signalling Unit
Beta Cell Signalling
Group Leader: Professor Trevor Biden

Increased beta cell death and disruption of beta cell function are characteristics of both Type 1 and Type 2 diabetes. In the last year we have discovered that the enzyme protein kinase C (PKC), 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 now shown that fatty acids disrupt the movement of secretory proteins within beta cells and that this involves a toxic lipid metabolite, ceramide. Our ongoing work is focused on delineating how and where this disruption occurs.

Islet Biology
Group Leader: Dr Ross Laybutt

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

Insulin Signalling
Group Leader: Dr Carsten Schmitz-Peiffer

A major interest of our group is the role of the protein kinase C (PKC) family of enzymes in modulating insulin action. We are currently using proteomic approaches to identify the downstream targets of specific PKC members, which will provide insights into the molecular mechanisms by which they control glucose and lipid metabolism. In collaboration with commercial partners we are testing the use of PKC inhibitors in improving the control of blood glucose, which underscores the importance of these enzymes as therapeutic targets. In addition, we are examining lipid metabolites which disrupt insulin signaling and how these contribute to insulin resistance. Our recent studies suggest that these accumulate in insulin target tissues in response to inflammatory processes initiated by fat oversupply, opening a new avenue for investigation.

Cellular Systems Biology
Group Leader: Professor David James

Our group combines systems biology, cell biology and signal transduction-based approaches to study normal insulin action and the progression to diabetes. We are currently using global mass spectrometry methods to study changes in protein phosphorylation as a fingerprint of cellular behaviour on a rapid timescale. We are also using sophisticated microscopy technology to study one of the most important actions of insulin to stimulate the insulin-dependent movement of the glucose transporter GLUT4 to the plasma membrane in fat cells. In each of these areas we are applying interdisciplinary approaches involving statistics, bioinformatics and mathematical modelling so that we can ultimately build a dynamic model of metabolism and how it responds to environmental change.

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 muscle. 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. Lastly studies using traditional Chinese medicines aim to help identify new insulin-sensitising agents that could be more useful than current therapeutics.

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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 10 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.

Scientific Program

Type 1 Diabetes Prevention Study, INIT II

This is a Phase 2, multicentre, 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.

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

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

Use of BAFF Blockers to Prevent Type 1 Diabetes in Mice

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 mice, this study aims to test the hypothesis that B cell depletion, by way of BAFF-blockade, will restore tolerance to islets and prevent diabetes occurrence.

Ravenna Tucker
CEO
DVDC Limited

Highlights

- Received confirmation of a further $6.5 million over 5 years from NHMRC.
- Renewed the Sponsorship Agreement between DVDC and Melbourne Health in respect of the INIT II Study.
- Progressed negotiations to open a clinical trial site in Munich, Germany, for the INIT II Study.
- Held a forum, A Day of Type 1 Diabetes, at Garvan on 17 May.
- Developed a package of standard operating procedures to cover all aspects of clinical trials administration and conduct.

Membership of the DVDC Board

Professor Don Chisholm AO FRACP (Chair)
Senior Principal Research Fellow, Diabetes & Obesity Research Program, Garvan

Professor John Shine AO FAA
Executive Director, Garvan

John Dakin
Chief Operating Officer, Garvan

Paul Eisen
VP Sales & Marketing, Australia & Asia Pacific, KarmelSoniX

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

Stephen Higgs
Chair of the Board of Directors, JDRF Australia

Christina Hardy
Director, Business Development & Legal Affairs, Garvan

Membership of the DVDC Scientific Advisory Committee

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

Dr Robert A Goldstein MD PhD
Senior Vice President, Scientific Affairs, JDRF International

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

Professor Leonard C Harrison
Head, Autoimmunity & Transplantation Division, Walter & Eliza Hall Institute of Medical Research,

Professor Peter Colman
(alternate to Professor Harrison)
Department of Diabetes & Endocrinology, Royal Melbourne Hospital

Stephen Higgs
Chair of the Board of Directors, JDRF Australia

Dr Dorota Pawlak
Research Development Manager, JDRF Australia

Dr Roland Tisch
Department of Microbiology & Immunology, University of North Carolina at Chapel Hill USA

The pancreas includes up to one million ‘islets’ of Langerhan’s, clusters of different types of cells, including the beta cells that make insulin. This image shows a single islet. Photograph by Associate Professor Shane Grey.
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

- Established that discrete regions on the cell surface termed ‘lipid rafts’ enable T cells to respond to growth hormones (Cytokines).
- Showed that administration of a drug to block IL-21, a key regulatory molecule of the immune system, protects transplanted insulin-producing pancreatic cells and reverses Type 1 diabetes in mice.
- Demonstrated that the level and balance of gut bacteria can affect whether or not mice predisposed to developing Type 1 diabetes succumb to the illness – and that the same mice without any bacteria always become diabetic.
- Identified a new group of immune cells (a subset of T cells) that for the first time directly link two autoimmune diseases, Type 1 diabetes and Sjogren’s syndrome.
- Started a clinical trial program with Novartis to test the effect of a promising therapeutic target for the treatment of Type 2 diabetes.
- Showed that the STAT3 gene plays a critical role in generating ‘memory’ B cells and plasma cells, the two kinds of immune cell that help our bodies remember an invading microbe and then fight it in the future.
- Clarified how a pivotal class of immune cells known as ‘T follicular helper cells’ are generated. These cells play a critical role in helping the white blood cells known as B cells make long-lived high-potency antibodies.
- Proved the longstanding theory that foreign microbes entering the body can ‘trick’ the immune system into producing potentially disease-causing antibodies against its own tissues.
- Oversaw the installation and establishment of the Garvan two-photon intravital imaging system that allows cell movement to be analysed within living tissues.

People Highlights

- Five Immunology Program staff (Dr Jenny Gunton, Cecile King, Tatyana Chitanova, Cindy Ma, Tri Phan) were awarded prestigious NHMRC Career Development Awards (CDAs). This represents half of all the Biomedical CDAs awarded across NSW.
- Five NHMRC Project Grants were awarded to Immunology Program staff (total of $2.33m funding over the next three years).
- Professor Jonathan Sprent was awarded an NHMRC Excellence Award as top ranked Senior Principal Research Fellow for 2009.
- Associate Professor Robert Brink was awarded an NHMRC Senior Research Fellowship.
- Ms Kendle Maslowski was awarded an NHMRC Overseas Biomedical Training Fellowship.
- Dr Daniel Christ obtained three separate grants from the Australian Research Council to advance his studies in the development of antibody-based therapeutics.
- Dr Tri Phan obtained Cancer Institute NSW funding to develop in vivo confocal endomicroscopy for analysis of bowel and oesophageal cancer.
- Shane Grey and Robert Brink were appointed as Associate Professors at the University of NSW.
- Professor Jonathan Sprent was appointed to the Board of Reviewing Editors for the top international journal Science.
- Dr Cecile King was invited to write a review for Trends in Immunology, was a plenary speaker at the Brisbane Immunology Conference, and received a Rebecca L Cooper Foundation award.
Helen McGuire won the 2010 Garvan PhD thesis.

Dr Stuart Tanyge led a team of Dr Cindy Ma received the 'Publication of the Year' award from the journal Immunology & Cell Biology.

Santi Suryani was awarded a Pfizer Diabetes Research Innovation Award for her work as an oral presentation at the Gordon Conference on Immunobiology (Switzerland), the International Conference of Immunology (Kobe Japan) and the Australasian Society of Immunology (Perth).

Santi Suryan was awarded a Pfizer Fellowship which allowed her to work for three months in Pfizer Drug Discovery in La Jolla California.

Dr Cindy Ma received the 'Publication of the Year' award from the journal Immunology & Cell Biology for a paper published in 2009.

Dr Stuart Tanyge led a team of applicants who were successful in receiving $500k from the Cancer Institute NSW to upgrade the Garvan Flow Cytometry Facility.

PhD students Tyra Chan, Elaina Marino and Alex Vogelzang all had their doctoral theses formally accepted by the University of NSW.

Helen McGuire won the 2010 Garvan Student Prize, awarded for best PhD thesis.

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 we can sometimes distinguish between the self and foreign antigens. One of the unknown questions is that central to maintaining the immune system’s homoeostasis 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 Leaders: Associate Professor Robert Brink and Emeritus Professor Antony Basten AD FAA FFAV

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 to target them for destruction and elimination. Autoimmune diseases such as rheumatoid arthritis, Grave’s and myasthenia gravis 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 deregulated, 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, signaling 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 1 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 1 diabetes, enable creation of a ‘death-defying’ beta cell as a novel cure.

Immunology & Immunodeficiency

Group Leader: Dr Stuart Tanyge

Our focus is on understanding the development of B cells – the population of white blood cells responsible for the production of protective antibodies – and the 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 can best and faster following subsequent exposure to the same infectious agent. The development of immunological memory involves interactions between B cells and helper T cells – another subset of immune cells. Thus, a major focus of our work is to understand exactly how helper T cells instruct B cells to produce antibodies. We are also studying several genetic conditions of the immune system, and corresponding mouse models, that result in immunodeficiencies – disorders whereby affected individuals are unable to mount appropriate immune responses following exposure to some infections or pathogens. These diseases include X-linked lymphoproliferative disease, common variable immunodeficiency, 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 Tatjana Chitnova

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
Group leader: Dr. Pablo Silveira

Our ultimate goal is to prevent the immune system attacking the insulin producing beta cells of the pancreas, which leads to Type 1 diabetes. Our research aims to identify the faulty mechanisms that allow 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: Dr. Jenny Gunton

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

Translational Immunology
Group leader: Professor Charles Mackay FAA

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

Cooperative Research Centre for Asthma and Airways
Head: Professor Charles Mackay
Group leader: Dr. David Zahra

As a node of the CRC for Asthma and Airways, our group focuses on the development of a promising therapeutic that neutralises the function of the cytokine GM-CSF. GM-CSF has been linked to a number of inflammatory diseases including asthma and rheumatoid arthritis, and we have developed an antibody that blocks this cytokine. The potential therapeutic is protected by two provisional patents and is now ready for pre-clinical and toxicity studies. Negotiations with pharmaceutical companies are ongoing with the aim to fully license the therapeutic for pre-clinical and clinical development. We also hope to develop a therapeutic that stimulates the G-protein coupled receptor GPR43, so releasing anti-inflammatory properties.
"There are over a billion neurons in our brains – roughly the number of trees in the Amazon rainforest. When you realize that each neuron has up to 75,000 synapses, each sending signals to other neurons, you probably have as many connections in your brain as there are leaves in that rainforest. It’s almost inconceivable – infinitely more complex than most people realize.

Out of all this, I’d like to know the answer to a couple of fundamental questions. First, where are the decisions being made? In other words, is there some kind of central controlling mechanism at work, or are many different factors involved that need to work together to achieve a balance? Second, why do we have so many different kinds of neurotransmitters in each cell – what specific purpose do they all have? While we like to believe we are sophisticated in our understanding, we only have an inkling how our brains and nervous systems actually work."

Professor Herbert Herzog
Leader Neuroscience Program
People Highlights

Professor Herbert Herzog was an invited speaker at the Satellite Symposium of the International Congress of Obesity in Stockholm, Sweden and the International Congress of Endocrinology in Kyoto, Japan.

Associate Professor Amanda Sainsbury-Salis was invited to present keynote seminars at the Annual Meeting of the Neurology Association of Australia and New Zealand as well as at the Annual Conference of the Professional Clinical Hypnotherapists of Australia.

Dr Sharon Oleskevich was an invited speaker at the Sensory Neuroscience Symposium, University of Western Sydney, Sydney.

Dr Bryce Vissel was reappointed as a member of the advisory board for Parkinson’s NSW, appointed to the Editorial Board of Journal of Neurochemistry, the clinical trials group of the Australian and New Zealand Spinal Cord Injury Network and a Network Facilitator for MS Research Australia. He was also appointed onto the advisory board for Baxter Pharmaceuticals in the United States.

Professor Ken Ho was invited to speak at the International Endocrine Congress in Tokyo, and to run a Meet-the-Professor Forum at the US Endocrine Society in San Diego and at the Asia-Oceania Congress of Endocrinology in Kuala Lumpur.

Dr Paul Lee was invited to speak at the Annual Meeting of the International Society for Pediatric and Adolescent Diabetes in Buenos Aires, was winner of the 3-minute thesis competition, Faculty of Medicine University of NSW and recipient of the People’s Choice Award, winner of the Poster Award at the St Vincent’s and Mater Health Research Symposium and was awarded a Post-Doctoral Fellowship from the Research and Education Foundation, Royal Australasian College of Physicians.

Dr Sharon Oleskevich was invited to speak at the Satellite Symposium of the International Congress of Obesity in Stockholm, Sweden and the International Congress of Endocrinology in Kyoto, Japan.

Dr Vita Birzniece was recipient of an Outstanding Abstract Award and winner of the Presidential Poster Competition at the US Endocrine Society, as well as recipient of travel awards from the GRS and IGF Societies and Qantas.

Dr Lei Zhang was selected to present an oral abstract of her research at the International Congress of Obesity in Stockholm, Sweden.

Dr Shu Lin was awarded an NHMRC Career Development Fellowship.

Louise Purcell received a Qantas travel award to present the results of her PhD research into the causes and consequences of Prader Willi Syndrome at the meeting of the International Prader Willi Syndrome Organisation Conference in Taipei.

Young researcher Ayse Zengin was awarded a Qantas travel award and Ins Wong was awarded a University of NSW travel award, both to attend the ASBMR Scientific Meeting in Toronto.

Ins Wong won The Outstanding Abstract Award of the 2010 ANZBMS annual meeting.

Research Groups

Adult Stem Cell
Group leader: Professor John Shine AO FAA

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

Eating Disorders
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 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
Group leader: Dr Sharon Oleskevich

Hearing loss due to noise trauma is one of the most common sensory disabilities, 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 benefit the young and ageing community suffering from noise-induced hearing loss.

Auditory Anatomy & Neurophysiology
Group leader: Professor David Ryugo

The Auditory Anatomy and Neurophysiology Research Group focuses on brain mechanisms of hearing with a special emphasis on studying how certain brain circuits change as a result of hearing loss. Our working hypothesis is that neuronal circuits are established to extract different physical features of the acoustic stimulus. These features, including frequency, location, and loudness, are processed by the brain to produce cognition of speech, music, danger, and so on. Additional circuits contribute to enhancing signals from noise or enable the following of one voice among several. Hearing loss (imcomplete deafness) impairs our ability to perform some of these functions. Our goal is to identify the circuits that are affected so that we can plan strategies to treat and restore these functions.

Neurodegenerative Disorders – Repair & Regeneration
Group leader: Dr Bryce Vissel

The Neurodegeneration Research Group is working to understand and treat Parkinson’s disease, Alzheimer’s disease and spinal disorders. Our goal is to harness the nervous system’s own repair mechanisms, in order to stimulate the formation of new nerve cells and their connections. We also investigate approaches to block nerve cell loss. Our team has identified new ways to stimulate brain repair as well as potential approaches to prevent neurodegeneration. We aim to develop new therapeutic approaches with a goal of running clinical trials. Our research outcomes have significant theoretical and clinical implications for impacting the lives of people who confront 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 formation and strength and the coordination of regulating body weight and bone formation. Our investigations involving the effect of neurotransmitter Neuropeptide Y (NPY) have identified a novel and powerful pathway for stimulating the production of bone and increasing bone strength, suggesting an approach to new treatment.

Neurosignalling
Group leader: Dr Adam Cole

Neuroplasticity is the ability of the brain to change and refine itself in response to particular experiences and circumstances. This process is especially important for higher order functions, such as calculation, learning and memory formation. Defects in neuroplasticity are one of the earliest symptoms in the development of neurodegenerative diseases, such as Alzheimer’s disease. The Neurosignalling group focuses on two enzymes that are important regulators of neuroplasticity and are known to be defective in Alzheimer’s disease: Cdk5 and GSK3. In particular, we focus on the discovery of new brain-specific targets of these enzymes. 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 and dementias, including Alzheimer’s disease.

Neuro-Pan
Group leader: Dr Greg Neely

One of the Neuro-Pan 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. 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. 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.

Neuro-Endocrine
Group Leader: Professor Ken Ho

The pituitary gland produces key hormones that control body growth, strength, appetite, metabolism, mood and reproduction under the control of the brain. Our group’s major focus is on understanding how the brain controls body metabolism, composition and physical function through pituitary hormones. Projects include the investigation of the sympathetic nervous system (SNS) in the control of body fat and muscle. One aspect looks at the metabolic consequences of beta-blockers, which are a class of drugs commonly used to treat blood pressure, and the therapeutic application of selective beta agonists to enhance energy metabolism and protein synthesis. A new body of work explores the physiology of brown fat in people, understanding what controls its activity and how this can be harnessed for the treatment of obesity. Complementary work in the laboratory addresses the cellular and molecular mechanisms by which sex steroids modify the action of Growth Hormone and seeks to identify novel Growth Hormone regulated genes.
The skeleton is a fascinating structure. We tend to think of it as something that’s finished, fixed, done, like the shell of a building, but it’s nothing like that. In fact, it’s constantly being renovated in a never-ending maintenance program. Your skeleton is a little bit different now than when you got up this morning.

There are cells that remove bone and cells that replace bone; changes that happen on the bone surface. At the same time there are other bone cells, buried inside bone throughout the skeleton, which seem to monitor this process. Known as osteocytes, they send out signals saying, “need more bone here” or “need bone removed there”, depending on the stresses we’re putting on our skeleton throughout life. We only understand a fraction of these processes and control pathways, but we do know that our skeleton is an incredibly sophisticated structure that is in constant communication with other tissues and organs in the body, including the brain.”

Professor John A Eisman AO
Osteoporosis & Bone Biology

Research 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.

Research Highlights

- Demonstrated the association between fragility fracture and premature mortality in men and women, younger and older.
- Extended our prognostic models for predicting fracture risk for men and women, implemented in www.fractureriskcalculator.com, widely used by doctors and patients worldwide.
- Validated our nomograms for absolute fragility fracture risk in collaboration with colleagues from the Canadian Multicentre Osteoporosis Study (CaMOS). Similar collaborations are underway with the Geelong Osteoporosis Study (Melbourne), CAIFOS study (Perth) and other major cohorts in Norway, Holland, UK and New Zealand.
- 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.
- Identified novel chromosomal regions that harbor osteoporosis genes in the world’s first search for osteoporosis genes, as part of international collaborations using genome wide analysis advanced technology.
- Demonstrated the frequency of vitamin D insufficiency in general populations and in severely ill individuals in hospital. These findings suggest that vitamin D deficiency contributes to in-hospital mortality in the intensive care setting.
- Demonstrated that neurotransmitters play a direct role in the regulation of bone mass, through receptors expressed upon the osteoblast (bone forming cell), a function that has been considered purely brain mediated until now. Specifically, neuropeptide Y (NPY) directly controls the cells that make bone.
- Revealed that osteoclasts (bone removing cells) play a role in the actions of PTH, the only clear-cut anabolic treatment available for osteoporosis.
- Detailed the actions of neuropeptide Y in control of bone stem cell function.
- Defined the role of peripheral neuropeptide Y Y2 receptors in the regulation of bone mass, showing the dominance of centrally expressed receptors in this action.
- Demonstrated an association between beta-blocker use and reduced fracture risk in elderly men and women.
- Demonstrated that genetic profiling could enhance the prognosis of fracture.
The Royal Australian College of General Practitioners Guidelines for Osteoporosis Management, chaired by Professor Eisman, supported by the Federal Department of Health, was approved by the NHMRC.

Garvan bone researchers were awarded five oral presentations and gave seven poster presentations at the 32nd Annual Scientific Meeting of the American Society of Bone and Mineral Research (ASBMR) in Toronto.

Bone Program students had the following successes: Ayse Zengin was awarded a Qantas Travel Grant and Iris Wong an University of NSW travel award to attend the ASBMR Annual Scientific Meeting in Toronto.

Iris Wong won the Outstanding Abstract Award of the 2010 Australian and New Zealand Bone and Mineral Society annual meeting.

People Highlights

- Professor John Eisman was appointed by the American Society of Bone and Mineral Research to Chair and bring together an international taskforce on System Approaches to Osteoporotic Fracture Secondary Prevention.
- Professor Eisman is Co-Chair of NSW Health Agency for Clinical Innovation musculoskeletal-related conditions team, which has won support for a Systems Approach to Osteoporotic Fracture Secondary Prevention in NSW hospitals.
- Associate Professor Jacqueline Center was awarded an NHMRC Clinical Practitioner Fellowship.
- The NHMRC has awarded a three-year grant on vitamin D to Osteoporosis and Bone Biology.
- Professor Tuan Nguyen was invited by the Vietnam Ministry of Education and Training to give a key lecture on scientific publication in a World Bank sponsored conference on higher education.

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 the initial findings in DOES.

Our search for new osteoporosis genes is continuing in large-scale international collaborations.

We are developing tools to predict those at high (and low) risk for osteoporosis and fractures. This insight will direct the focus of preventative activities on osteoporosis or other health concerns, as most appropriate.

Establishing how clinical factors and genetic factors interact to affect bone biology will help identify those individuals who would most benefit from existing therapies, as well as helping to identify targets for novel therapies.

Bone Biology

Group Leader: Dr Paul Baldock

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

Fracture Prevention – Clinical Studies

Group Leader: Professor John Eisman

Our clinical studies group continues to participate in multicentre international clinical trials evaluating potential osteoporosis treatments that are in the final stages of pharmaceutical development. Involvement in these studies helps ensure we remain at the cutting edge of knowledge of novel therapies. It also provides an entry pathway to pharmaceutical interest in our novel developments as well as providing access to major clinical database sets in which we can explore and validate our Dubbo findings.
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, holds mouse production colonies under clean room conditions for Garvan and other medical research organisations in NSW. Services offered include the import and export of mice, rederivation, embryo and sperm freezing, and DNA preparation.

**The Biological Testing Facility**, located at Garvan in Darlinghurst, receives mice from ABR for holding in specialised experimental zones to enable quality animal-based 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** is a unique resource dedicated to the conduct of research in people. It provides a vital interface between discoveries in the laboratory and their evaluation in humans. The facility, staffed by highly skilled nurses and clinical investigators, has a range of support services and state-of-the-art equipment to evaluate new therapies.

Peter Wills Bioinformatics Centre applies techniques derived from disciplines such as applied mathematics, statistics and computer science to understand, organise and analyse biological data. This includes the housing of both clinical and microarray data, and the building of computer programs for querying and analysing these datasets. 2010 was a period of growth for the centre, with a successful equipment grant enabling the establishment of a High-Performance Computer facility as well as the expansion of data-storage. The centre grew its microarray archive, calarray and extended the GenePattern bioinformatics analysis environment. It also remains actively involved in the American National Cancer Institute’s cancer Biomedical Informatics Grid (cBiUG) and has begun using ‘machine virtualisation’. During 2010, centre staff collaborated on over 30 research projects, published four research papers, and were jointly successful in equipment, project and program grants.

**MLC Community Foundation Flow Facility** provides cell analysis and cell sorting services to the Garvan Institute, members of the St Vincent’s Research Precinct and external users including Children’s Cancer Institute Australia, University of NSW and St George Hospital. 2010 saw the installation of the world’s first 7 Laser BDInflux™ Cell Sorter, and the first 7 Laser LSRII analyser. The facility now houses three cell sorters and six flow cytometry analysers. Flow cytometry is a technology that allows simultaneous analysis of the physical, biochemical and molecular characteristics of single cells or particles suspended in a fluid stream. Cell analysis and sorting are frequently used to identify the various cell types present in biological tissues and to determine their developmental or functional relationships. It has wide-ranging applications in immunology, haematology, infectious diseases and cancer. The facility is supported by a generous grant from MLC.

**The 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.
_ Conducted external Occupational Health and Safety (OHS) audits covering responsibilities and accountabilities, consultation, risk management and contractor safety, in line with Garvan’s commitment to maintaining the highest possible standards of work safety. Also provided OHS training, presented in a ‘mock court’ style, for all managers and supervisors to reinforce their responsibilities to their fellow workers.

_ Increased the capacity of Garvan’s computer network tenfold. Effectively an information ‘super highway’, the network connects every desktop computer, laptop, printer and research instrument to every other and to a suite of servers. Garvan and the University of NSW collaborated closely in designing and implementing change, as the Garvan network forms part of the larger campus network.

_ Further reduced water consumption, aided by a collaboration with Sydney Water which commits both organisations to water saving initiatives. See graph opposite.

_ Established the spaces required to house two large state-of-the-art microscopes – an electron microscope as well as a two-photon microscope (which takes images deep inside living tissue). Both microscopes were acquired in 2010 and dramatically expand the Institute’s imaging capabilities.

_ Increased the number of mouse cages held at the Australian BioResources (ABR) facility from 8,000 in January to 9,500 by the end of 2010, bringing capacity to 65%. At the same time, signed new partnership agreements with researchers from the ANZAC Institute, Monash University and the University of Wollongong, increasing the number of partners from seven to ten. Preparation for the introduction of new services such as sperm freezing and microinjection began with the appointment of a Scientific Services Manager mid-year.

_ Started renovating the former rodent breeding area of the Biological Testing Facility at Garvan’s premises in Darlinghurst. This has provided additional procedures rooms, an expanded immunodeficient suite and specialised labs for hearing studies.

_ Co-supervised an Industrial Design student from UTS (University of Technology Sydney) who designed a trolley for use in Tissue Culture, to extend storage space and provide additional work surfaces. The trolley will be tested at Garvan and The Kinghorn Cancer Centre to assess its usefulness.

_ Constructed an AQIS-compliant drosophila (fly) facility at Garvan, necessary for the research of a neuroscientist who is comparing the functions of fly genes to their human equivalents.

_ Developed a major new information system for the management of mass spectrometry experimental results.

_ Released improved versions of the database that tracks Garvan Water Usage.

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Mrs Janice Gibson and the Ernest Heine Family Foundation are committing $3 million over 5 years for the establishment of a named Chair in Osteoporosis Research. Professor John Dzien, Director of Osteoporosis and Bone Biology at Garvan, seated at table (left to right) with Foundation Trustees Trevor ‘Tom’ Balletti and Tony Salier. Acting Garvan Foundation CEO, Gabriella Lang stands behind.

GARVAN COMMUNITY

Life Governors

Alind Pty Limited
Amadeus Energy Limited
Mr John Armati
ASK Group
Australian Cancer Research Foundation
The Blundy Family
Mr Charles P Curran AC
The Curran Foundation
Peter & Val Duncan
Lady Mary Fairfax AC OBE
Ferris Family Foundation
Mr Laurence Freedman AM
Mr & Mrs Berel & Agnes Ginges
Mr Laurence Freedman
Ferris Family Foundation
Lady Mary Fairfax
Mr Charles P Curran
The Blundy Family
Australian Cancer Research Foundation
Allind Pty Limited
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Dr John T onkin
Mr Laurie Sutton
Mr Tim & Mrs Sally Sims
The Bill & Patricia Ritchie Foundation
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MLC Community Foundation
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Mr Ralph & Mrs Lorraine Keyes
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Ms Elizabeth Lee
Mr Keith Line
Mrs Adel Leutjohm
Ms Maria Lydaki
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Mr Lance Matheson
DJ McCarty
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Wil & Mabs Melville
Mrs Mary Miller
John K Moody
Miss Helen Morgan
Mrs Mary & Mr Herbert Morris
Mrs Carol A O’Carroll
Mr Peter Olive
Mrs Lesley Powell
Mrs Judy Radecki
Ms Helen Richards
Kathy Rockwell
Tanya Reddan
In memory of Sonia Gabrielle Saba-Losey
Ms Coral Saunders
Miss Theima Shepherd
Mr Bruce Prior Smith
Kathryn Ann Smith
Mrs Cynthia Southwell
Mrs Liese-Lane Spring
Ms Nicola Stahl
Mrs June Strange
Mr & Mrs Peter Sturrock
Mr Leonard Towers
Mr & Mrs Eric & Pauline Vail
In loving memory of Lyndall Weiss
Mrs Judith Wheeldon AM
Dr Yeonne White
Mrs Jean Whittaker
Dr Eva Wicks
Ms Barbara Williams
Ms Faye Margaret Williams
Mrs S Wilson-Pearson
Miss June Yuan

Gabriella Lang stands behind.
Dr Tri Phan checking the laser alignment on the new two-photon microscope, a sophisticated piece of equipment that makes it possible to observe cells inside living tissue. Purchase of the microscope was made possible by a generous donation from Peter and Val Duncan.
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 Australia. Mr Ferris is Chairman of the Health and Hospitals Fund Advisory Board as part of the Federal Government’s Nation-Building Funds initiative. Former directorships include: Chairman, Australian Trade Commission (Austrade), Austar United Communications Limited, and Bradken Resources Pty Ltd. Mr Ferris is also a director of the Garvan Research Foundation. Mr Ferris was made an Officer in the Order of Australia in 1990 for services to the export industry and in 2006 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.

Nicholas Curtis
Chairman of the Queensland (Australia) Major Events Corporation and the Museum of Contemporary Art.

Annette Cunliffe OAM
Nominated by the Sisters of Charity (From March)

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 1996-02 and since 2002 Annette has been Leader of the Sisters of Charity of Australia. She has held the positions of President of CLRI Conference of Leaders of Religious Institutes (NSW) and Inaugural Chair of the Stewardship Board of Catholic Health Australia and served on a number of incorporated boards.

Martin Hoffman
Treasurer
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 OAM
Nominated by the Sisters of Charity (From March)

Mr Geoff Dixon held the position of Managing Director and Chief Executive of Qantas Airways Limited from 2000–08. After joining Qantas in 1994 he was appointed Deputy Chief Executive in 1998 and then to the board of directors in 2000. Mr Dixon currently sits on the boards of publicly listed Australian companies, Crown Limited, Consolidated Media Holdings Limited, and Facilitate Digital. He is Chairman of Tourism Australia, Chairman of the Queensland (Australia) Major Events Corporation and the Garvan Research Foundation. He also sits on the boards of The Great Barrier Reef Foundation and the Museum of Contemporary Art.
John Horvath AO
Nominated by the Federal Minister for Health

Professor John Horvath was the Australian Government Chief Medical Officer from 2003-09. He is currently continuing to advise the Department of Health & Ageing and the School of Medicine, University of Sydney, and holds the position of Honorary Professor of Medicine. He is currently a member of council of the NHMRC, Chairman of the Healthcare Committee and of the Prosthetics Listing Advisory Committee of the Australian Government. Professor Horvath is a member of the boards of 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 9th and Concord Repatriation General hospitals. He is also known as a leader in a range of medical training and workforce organisations. He is also a former president of the Australian Medical Council and the NSW Medical Board.

Anne Keating
Nominated by the NSW Minister for Health

Ms Anne Keating is a company director and holds board positions in a range of industries including advertising, banking, and property. She is on the boards of the Goodman Group Limited, Ardent Leisure Group Limited, Reva Medical Inc and Clearview Wealth Limited. Ms Keating is also a member of the RIS 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, 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 1993-01.

Lisa McIntyre
Nominated by the Federal Minister for Health

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

Greg Paramor
Nominated by the Garvan Research Foundation

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

Carol Pedersen RSC
Nominated by the Sisters of Charity (Until February)

Sister Carol Pedersen graduated as a trained nurse at St Vincent's Sydney in 1963 and is a Sister of Charity. She holds a PhD from University of NSW and a BSW (Hons 1) from the same institution. She also holds an Advanced Diploma from the Sydney College of Homeopathic Medicine, and has completed postgraduate work, obtaining an Associate Diploma in Advanced Homeopathic Medicine. For over 20 years Sister Carol was a member of various human research ethics committees, and was active at national, state and local levels in the development of alcohol and drug services. Sister Carol is currently providing pro bono clinics in rural areas and the bush.

Steven Rubic
Nominated by the Sisters of Charity

Mr Steven Rubic was appointed CEO of St Vincent’s & 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 the Garvan Research Foundation, the Health Industry Superannuation, Macquarie University Council, a member of Australian Commission on Safety and Quality Health Care (Private Hospital Sector Committee) and is a past chairman of the NSW Private Hospitals Association. He is a fellow of the Australian Institute of Company Directors and Australian Institute of Management.

Peter Smith
Nominated by the University of NSW

Professor Peter Smith is Dean of Medicine at the University of NSW. He specialised in paediatric clinical oncology 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, RAAFSR and Clinical Director, Health Administration and Education, Directorate of Health Reserves, Air Force and has served as a consultant to government, including as Chair of the Inquiry into Vietnam Veterans’ Cancer Incidence and Mortality. Peter is currently a director of St Vincent’s Health Australia, Neuroscience Research Australia and a number of other research centres and institutes.

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 Ethics 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.
Bruce Baird AM (From December)

The Hon Bruce Baird has an impressive career spanning the Australian Trade Commission and the parliaments of NSW and the Commonwealth. Bruce 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 1984-95, 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 1992-95. 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 Gavit, 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 a consultant and company director for a range of business, health and community organisations. In addition to the Garvan, she serves as a non-executive director for the NSW Clinical Excellence Commission, NSW Agency for Clinical Innovation, and the Australian Brandenburg Orchestra. Ms Conrad has extensive experience in strategy, marketing and business development. In her previous executive career, she founded and ran the retail store chain, Conrads Warehouse, and held executive positions in the Consumer Products Practice Group for Asia Pacific. She is currently a member of Chief Executive Women, a small active network of Australia’s top women leaders. Prior to joining Egon Zehnder International she worked at Procter & Gamble in both the US and Australia. Ms Allen has an MBA from Harvard Business School and a Bachelor of Arts from Smith College. Ms Allen joined the Foundation Board in 2007.

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

Lyn Gearing

Ms Lyn Gearing was appointed to the Garvan Foundation Board as a representative of the Sisters of Charity. Ms Gearing is currently a director of Queensland Investment Corporation Limited, Hancock Natural Resource Group Australasia Pty Limited, IMB Limited, Global Mining Investments Limited, and one other not for profit organisation. 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.

Loftus Harris AM

Mr Loftus Harris is a non-executive director on various boards in NSW, Victoria and Queensland, a 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.

Byram Johnston OAM

Mr Byram Johnston is the Chief Executive Officer of MainstreamIPQ, a company providing back office processing and administration services to fund managers and superannuation funds. Prior to establishing this business he spent over 30 years as a management consultant. He serves on the board of a number of companies. Mr Johnston joined the Foundation Board in 1997.
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 a director of Coca-Cola Amatil Limited, the University of NSW Foundation Limited and Kimberly 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 Institute of Building 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 Goldbeach 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 Most Excellent Order of the British Empire. He is the Order of Australia and a Commander of the University of Sydney. Mr. Landerer is a Member of business and commercial law. He is also a fellow of Macquarie University in business and commercial law. He is also a fellow of University of Sydney.

Mr. Simon Mordant is Co-Chief Executive of Greenhill Calburn, 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 Deputy Commissioner for Australia at the Venice Biennale. Mr. Mordant joined the Foundation Board in 2009.

Following nurse training at the Mater Hospital in Brisbane, Sister Clare entered the Sisters of Charity. 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.

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Paulina Pilkington (resigned 2009) (Until July)

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

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 corporates and governments in Australia and overseas. Mr. Rees joined the Foundation Board in 2008.

Mr. Steven Rubic was appointed CEO of St Vincents & Mater Health Sydney in April 2008. Prior to this he was Executive Director of St Vincents’ Private Hospital a position he held since 1997. He is currently a board member of the Garvan Institute, the Health Industry Superannuation, Macquarie University Council, a member of Australian Commission on Safety and Quality Health Care (Private Hospital Sector Committee) and is a past chair of the NSW Private Hospitals Association. He is a fellow of the Australian Institute of Company Directors and Australian Institute of Management. Mr Rubic joined the Foundation Board in 2008.

Professor John Shine is Executive Director of the Garvan Institute of Medical Research. He is Professor of Molecular Biology and Professor of Medicine at the University of NSW. 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-Chair of the National Health and Medical Research Council (NHMRC). 

Mr. Karim Temsamani manages Google’s global mobile business and operations, based in Mountain View, California. Prior to this, he managed for three years Google’s domestic business and strategic partnerships in Australia and New Zealand. Mr. Temsamani joined Google from Fairfax Media, where he was Group Director, Fairfax General Magazines (responsible for growing the profile and advertising revenue of Fairfax’s suite of inserted magazines) and Commercial Director for Newspapers (responsible for agency and group sales, trade marketing and business development). He was the Publisher and Vice President of Who Weekly at Time Inc South Pacific from 1999-02 and has previously served in a variety of senior capacities with Hachette, including the positions of Regional Business Publisher in Hong Kong (1995-96), Associate Publisher for Korea in Seoul (1996-97), and Managing Director for Hachette in Sydney (1997-99). Mr Temsamani joined the Foundation Board in 2008.
Type 1 diabetes in progress. Pancreatic insulin-producing cells, stained red, are being destroyed by immune cells (B cells), stained green. Photograph by Associate Professor Shane Day.

**A**


Anderson LR, Sutherland RL, Butt AJ. BAG-1 overexpression attenuates luminal apoptosis in MCF-10A mammary epithelial cells through enhanced RAF-1 activation. *Oncogene* 2010; 29:527-38.


Bartos C, Gross BS, Qu W, Statham AL, Hacker NF, Sutherland RL, Clark SJ, O’Sheen PM. Collagen and calcium-binding EGF domains 1 is frequently inactivated in ovarian cancer by aberrant promoter hypermethylation and modulates cell migration and survival. *Br J Cancer* 2010; 102:87-96.


Brummer T, Schmitz-Peiffer C, Daly RJ. Docking proteins. *FEBS J* 2010; 277:4356-69.

**B**

ovarian carcinoma, but differentially (TPD52) are frequently overexpressed in C, Hacker NF, Sutherland RL, Defazio A, Byrne JA, Maleki S, Hardy JR, Gloss BS, 2010; 12 Suppl 2:159-67.


Co-expression of TPD52 is frequently overexpressed in ovarian carcinoma, but differentially associated with histological subtype and patient outcome. BMC Cancer 2010; 10:497.

BMC Cancer 2010; 9.

homeostasis of CD4+ T cells. Not ImmunoL 2010; 11:547-8; author reply 548.


Bone during the growth phase – the dark blue osteoblasts, or bone forming cells, can be seen in the bottom third of the image. Photograph by Dr Paul Baldock.

### Garvan Institute of Medical Research

#### Income Statement

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<td>Commonwealth Government Grant (TKCC* Construction)</td>
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<td>14,900</td>
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<td>Commercial Collaborations</td>
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<tr>
<td>Garvan Research Foundation</td>
<td>2,562</td>
<td>2,714</td>
<td>4,689</td>
<td>5,174</td>
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<tr>
<td>Garvan Research Foundation (TKCC* Construction)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Accumulated Surplus Brought Forward</td>
<td>308</td>
<td>9,914</td>
<td>11,099</td>
<td>16,571</td>
<td>32,512</td>
</tr>
<tr>
<td>Unrealised gain/(loss) on investment</td>
<td>-</td>
<td>-</td>
<td>(7,407)</td>
<td>1,922</td>
<td>(142)</td>
</tr>
<tr>
<td>Other Income (Insurance Claim Facade)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2,750</td>
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<tr>
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<td>Administration and Information Technology</td>
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<td>3,771</td>
<td>5,321</td>
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<td>Building and Scientific Operations</td>
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<td>Building Cost - Facade</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>Total Operating Expenses</td>
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<td>37,493</td>
<td>44,798</td>
<td>44,351</td>
<td>46,974</td>
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<td>(1,180)</td>
<td>(1,189)</td>
<td>(1,657)</td>
<td>(1,659)</td>
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<td>Property, Plant and Equipment Depreciation</td>
<td>(2,449)</td>
<td>(2,433)</td>
<td>(2,390)</td>
<td>(2,597)</td>
<td>(2,670)</td>
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<td>Transfer from/(to) Building Reserve</td>
<td>(1,353)</td>
<td>1,047</td>
<td>1,047</td>
<td>1,047</td>
<td>-</td>
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<tr>
<td>Endowment Grants from Garvan Research Foundation</td>
<td>10,965</td>
<td>2,210</td>
<td>3,953</td>
<td>6,388</td>
<td>1,604</td>
</tr>
<tr>
<td>Endowment Earnings</td>
<td>2,181</td>
<td>2,589</td>
<td>1,700</td>
<td>958</td>
<td>1,192</td>
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<td>Donations &amp; Bequests direct to/(from) Endowment Fund</td>
<td>-</td>
<td>-</td>
<td>5,393</td>
<td>(5,000)</td>
<td>-</td>
</tr>
<tr>
<td>Unrealised gain/(loss) on investment</td>
<td>-</td>
<td>-</td>
<td>(7,407)</td>
<td>1,922</td>
<td>(142)</td>
</tr>
<tr>
<td>Net Income</td>
<td>23,074</td>
<td>6,350</td>
<td>3,028</td>
<td>20,683</td>
<td>7,960</td>
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<tr>
<td>Accumulated Surplus Brought Forward</td>
<td>308</td>
<td>9,914</td>
<td>11,099</td>
<td>16,571</td>
<td>32,512</td>
</tr>
<tr>
<td>Transfer from/(to) Research Program Reserve</td>
<td>(107)</td>
<td>(2,526)</td>
<td>380</td>
<td>(2,189)</td>
<td>1,133</td>
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<tr>
<td>Transfer from/(to) Endowment Reserve</td>
<td>(11,809)</td>
<td>(3,664)</td>
<td>1,847</td>
<td>(2,530)</td>
<td>1,190</td>
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<td>Transfer from/(to) Infrastructure Expense Reserve</td>
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<td>1,035</td>
<td>207</td>
<td>(23)</td>
<td>333</td>
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<td>Accumulated Surplus Carried Forward</td>
<td>9,914</td>
<td>11,109</td>
<td>16,571</td>
<td>32,512</td>
<td>43,128</td>
</tr>
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</table>

* The Emotions Cancer Centre (TKCC)
** The figures in 2006 and 2007 have been adjusted to improve the comparability with 2008.
### Garvan Institute of Medical Research

#### Balance Sheet

<table>
<thead>
<tr>
<th></th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
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</thead>
<tbody>
<tr>
<td><strong>Current Assets</strong></td>
<td>$15,249</td>
<td>$18,226</td>
<td>$21,114</td>
<td>$52,136</td>
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<td>$84</td>
<td>$84</td>
<td>$84</td>
<td>$84</td>
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<tr>
<td><strong>Total Assets</strong></td>
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<td>$90,573</td>
<td>$106,538</td>
<td>$142,062</td>
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<td>Provisions**</td>
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<td><strong>Total Liabilities</strong></td>
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<td>$16,571</td>
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<td>$43,128</td>
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<tr>
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<td>$76,990</td>
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<td>$103,539</td>
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</table>

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

---

### Garvan Research Foundation

#### Statement of Funds

<table>
<thead>
<tr>
<th></th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Donations &amp; Pledges</strong></td>
<td>$3,826</td>
<td>$4,961</td>
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<td>$55</td>
<td>$19</td>
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<td>Grants to TKCC Joint Venture Partner</td>
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<td><strong>Accumulated Funds Carried Forward</strong></td>
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<td>$109</td>
<td>$507</td>
<td>$(20)</td>
<td>$248</td>
</tr>
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<td><strong>Represented By:</strong></td>
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<tr>
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<td><strong>Net Assets</strong></td>
<td>$78</td>
<td>$109</td>
<td>$507</td>
<td>$(20)</td>
<td>$248</td>
</tr>
</tbody>
</table>
Equipment photographed on the cover is the first 7 laser BDInflux™ Cell Sorter installation in the world, being operated by Nabil Abi-Rig.