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prince henry's institute
science for better life ™

prince henry's institute
2004/05 annual report

Contents

Cover and inside cover photo:
Morag Young, Senior Research Officer,
Endocrine Genetics group
Photographer: Chris Kapa

Our Vision

To improve health through hormone research

Our Mission

To improve quality of life through the investigation of hormones in the fields of reproductive health, cancer, diabetes, obesity and cardiovascular disease

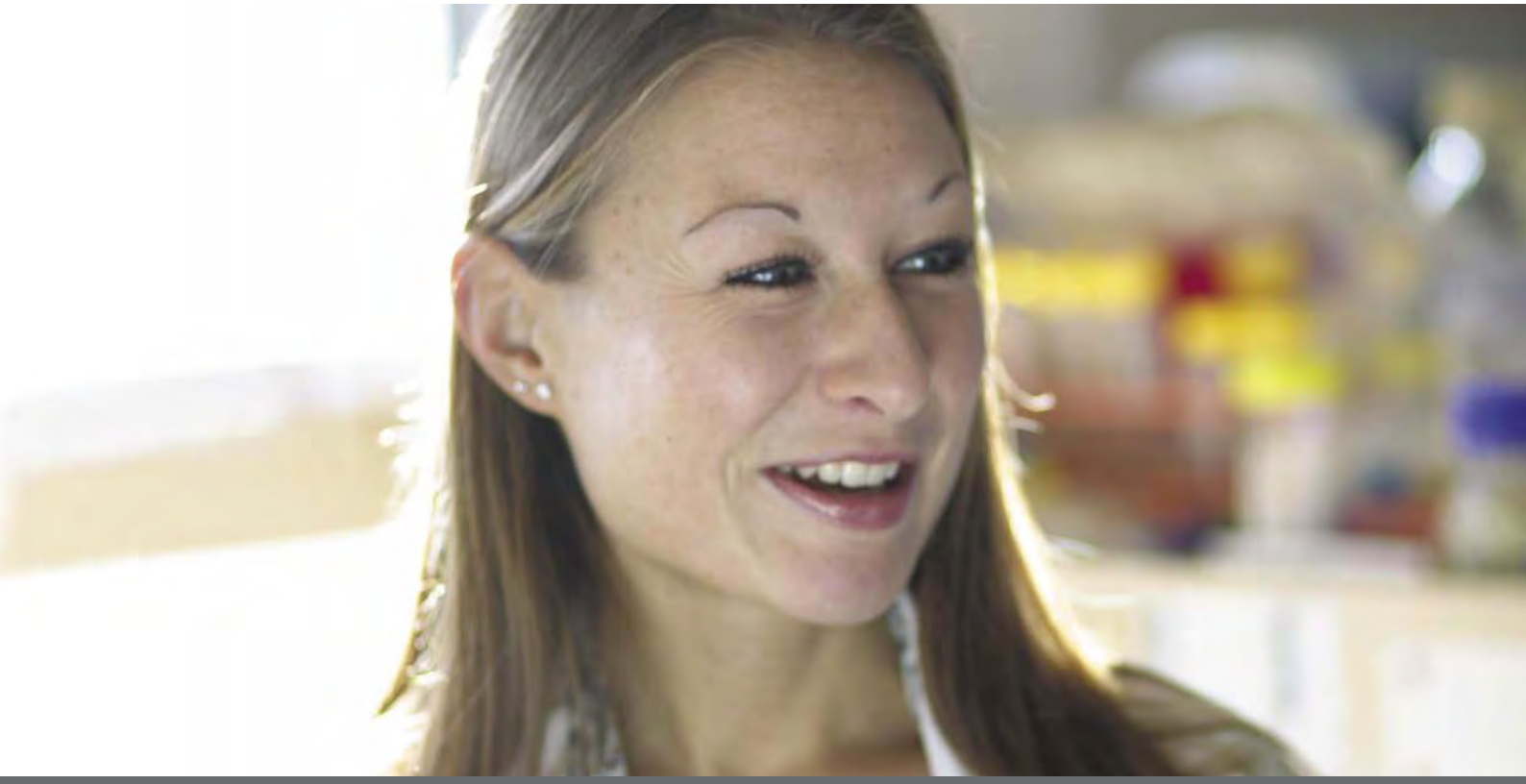
Our Aims

- **Improve** early detection, diagnosis, prevention and treatment of disease
- **Contribute** to national and international health priorities
- **Lead** in the publication of new scientific knowledge
- **Enhance** scientific education through innovative research
- **Increase** community awareness through the promotion of research

Our Values

- **Quality and integrity** in our research
- **Empathy** for those we help
- **Leadership and excellence**
- **Passion and discipline** for the work we do
- **Cooperation and creativity** in our field

Science for Better Life



Prince Henry's Institute has a fresh new logo and tagline

A long term goal of the Institute has been to develop a fresh new image. This new marketing initiative will help us to better communicate our research and commitment to improving human health.

Science for Better Life represents our vision to help people have better, healthier lives. We have also chosen to shorten our name. We believe this new initiative will help to raise the public profile of the Institute, nationally and internationally.

During this process, we have been extremely fortunate to have the assistance of advertising agency Tribal DDB. We would particularly like to thank Creative Director, Heath Rudduck for the logo design and Director, David Pisker, for their ongoing expertise, passion and guidance.

Members of the Institute Development Board, Institute staff and friends have contributed to this process. This has included external and internal focus groups with stakeholders, Board members, staff and supporters.

The Development Board, led by Chairman John Robinson, has been instrumental in driving this initiative forward which also includes the development of a new Vision, Mission, Aims and Values.

We have received extensive support for this new direction and hope that all our supporters will embrace it also.

About Prince Henry's Institute

Our Credentials

For nearly forty years, Prince Henry's Institute (PHI) has maintained a reputation for excellence in the field of endocrinology, the study of hormones.

Beginning as the Medical Research Centre for Prince Henry's Hospital (1969-1990), PHI is now an independent Institute based at Monash Medical Centre in Clayton, Melbourne, Australia.

PHI is a World Health Organization Collaborating Centre for Research in Human Reproduction, one of only two in Australia. The standing of the Institute was also confirmed in an independent review conducted in 2003 that placed it as one of the top ranking research institutes in reproductive health worldwide.

Prince Henry's Institute is

- An Accredited Institute of the National Health and Medical Research Council of Australia
- An Affiliated Institute of Monash University
- A Partner of the Monash Health Research Precinct
- A Member of the Monash Institutes of Health
- A Member of the Victorian Breast Cancer Research Consortium Inc
- An Alliance Partner with the National Australia Bank Ovarian Cancer Research Foundation

PHI's funding is derived from competitive international and national government grants, charitable trusts and foundations, the corporate sector, private philanthropy and public donations.

What are hormones?

Hormones play a major role in the body's communications system. Much like the way the brain and limbs communicate by sending electrical signals along the nerves, the body's organs communicate by sending hormones to one another in the blood stream.

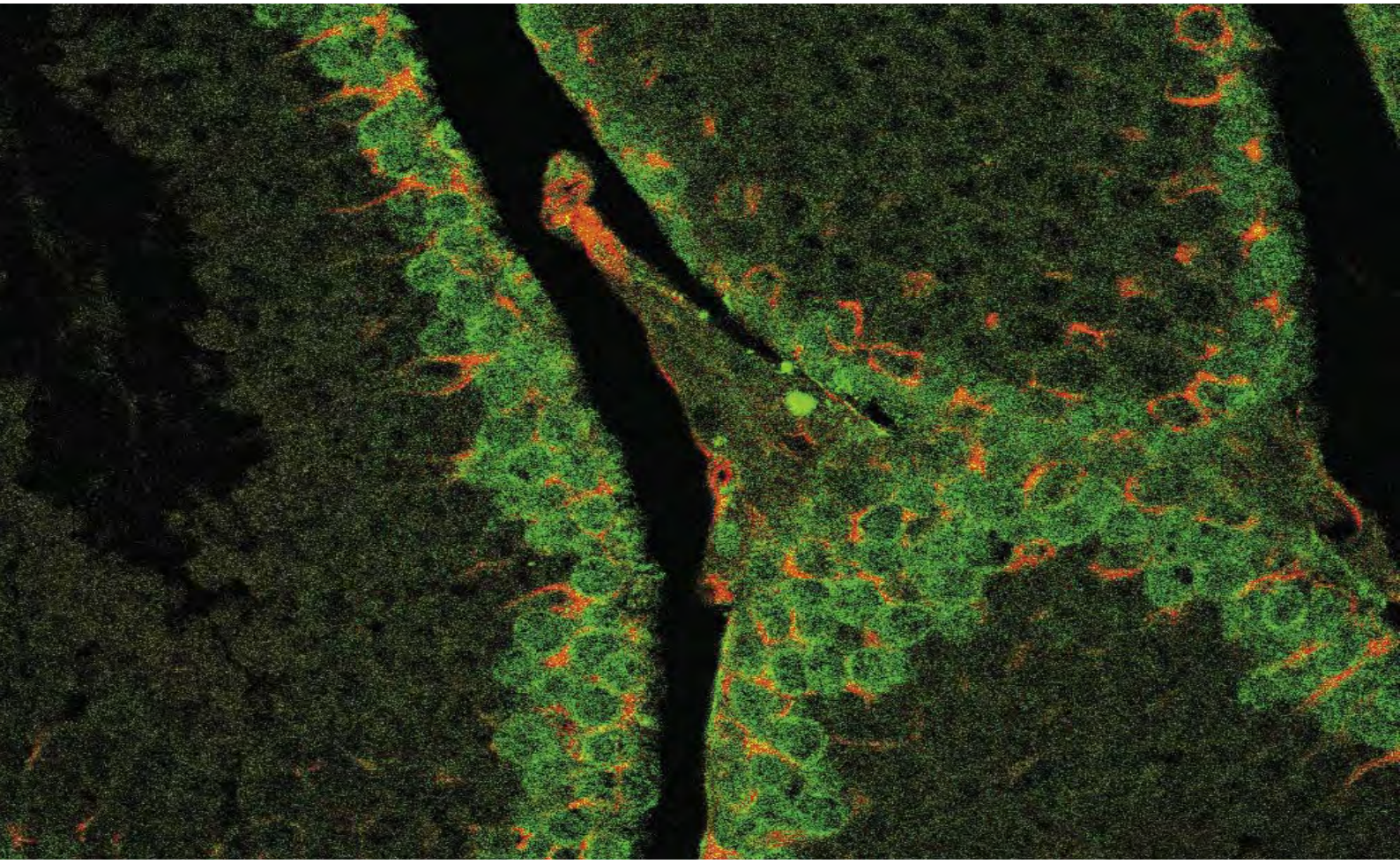
Hormones also communicate between cells in an organ. When hormones reach a target cell they bind to specific sites called receptors and cause many different effects which control the function of that cell. Hormones not only control normal functioning in the body, but can also contribute to the onset of disease. Subtle hormonal changes and irregularities can provide an early warning that something is wrong in the body.

The earlier such abnormalities are detected the more effective the treatment.

The use of hormones in both the early detection and treatment of cancers in the breast, ovary and uterus is a major focus of the Institute. Hormonal dysfunction also impacts conditions such as male and female infertility, diabetes, obesity, heart disease and sex determination.

Photo opposite: Jayne Sierens, Research Officer, Sex Hormones in Action research group

Research Highlights



Confocal Microscope image: Sertoli cells

Oestrogen linked to male libido

Discovered that lack of oestrogen causes a total loss of sex drive in male mice

Protein discovery has dual role in breast cancer

Observed that the protein LRH1 stimulates breast cancer growth both via fat tissue in the breast and in breast tumours

Target for male infertility

Showed that the protein LRH1, a key factor in oestrogen production in females, also regulates oestrogen production in the male testis and hence may be a target for infertility treatments for men

Sex determining factor in the brain

Discovered that men produce the testes-determining protein, SRY in brain regions associated with sexual behaviour

Clue to obsessive compulsive disorder

Discovered a lack of oestrogen caused obsessive compulsive disorder symptoms such as excessive grooming in male mice

Target for female contraceptive that reduces HIV virus

Established a target for a new female contraceptive that prevents both pregnancy and HIV infection

Collaboration for contraceptive development

Invited to join a new initiative from Schering AG (Germany) aimed at developing entirely new forms of contraception for women

Reproductive function restored

Found that a key peptide restores reproductive function in animals that have a deficiency in brain and pituitary hormones

Early sperm cells restored

Discovered that follicle stimulating hormone restores early sperm development in an infertile male animal

Sertoli cells respond to hormone treatment

Proved that adult Sertoli cells, essential for the nutritional structural support for developing sperm, respond to hormone treatment and hence could be a target for male infertility

Australian ovarian health study

Collaborated on an Australian-first ovarian health study to measure ovarian function in postmenopausal women

Treatment of ovarian cancer

Initiated tests of a novel ovarian cancer drug using tumour cell lines

Hormone treatment reverses heart disease and benefits kidney

Showed that blocking a mineralocorticoid receptor not only reverses heart disease, but may also have beneficial effects in the kidney

Community Highlights

• **Young Australian of the Year in Science and Technology (2002)**, Dr Kara Britt of PHI was a guest speaker at the r u MAD (Are You Making a Difference) Youth Ambassador's conference in October 2004. The conference was presented by the Education Foundation, held at Government House and the Victorian Arts Centre. Dr Britt spoke to over one hundred school children about her scientific career and her efforts to make a difference in medical research.

• Oestrogen and its role in men and women was the focus of a presentation to members of the **Health Law Committee of the Victorian Law Institute**, held at Middleton's law firm in March 2005. Lawyers and health professionals attended the information session. Dr Margaret Jones led a lively discussion after her presentation "Oestrogen, Not Just a Reproductive Hormone".

• Prince Henry's Institute presented to the meetings of the Regional and the Metropolitan Captains of **Women's Golf Victoria** in October 2004. Presentations by Professor Lois Salamonsen and Dr Ann Drummond were well received by the female audience.

• Thousands of students investigating a career in science attended the **Sci Tech Conference held at the Telstra Dome** in August 2005. As part of an Australian Society for Medical Research (ASMR) stall, Dr Morag Young of PHI, fielded questions from undergraduate students from universities throughout Victoria.

ASMR Medical Research Week 5 – 9 June, 2005

• Prince Henry's Institute participated at the 2005 **ASMR Medical Research Week EXPO at Federation Square**, Melbourne. The Institute's interactive and educational display was voted best stall of the day by radio sponsor Radio 3RRR. Scientists Dr Sarah Meachem and Pavel Sluka were interviewed as part of a live broadcast by the station.

• The Institute hosted two tables at the **Victorian ASMR Medical Research Week Dinner** at the Crown Palladium at Southbank, Melbourne. Guests and supporters of PHI included members from the Jack Brockhoff Foundation, Lord Mayor's Charitable Fund, the Ovarian Cancer Research Foundation, Blake Dawson Waldron, Middletons Lawyers, and New Scientist magazine.

• Young scientists Natalie Hannan, Chelsea Stoikos and Tu'uhe Kaitu'u from PHI presented research into pregnancy and uterine biology in the **ASMR tour of regional high schools**. The tour held in Sale, Traralgon and Warrigal was dedicated to encouraging students into a career in science. The scientists were interviewed on ABC regional radio.

Research Assistant Alex Umbers helps Matt Travaglione, aged 12, enter the hormone competition.

Media Highlights

Snapshot in the Media

Prince Henry's Institute has continued to gain extensive media interest and exposure. Research discoveries have been reported in Australian and worldwide media outlets including print, radio, tv and the internet. Some highlights from the previous year include:

• Research into sex determination and transsexualism, featured on the ABC Four Corners televison program "The Gender Puzzle". The program discussed the complexities and difficulties of people with conditions such as intersex and transsexualism.

• Research linking oestrogen to Obsessive Compulsive Disorder in male mice, received coverage in popular international science magazine New Scientist. The magazine's global website also featured the story.

• Research linking oestrogen to male sex drive gained extensive coverage in Australia and Europe. It featured on ABC TV science program Catalyst "Oestrogen Men".

• The cover of The Age Good Weekend magazine promoted a feature article on Prince Henry's Institute's collaborative research investigating male infertility and quality of sperm production.

2005 Young Scientist of the Year Award

PhD scholar Ms Christine White, 27, of the Uterine Biology Group at Prince Henry's Institute, is the winner of the 2005 Young Scientist of the Year Award.

Jacqui Schade (left) and her son Sean Queantal with Christine White, 2005 Young Scientist of the Year Award winner (Source: The Australian)

The national award is presented by The Australian newspaper and the British Council Australia. Christine received the accolade for her entry explaining how poor communication between a human embryo and its mother's womb may prevent pregnancy.

It is estimated that 40 – 50% of pregnancies end in miscarriage, and 75% of these miscarriages are due to failure of embryo implantation. The research clarifies that a factor called interleukin-11 plays a critical role in the implantation process and may provide new targets for an infertility test or treatment. Entrants were asked to write an original news story about their research in a style suitable for publication in The Australian newspaper.

Christine's media debut included a live interview on ABC Radio and a pre-recorded interview on Radio Australia, reaching Asia and Europe.
As part of the award, Christine trained as a science journalist in newsrooms at The Australian in Sydney, The Times in London and with the science news team at the Science Museum in London.

Chairman's Report

The Institute has continued to make excellent progress across the spread of its research activities and this is presented in some detail in the body of this report. We have also made solid progress in improving the infrastructure necessary to support our research efforts.

Construction of the first stage of the Monash Health Research Precinct Limited building is nearing completion on the Clayton campus and is expected to be ready for occupancy later in the year. This development has been made possible by building grants received by Prince Henry's Institute and Monash University from the Commonwealth and State governments. Southern Health has contributed the land on which the Precinct building is being constructed, demonstrating the co-operation that underpins this research precinct concept. The additional research laboratory space created opens up a range of opportunities for Prince Henry's Institute.

We are already engaged in a number of collaborative research projects with the Monash Institute of Medical Research and the new Precinct facility will allow this cooperation to be extended into new research consortia. The additional space available to Prince Henry's will mitigate the difficulties that result from overcrowding and in addition provide the opportunity to attract new research groups to the Institute. In his Director's report Professor Evan Simpson mentions the introduction of equipment into the Institute to allow the application of Proteomics to a number of our ongoing research projects. The adoption of this new technology requires provision of space for new equipment and the personnel to operate it.

Although completion of Stage 1 of the Research Precinct is a major step forward, it does not resolve all of the space issues that impact on the precinct members and Stage 2 is currently under active consideration.

On the matter of research funding, Prince Henry's has again received good recognition of the quality and relevance of its research through competitive, peer reviewed, National Health & Medical Research grant support. This year we have for the first time received proportionate research infrastructure funding from the Commonwealth Government to cover expenditure outside of direct research grants and we have continued to receive funding support from the State Government. The Institute in recent years has also placed increased emphasis on seeking research funding from non-government sources and we have been successful in gaining support from a number of international corporations and research bodies. Income from the commercialisation of various research programs has also increasingly supplemented our general income.

Prince Henry's, however, is an independent research institute and we remain very dependent on the philanthropic support of individuals, charitable trusts and local research foundations. The National Australia Bank Ovarian Cancer Research Foundation has, for example, continued to provide strong funding support during the year for our work to discover an early detection test for this disease.

We continue to work hard to lift the profile of the Institute and publicise the important work we are doing to improve health outcomes. We have established a Development Board to assist this effort and valuable pro bono assistance has been provided by Tribal DDB in making the Institute more visible to the community at large.

The key to our success as an internationally regarded endocrinology research institute is the quality of our researchers and it has long been the case that Prince Henry's has attracted people of the highest calibre. Evan Simpson in his Director's Report mentions some of the achievements and the international recognition of our researchers. This recognition reaches to the highest levels in the Institute and both our Director and Deputy Director have received important international awards.

Professor Evan Simpson has been recognised by the US Endocrine Society with the 2005 Roy O Greep award. This is in recognition of his contribution to the understanding of hormones, in particular oestrogen and its enzyme aromatase. Professor Jock Findlay AM our Deputy Director has been awarded the 2006 Dale Medal by the UK Society for Endocrinology. This is the highest accolade bestowed by the Society and only five Australians have ever received the award. It is made in recognition of his contribution to reproductive health research.

In closing, I would like on behalf of the Institute Board to congratulate our Director and Deputy Director on their personal achievements and to also recognise the valuable work being conducted by the Institute's Research Managers and to thank them and their dedicated research staff for the good progress made during the past year. The Institute's administrative staff have also made a valuable contribution and their efforts are integral to our success. I would also like to pay tribute to all those who have supported the Institute during the past year with direct funding, general donations and pro bono work. We greatly value your assistance in the important work that we do.

John Robinson
Chairman

Institute Governance and Board of Directors

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Chairman

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Mrs J Hibbins
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Mr J Robinson
Mr R Fynmore AO

Roy O. Greep Award

The US Endocrine Society has recognised the outstanding achievements of Professor Evan Simpson by awarding him the 2005 Roy O.Greep Award.

The 2005 Award was given in recognition of Professor Simpson's contributions to our understanding of hormones, particularly oestrogen and its enzyme, aromatase. As the recipient of the Award, Professor Simpson presented a Plenary Lecture at the US Endocrine Society Annual Meeting in San Diego in June 2005.

Professor Simpson is recognised as the world leader in the area of oestrogen biosynthesis. Over the last 25 years, his work has shown that oestrogen plays an important role in the development of breast cancer, the maintenance of bone mineralisation and cognitive function.

Professor Simpson's lab was the first to clone the cDNA and subsequently the human gene encoding aromatase, the enzyme responsible for oestrogen biosynthesis. His work has major significance for the future use of aromatase inhibitors for breast cancer treatment.

Professor Simpson's group has, in collaboration with clinical investigators, studied aromatase levels in oestrogen deficient humans and created a mouse model of oestrogen deficiency, the ArKO mouse.

These studies have revealed many new and unexpected roles for oestrogens, including roles in male libido and in the prevention of obesity.

Professor Simpson has published over 350 peer reviewed articles and invited reviews and book chapters. He is one of the four most cited scientists in Australia, in the field of Biochemistry and Cell Biology.

He has received numerous awards including the Trans-Atlantic Medal and the Asia and Oceania Medal from the UK Society for Endocrinology, and the President's Scientific Achievement Award from the US Society for Gynecological Investigation.

Since 1998, Dr Simpson has provided leadership as Director of Prince Henry's Institute. He has mentored over 60 PhD students and postdoctoral Fellows, many of whom hold senior positions in obstetrics/gynaecology and endocrinology worldwide.

As a Group Leader in the Victorian Breast Cancer Research Consortium his current research is directed towards discovering new and better therapies for breast cancer prevention and treatment.

Director's Report

This year has been notable on account of several landmark steps which we have taken. The first of these, as our Chairman has mentioned in his report, is to acquire new space so that we can expand our research activities. This is a culmination of our success, together with the University, in obtaining funding from both the Commonwealth and State Governments in order to construct the new research building on the Monash Medical Centre site. As John Robinson also mentioned, the land was given to us by Southern Health and we are very grateful for that support. Our share of the new building is the whole of the fourth floor and almost half of the third floor. This represents a considerable expansion of our total available space. The building should be ready for occupancy later this year. Acquisition of this increased space will allow us to achieve a long term cherished goal, namely to expand our research activities by bringing in new research groups. To this end we have advertised internationally for new group leaders. The response has been most encouraging and we now have a short list of several outstanding leadership role candidates. In addition we have been able to identify several excellent younger candidates who, if we are able to recruit them, will help to fill what has long been recognized as a serious gap in our ranks.

Proteomics Technology

Another major initiative which we are undertaking is our investment in the technology of proteomics. Proteomics is to protein analysis what DNA micro arrays are to gene expression analysis, namely, the ability to identify large numbers of proteins in samples from tissues, cells and body fluids.

With the support of the **National Australia Bank Ovarian Cancer Research Foundation**, the Institute has been able to acquire a Ciphergen protein chip SELDI-TOF MS (surface enhanced laser desorption/ionization time-of flight mass spectrometer) proteomic system. This technology provides a platform for the detailed analysis of the patterns of proteins in tissues and body fluids such as blood, uterine washings and peritoneal fluid, and will be used by our colleagues Dr Martin Oehler and Associate Professor Tom Jobling in their search for early detection markers of ovarian cancer.

This technology is readily applicable to other projects in the Institute, including the identification of cancer-specific proteins and related signalling factors produced by the uterus and breast as candidate markers of early stage disease.

Ovarian Health Study

Prince Henry's Institute is involved in an ovarian health program for post-menopausal women who are at risk of developing ovarian cancer. The combined blood test, which we have previously reported, consists of the combination of CA125 and the hormone, inhibin. This was developed by Prince Henry's Institute and **Diagnostic Systems Laboratories Inc**., in Texas, and is being tested for the first time in this study. This study is in collaboration with **Monash University** and the **Jean Hailes Foundation**, and is jointly funded by the **National Australia Bank Ovarian Cancer Research Foundation**, **Diagnostic Systems Laboratories Inc**., and **Inhibin Pty Ltd.**

Schering AG Agreement

A leading German pharmaceutical company, **Schering AG** has recently set up a new initiative to identify new targets for female contraception. Members of the Institute's scientific team have been invited to join the Consortium which is providing substantial funding for further work at Prince Henry's Institute and a potential endometrial target already identified in the Uterine Biology Laboratory, directed by Professor Lois Salamonsen. This is only one of five groups selected world-wide for this initiative and the choice clearly recognises the globally significant research expertise at Prince Henry's Institute in terms of female reproductive health.

Funding Matters

This year we are the beneficiaries of a new initiative by the **Commonwealth Government** to provide infrastructure support to independent medical research institutes amounting to 20% of peer-reviewed **NHMRC** grant support. This is the successful conclusion to a long campaign involving us as a member of the **Australian Association of Medical Research Institutes (AAMRI)** to persuade the Commonwealth Government to invest in this fashion. This year we received $4.1 million in peer-reviewed grants (up from $3.8 million last year), and most of this is from the NHMRC, so clearly this is a substantial new source of much needed infrastructure support.

In addition to this we continue to receive international funding from the **World Health Organization** for research into the development of female contraceptives and for research into uterine biology; from **CONRAD/CICCR** to provide funding for research into new targets for female contraception; and from the **National Institutes of Health** of the USA for improving long-acting contraceptives such as Implanon. We also continue to receive support from Australian funding bodies including the **Victorian Breast Cancer Research Consortium Inc**., for investigating ways to better improve diagnosis and treatment of breast cancer, from the **National Australia Bank Ovarian Cancer Foundation** for our ongoing research seeking early detection markers for ovarian cancer, and from **Merck & Co Inc (USA)** for improving treatments for cardiac fibrosis and heart disease in patients with the Metabolic Syndrome.

One disappointing outcome, during the period under review, was the failure of the huge effort on the part of the biomedical research community to persuade the Commonwealth Government to accept the findings of the Investment Review which was presented to them last year, as a joint effort by Research Australia, AAMRI, the Australian Society for Medical Research and other agencies. Once again Prince Henry's Institute was heavily involved in this effort. The review recommended a doubling of the NHMRC budget following the completion of the Wills round to a sum approaching $1 billion annually. This would place us in line with the other OEDC countries. We must and will continue our efforts in this direction in time for the next Commonwealth budget.

Commercialisation

Our royalty stream on sales of inhibin products in the USA continues to flow at a pleasing rate, and prospects for new markets are very encouraging, in particular for the inhibin-based diagnostic test for ovarian cancer.
Antibodies Australia, at Prince Henry's research facility in Werribee, has continued to produce a range of antibodies available for sale to the Australian research market.
A number of orders have been filled and customer response is very positive.

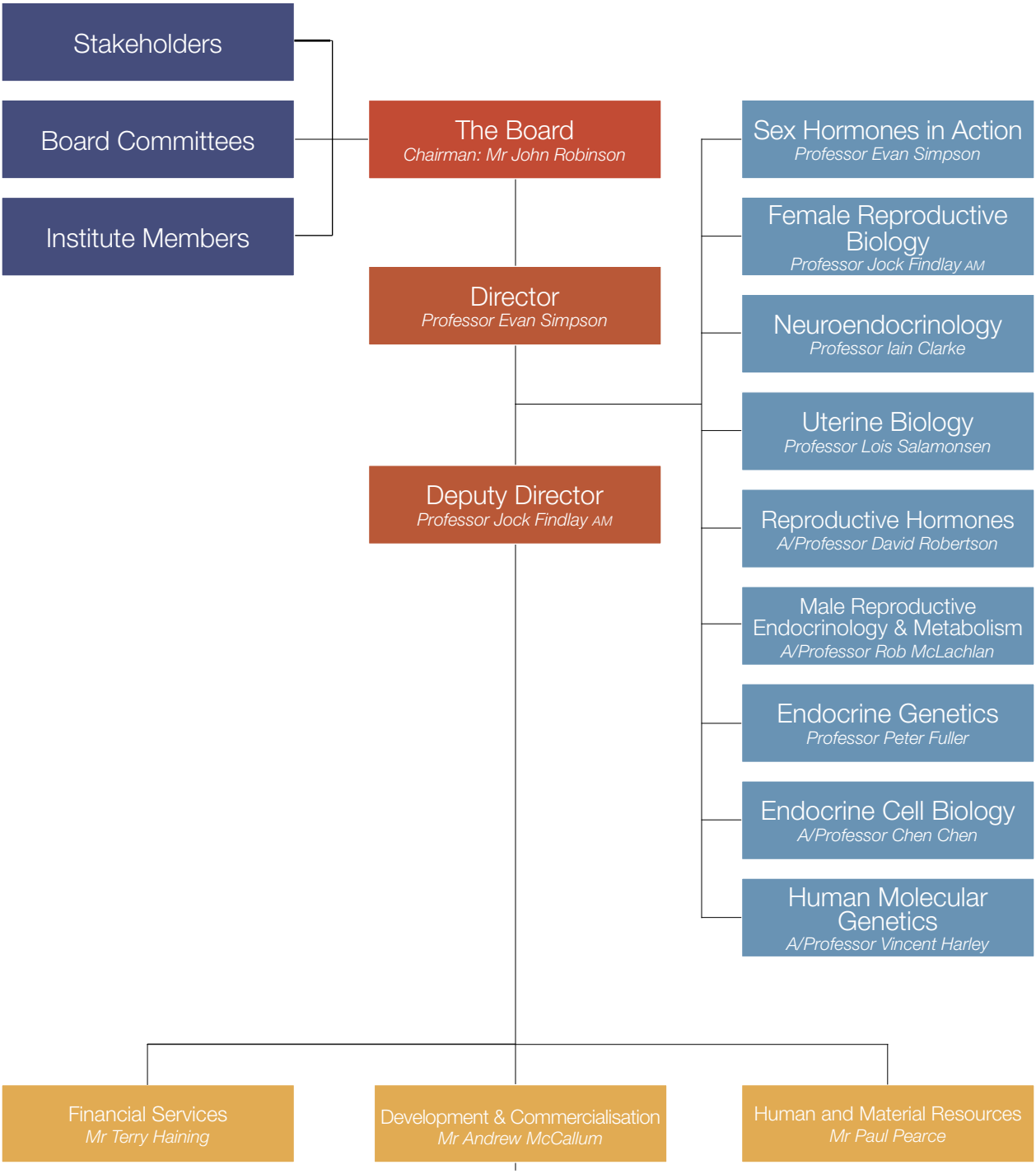
Branding Strategy

Driven by the Development Committee and with the expert guidance of advertising agency, **Tribal DDB**, Prince Henry's Institute has embarked upon a new branding strategy to communicate more effectively with the public and potential donors. The Institute has embraced this new direction, new logo and tagline, as it is an important step for improving marketability and fundraising appeal.

So in conclusion, this year has witnessed both an expansion of our activities as well as the development of new directions. Both of these represent the fruition of many years of patient work towards these goals. I am confident that the outcome will only be to the Institute's benefit.

Evan Simpson
Director

Organisational Structure



Dale Medal Award

Professor Jock Findlay AM has been awarded the 2006 Dale Medal from the UK Society for Endocrinology

The Dale Medal is the highest accolade bestowed by the UK Society for Endocrinology and acknowledges excellence in hormone research. Professor Findlay is one of only five Australians to have won the award. He was recognised for his contribution to reproductive health research, in particular a better understanding of the ovary, leading to improved knowledge of fertility and treating infertility in women.

Professor Findlay has worked in this field for more than 30 years and was one of the original collaborators on the first paper on hormone replacement in women receiving IVF (in vitro fertilisation) treatment. He has served on a number of advisory committees for the Reproductive Health and Research Department of World Health Organization (WHO) in Geneva, Switzerland and ultimately was Chair of the WHO Scientific and Technical Advisory Group on Reproductive Health.

In 2001, Professor Findlay was recognised in Australia for his contributions by being made a Member of the Order of Australia.

He is currently Chairperson of the Infertility Treatment Authority of Victoria, and Chair of the National Health and Medical Research Council Embryo Research Licensing Committee. He is also a National Health and Medical Research Council Fellow and receives substantial support from the Federal Government.

At present, Professor Findlay's research centres on the hormonal control of egg development in the ovary which has implications in understanding ovulation, the regulation of the lifetime of eggs which determines the length of fertility, and the time of the menopause. He is also collaborating with other scientists at Prince Henry's Institute on a project investigating new methods of contraception.

Proteomics Technology

A New Era of Research

A state-of-the-art Proteomics facility begins a new era of medical research at Prince Henry's Institute.

The technology has significant application for the diagnosis and treatment of conditions such as cancer, heart disease, diabetes and male and female infertility. Among the many advantages is the ability of Proteomics to detect extremely small quantities of novel proteins in blood serum in diseased states.

Where the 1990s saw enormous advances in medical research resulting from the genomics revolution, research has now moved forward to a period where the Proteomics revolution will provide even greater advances.

The introduction of Proteomics technology at Prince Henry's Institute will maximize the Institute's ability to create successful research outcomes. It will also facilitate the opportunity for national research collaborations to combat disease and provide better health for all.

The following health conditions and research projects are being investigated using Proteomics.

Diabetes

• Identification of the hormones secreted by fat cells that induce pancreatic beta-cell dysfunction, which occurs in type 2 diabetes.

Cancers

• Identification of novel proteins expressed in endometrial cancer cells and the regulation of these proteins by local growth factors.

• Identifying the key molecular events which lead to the development of a range of granulosa cell tumours, a form of ovarian cancer.

High Blood Pressure

• Investigation of the mineralo-corticoid receptor and aldosterone and their roles in high blood pressure.

Aged Health Research

• Identification of changes in protein production by pituitary growth hormone cells during growth hormone deficiency and after long term treatment with growth hormones.

Pregnancy

• Identifying key proteins required for preparation of the endometrium for embryo implantation, in women who fail to become pregnant.
• Further identification of two proteases, one previously not known, which are critical for the processes of uterine implantation and placentation, important for fertility and establishment of pregnancy.

Infertility

• Investigation of the genetic and hormonal factors in male fertility and testicular biology.

• Analysis of the protein profile of uterine samples taken from fertile and infertile women.

• Examination of new targets for treatment of infertility and for development into a new test for 'uterine receptivity' in women.

Photo: Proteomics Laboratory

Obesity Research

People who suffer from obesity have low levels of growth hormone which contributes to an increase in fat tissue

Appetite control

Obesity is unhealthy levels of excess weight and is the most common medical problem in our community. At least 15–20 per cent of the western world is obese, with a much greater number being overweight.

Appetite and the regulation of food intake are controlled by cells of the hypothalamus in the brain. Scientists aim to clarify how food intake is regulated with a view to understand how obesity occurs.

The Institute's research has detailed how food intake and weight can be altered by factors such as day-length. This helps in understanding the basic mechanisms that control appetite. We are especially interested in the interactions between nutrition and reproduction and the cellular functions that relate to both.

One very important factor in the regulation of food intake is the hormone leptin, which is produced by fat cells. Leptin acts as a 'barometer' informing the brain of the level of fatness. In thin animals, low levels

of leptin inform the brain of the lack of energy stores and reproduction ceases. Studies show that reproductive function in animals can be restored by infusion of leptin into the brain. We are currently studying the brain mechanisms underlying this response.

Appetite controlling hormones

Appetite controlling hormones regulate body weight, our fat/muscle ratio and are significant factors underlying obesity. Prince Henry's Institute is conducting research into the hormones leptin, orexin, ghrelin and growth hormone, to better understand this significant health condition.

People with obesity have low growth hormone levels, which contributes to an increase in fat tissue and a decrease in muscle mass.

Leptin, which is secreted from fat cells, acts on the brain to reduce food intake and increase energy expenditure. In obesity, however, the ability of leptin to reduce food intake is altered. Our research has shown that high levels of leptin act on the pituitary gland (at the base of the brain) to inhibit growth hormone secretion.

Potential targets for treatment of growth hormone deficiency may be via the hormones orexin and ghrelin. Our findings show that brain derived orexin acts on the pituitary to enhance growth hormone secretion.

Photo: Research Fellows Margaret Jones (left), Anne Corbould with Kerry McInnes, Research Officer (centre)

Ghrelin, which is produced in the stomach, circulates to the pituitary gland to stimulate the function of growth hormone cells.

By studying these phenomena in the pituitary gland, we will better understand the mechanisms causing growth hormone deficiency in obesity. By clarifying the way in which appetite controls hormone function, we hope to be able to correct growth hormone deficiency in obesity. In doing so, our research could assist the reduction of fat and increase energy expenditure and muscle mass.

Metabolic syndrome and oestrogen

With increasing obesity and sedentary lifestyle, the prevalence of Metabolic Syndrome is on the rise. This condition has been estimated to affect 20-30% of the middle-aged population.

Metabolic Syndrome is a group of closely related risk factors that contribute to the onset of diabetes and heart disease. The risk factors include obesity, especially when fat accumulates around the waist, insulin resistance and high blood pressure. There is an important but as yet not fully understood relationship between oestrogen and the development of these risk factors.

By utilising the ArKO mouse which cannot make its own oestrogen, we are conducting studies investigating how oestrogen contributes to maintaining the body's balance of fat tissue, sensitivity to insulin and a healthy heart.

The outcome of this work will provide a better understanding of how oestrogen can best be used as a therapy to prevent the development of the risk factors for the Metabolic Syndrome.

Funding

National Health and Medical Research Council of Australia
National Institutes of Health, USA
Merck & Co Inc.

Collaborators

Monash University, Melbourne
Victorian Institute of Animal Science, Melbourne
AgResearch, New Zealand
Shinshu University, Japan
Tohoku University, Sendai, Japan
Kitsato University, Japan
Fourth Military Medical University, Xi'an, China
National Cardiovascular Centre Research Institute, Osaka, Japan
LeHigh University, USA
MRC Reproductive Biology Unit, Edinburgh, UK

Cardiovascular Research

Research shows that cardiac fibrosis which leads to heart disease can be prevented and reversed

Photo: Professor Peter Fuller with PhD student Amanda Rickard and Senior Research Officer Morag Young

Investigating hormones and hypertension

Cardiovascular disease is the largest cause of death in Australia, accounting for 40% of all fatalities. The underlying causes of much cardiovascular disease and heart failure are hypertension (high blood pressure), stiffening of the heart (cardiac fibrosis) and chronic heart failure.

One of the critical determinants of blood pressure control is the body's ability to handle salt (sodium chloride). Research findings show that the most important factor in the control of salt balance is the hormone aldosterone.

Through better understanding of aldosterone and its role in the development of hypertension, our scientists hope to be able to assist in the development of improved treatments for cardiovascular disease and heart failure. This work is also investigating aldosterone and cardiac fibrosis (the stiffening of the heart) in heart failure.

Aldosterone is a steroid hormone secreted by the adrenal gland, which acts on the kidney and colon to increase sodium retention. Over-stimulation of this system leads to hypertension. Despite the link between aldosterone and cardiovascular disease, there is still little understanding of the basic molecular mechanisms of its action.

Like other steroid hormones, aldosterone primarily regulates cellular function by binding to an intracellular receptor. Once activated, this receptor switches genes on and off. A better understanding of the interaction of aldosterone with its receptor at a molecular level is the major focus of the Institute. In the design of novel therapies, drugs that are tissue specific are highly desirable. Studies are directed at understanding the basis of tissue specificity, particularly differences that may allow targeted therapy.

A consequence of the Institute's studies will be improved current treatment options for hypertension and cardiovascular disease.

Blocking aldosterone action in heart failure

High levels of the adrenal steroid hormone aldosterone are an independent risk factor for cardio-vascular disease.

In the landmark international clinical trial, Randomised Aldactone Evaluation Study (RALES) in 1997, the addition of a low dose aldosterone receptor blocker, on top of normal treatment, produced 30-35 per cent improvement in survival for patients with moderate to severe heart failure.

Fibrosis, or stiffening of the heart tissue, is involved in the progression of heart failure. Our research is investigating the role of aldosterone in the development of cardiac fibrosis. This work has revealed that cardiac fibrosis develops following activation of the aldosterone receptor and the initiation of inflammation, which we have shown to be a key step in this process.

This work suggests that the aldosterone receptor may be a significant regulator of inflammation in the blood vessel wall, in addition to the closely related glucocorticoid receptor, which is a well known regulator of inflammation.

Significantly, we have identified that blocking the aldosterone receptor not only prevents cardiac fibrosis and vascular damage, but also reverses this process. Our work also reveals that blockade of the mineralocorticoid receptor may also have beneficial effects in the kidney.

Results from our studies will provide the basis for the development of future pharmacological interventions and novel treatments for cardiac fibrosis, heart failure and hypertensive kidney disease.

Protective effect of hormones in chronic heart failure

Chronic heart failure occurs in two percent of the western population. Of these people, 65 per cent will die within five years. There is currently no effective treatment for this condition. Our work investigates the action of the hormone ghrelin in this condition.

Normally secreted by the stomach cells, this hormone has been found to have an important role in the heart. The specific receptor for ghrelin is highly present in the heart muscle cells. We have demonstrated that this hormone increases the contraction of heart muscle cells and protects them from programmed cell death which normally occurs in heart failure and in blocked coronary arteries.

We have also shown in animal studies that ghrelin protects the heart muscle cells and alleviates cardiac dysfunction and Cachexia. Research now aims to clarify the mechanisms by which ghrelin acts upon cardiac cells.

By further investigating the cellular mechanisms of ghrelin, scientists at the Institute will be able to show the potential use of this hormone in the treatment of chronic heart failure.

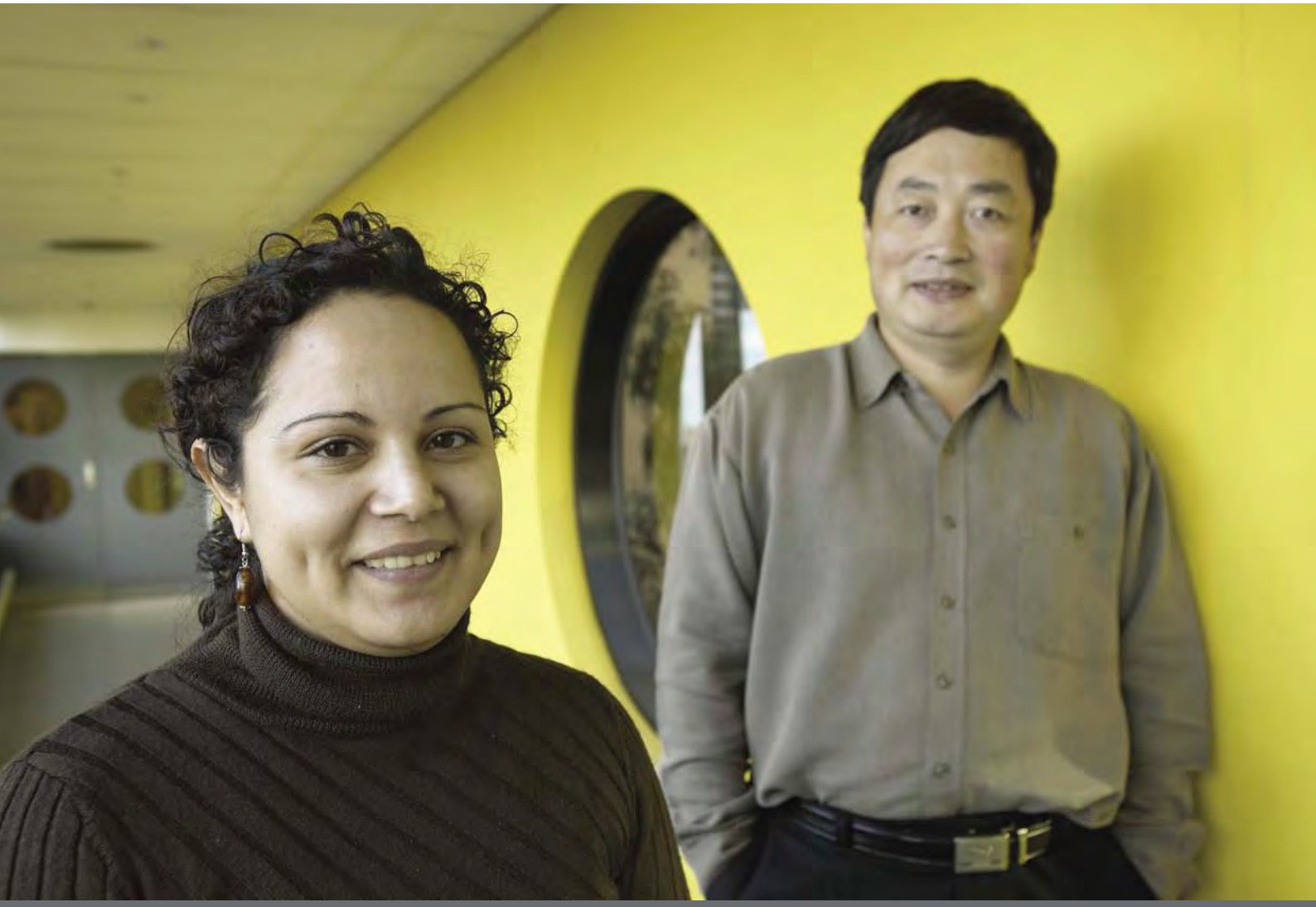
funding

National Health and Medical Research Council of Australia
National Heart Foundation of Australia
High Blood Pressure Research Council of Australia
Pfizer Pty Ltd
Merck & Co.Inc

Collaborators

Walter and Eliza Hall Institute, Melbourne
Chinese Academy of Medical Sciences, Beijing, China
Xavier Bichat Hospital, Paris, France

Diabetes Research



To reduce the number of Australians suffering from diabetes, we are investigating the role of genes and hormones in this disease

Genetic control of diabetes

The regulation of insulin in health and disease is poorly understood. Research has discovered a potential role of the human gene SOX13 and its protein in diabetes.

The SOX13 gene is produced in the developing embryo, particularly in cells that become the insulin-

producing beta cells of the pancreas. These cells are important as they are required for the normal metabolism of sugars in the body.

Research at the Institute has shown that the SOX13 protein turns genes on when it is in the nucleus of the beta cell. Scientists have observed high insulin levels in those cells containing SOX13 in the nucleus, the site where it is active. Moreover SOX13 forms a complex with SOX9 which greatly improves its action. Humans and mice lacking SOX9 develop diabetes. Research is aimed at dissecting the molecular mechanisms by which these two SOX proteins affect insulin production.

Insulin secretion and fat cells

Diabetes affects over one million Australians and is the fifth major cause of death. Type 2 diabetes, which accounts for 90% of all diabetes cases, occurs often in overweight and obese people.

These patients have a significant abnormality of insulin secreting cells in the pancreas, called beta cells. It is generally accepted that excessive fat cells evoke tissue non-responsiveness to insulin and damage the beta cell function. The mechanisms underlying this damage of beta cell function in obese patients is unclear.

Each individual hormone and factor produced from fat cells is currently under investigation.

Using a co-culture system, fat and beta cells have been put together to analyse the action of hormones and factors produced from fat cells on the beta cells. From this process several molecules have been identified and will be further investigated. It is hoped that continued research in this area will lead to new ways of preventing and managing type 2 diabetes in overweight and obese patients.

Oestrogen and diabetes

Scientists have discovered that mice lacking oestrogen develop diabetes. Studies show that as oestrogen-deficient mice get older, they develop increased body fat, insulin resistance and diabetes. These conditions can be prevented by administering oestrogen. This gives scientists insight into the role that oestrogen plays in the prevention of diabetes.

This research is significant for understanding the ageing process and health problems of postmenopausal women who cannot make their own oestrogen. It is also important for younger women who have a common condition called Polycystic Ovarian Syndrome (PCOS) characterised by ovarian failure. Both ageing and PCOS are associated with an increased incidence of diabetes.

Research Assistant Maria Hernandez with Associate Professor Chen Chen, Endocrine Cell Biology group

Funding

National Health and Medical Research Council, Australia
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Collaborators

Monash University, Melbourne
University of Melbourne
Central South University, Changsha, China
Fourth Military Medical University, Xi'an, China
University of Texas, Southwestern Medical Centre, USA

Sex Determination & Bone Disorders

Scientists have developed a human cell culture model that replays critical events in sex determination

Sex and genetics

In the human embryo, gender is determined at seven weeks gestation when a developmental decision is made in the gonad by the sex chromosomes (XY in males, XX in females). Whether you develop as a male or a female depends on whether you develop testes or ovaries.

If you have a Y chromosome, the SRY gene will be turned on and your gonads begin to develop into testes and male development begins. If you do not have a Y chromosome, your gonads begin to develop into ovaries and female development begins.

Our scientists are investigating genes, primarily SRY and SOX9, which disrupt formation of the human testis leading to various forms of intersex conditions.

Intersex conditions

Intersex is a condition where the physical sex of the person does not match the sex of their chromosomes (i.e. XY females and XX males). Defects in sexual development affect one in 4,000 births and their clinical management is a major paediatric issue.

SRY and SOX9 are crucial to male development. When they do not function properly, rare but traumatic conditions such as Swyer Syndrome and Campomelic Dysplasia can occur, where patients have male chromosomes but female genitalia.

In collaborative studies with the Ludwig Institute of patients with Swyer Syndrome, we have found that the ability of SRY to move into the nucleus of testes cells is blocked, so that SRY could not turn on genes required for testis development. This work led to the discovery of the calmodulin-mediated pathway by which proteins are imported into the nucleus. Unfortunately the majority of intersex conditions remain unexplained genetically.

We have developed a human cell culture model that replays critical events in gonad development. This system will enable scientists to discover new genes that may potentially cause intersex conditions, thus improving genetic diagnoses, counselling and treatment options.

Photo: Associate Professor Vincent Harley with Research Officer Stefan Bagheri-Fam

Diseases linked to intersex conditions

In addition, our research has demonstrated the effects of loss of SOX9 in Campomelic Dysplasia (CD), a human condition characterised by severe dwarfism, where males also have female genitalia.

Mice lacking the SOX9 gene show many features of CD including sex reversal and dwarfism. By analysing these mice, our understanding of the normal
roles of SOX9 in bone and testes formation is improved. Both humans and mice lacking the SOX9 gene also have other conditions including craniofacial defects and diabetes, which are also being studied.

Bone and face development

Craniofacial abnormalities occur in one-third of all birth defects and in most cases the genetic basis is unknown. Children affected with cleft palate frequently have respiratory and feeding difficulties neonatally which result in moderate to severe growth and development deficiencies in their first year.

Our studies show that the gene SOX9, which is critical in sex determination, is also important in the formation of the face and other bones. Research involves screening Pierre-Robin patients for genetic changes in a DNA element which controls SOX9 production in the face.

This research Identifying and understanding molecules that work to form the human face will provide new insights into why development does not proceed normally in patients with craniofacial anomalies. This is the first step towards improving diagnosis and clinical management of this very common and heterogeneous group of disorders.

Funding

National Health & Medical Research Council of Australia

National Institutes of Health, USA

Perpetual Trustees Ltd

Human Growth Foundation, USA

Collaborators

Ludwig Institute, Melbourne

Murdoch Children's Research Institute, Melbourne

Institute of Molecular Bioscience, Queensland

Institute of Human Genetics, University of Freiburg, Germany

Institute of Biomedical Investigation, Mexico

National Institute for Medical Research, London, UK

University of California Los Angeles, USA

Exploratory Hormone Research

Scientists are studying the hormone family of inhibin and activin to better understand their role in reproduction and disease

Discovering the role of inhibins and activins

Since the early eighties, scientists at Prince Henry's Institute have been researching the hormone families of inhibin and activin and their role in male and female reproduction.

These hormones play a key role in the regulation of follicle stimulating hormone (FSH) secreted from the pituitary in the brain, which in turn controls sperm production in the testis and egg production in the ovary. They also have a potential role in the treatment of a range of diseases.

Investigating inhibins in reproduction

A significant research discovery by Prince Henry's Institute in the eighties, was the isolation of various forms of inhibins. This showed that inhibins are important in the regulation of fertility. Our current field of research focuses on better understanding the role of inhibins in the body. In particular, we aim to examine the two forms of inhibins, A & B, which are believed to have differing functions in the body.

There is hope that further study in this field will lead to the discovery of the elusive inhibin receptor, and for the potential development of new treatments for infertility.

Blocking activin to combat disease

In collaboration with the Salk Institute, USA, we have discovered a novel compound important for disrupting the activin signalling system. This could help to develop ways to either block or enhance its action and may have a range of clinical applications for treatment for a number of conditions.

Our work has shown that blocking activin action impacts on scar tissue formation during wound repair.

Photo: Associate Professor David Robertson with PhD student Yogeshwar Makanji, Reproductive Hormones group

We have also shown that activin has a relationship with profound muscle and fat loss in conditions associated with AIDS and cancer.

Another research discovery is that this compound could also block the action of the protein, myostatin. We have shown that if this protein is blocked, it enhances muscle growth. This research may have particular significance for people with muscular dystrophy.

The Institute also hopes to define the role of activins in ovarian and testicular cancers, which may have implications for potential treatments of these diseases.

Premature ovarian failure

Premature Ovarian Failure causes women to experience menopause before the age of 40. This disease affects one in 100 women worldwide. Women who experience this condition stop ovulating, their menstrual cycle ceases, and they experience menopausal-related symptoms of infertility as well as increased risk of cardiovascular disease and osteoporosis.

In collaboration with Auckland University, Prince Henry's Institute is investigating the role that mutated hormone inhibin plays in the development of this disease. A mutation in the hormone inhibin, while not common, is prominent in the tissue of women who have suffered this disease.

Funding

National Health and Medical Research Council of Australia

Collaborators

SALK Institute, San Diego, USA
University of Auckland, New Zealand

Breast Cancer Research

Our research shows that the principal source of hormonally driven breast cancer in postmenopausal women, is local oestrogen production in the breast

Blocking oestrogen in the breast

One in twelve Australian women will suffer breast cancer at some point in their lives. Research at the Institute has provided evidence that the principal source of oestrogen driving breast cancer development in postmenopausal women is local oestrogen production in the breast itself.

Inhibitors of aromatase, the enzyme that produces oestrogen, are now coming into the realm of breast cancer therapy. These new treatments have been shown to improve the quality and length of life

The problem with these inhibitors, however, is that they also block aromatase activity everywhere in the body. Aromatase activity is important in the brain for memory, and in bone for preventing osteoporosis.

Our work is focussed on looking for ways to specifically block oestrogen in the breast whilst not affecting the production of the hormone in other important sites in the body. To achieve this goal, we are identifying factors that uniquely control aromatase production in the breast and which could therefore be targets for drug treatment.

Dual role of protein in breast cancer

Our research has provided some significant targets for the treatment of breast cancer. The protein LRH1, previously known for its role in the liver and the pancreas for controlling cholesterol and bile production, has been shown to play a dual role in breast cancer.

In 2002, our research team were the first to show that LRH1 has a direct connection with breast cancer via localised oestrogen stimulation. This is because LRH1 uniquely stimulates aromatase expression in the breast but not elsewhere.

Photo opposite: Colin Clyne, Research Fellow with Professor Evan Simpson, Sex Hormones in Action group

Current research indicates that LRH1 plays a dual role in furthering tumour growth. LRH1 causes the fat tissue surrounding a breast tumour to produce oestrogen which is required for tumour growth. Secondly, LRH1 is highly present within the tumour itself where it has a direct pathway to stimulate tumour growth.

We have demonstrated that LRH1 is a significant target for the treatment of breast cancer. Therefore drugs which might inhibit LRH1 activity could find utility as the next generation of breast cancer therapeutic agents.

The work is a collaboration between Prince Henry's Institute and SENDAI University Tohuko, Japan. It is supported by the Victorian Breast Cancer Research Consortium and the National Health and Medical Research Council of Australia.

Agnes Kovacic, PhD student, Sex Hormones in Action group

Funding

Victorian Breast Cancer Research Consortium Inc. Melbourne
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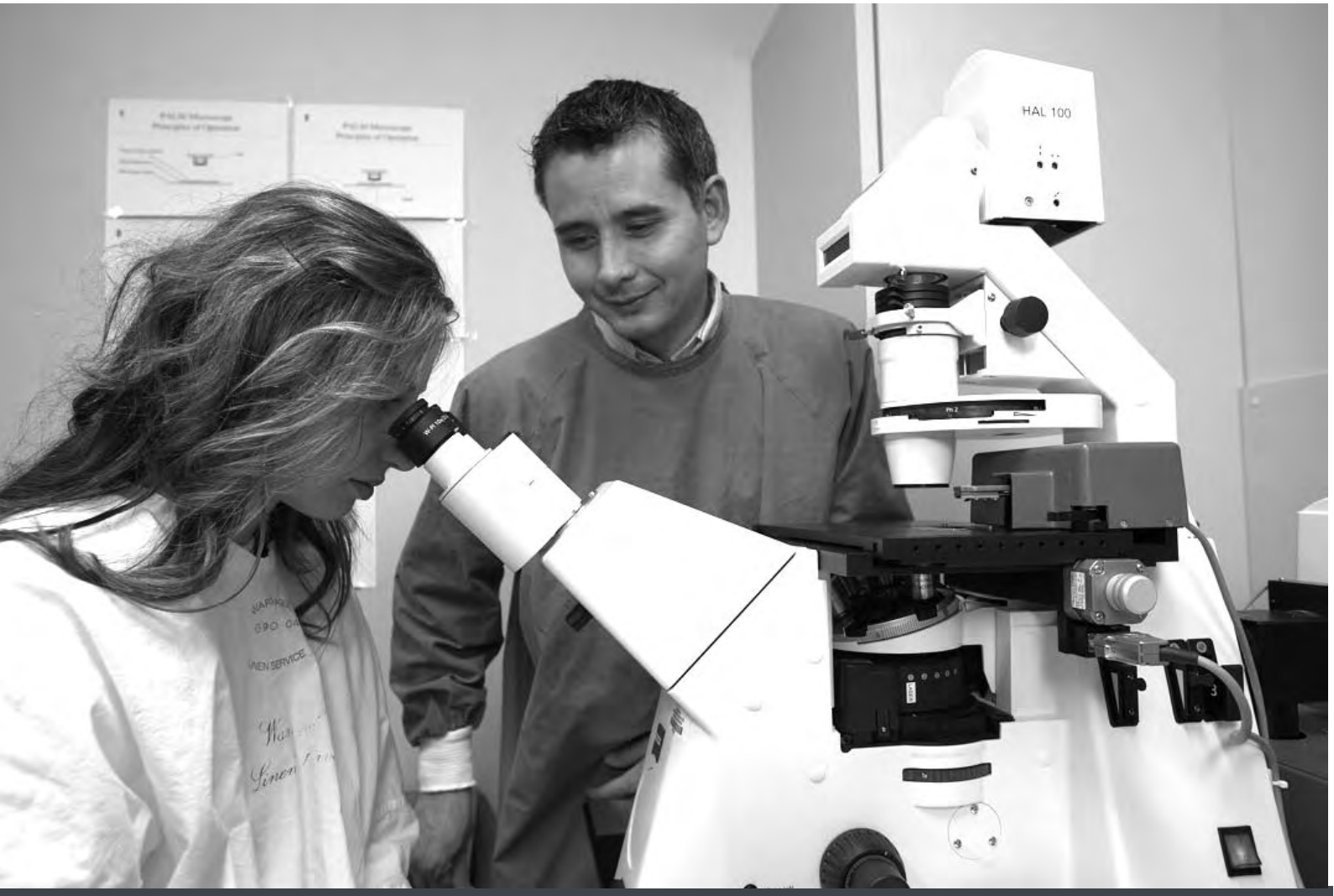
National Institutes of Health, USA

Collaborators

Victorian Breast Cancer Research Consortium Inc., Melbourne
Melbourne University
Tohoku University, Japan
Duke University, North Carolina, USA
University of Calabria, Italy

Ovarian Cancer Research



Using the latest technology, our scientists aim to identify early detection markers for ovarian cancer

Proteomics investigating ovarian cancer

One woman dies of ovarian cancer in Australia every ten hours. Although less common than breast cancer proportionally more women die from ovarian cancer. When diagnosed, ovarian cancer is usually well advanced and often spreads to other areas of the body decreasing chances of survival.

Using a new technology called Proteomics our main objective is to identify early detection markers for ovarian cancer.

The most promising tool for identifying new serum proteins and unique expression patterns of proteins (so called “protein signatures”) in women with ovarian cancer is proteomics – the study of protein shape, function and patterns of expression.

With the support of the National Australia Bank and the Ovarian Cancer Research Foundation (OCRF), the Institute has been able to acquire a Ciphergen ProteinChip SELDI-TOF-MS (surface-enhanced laser desorption/ionization time of flight mass spectrometer) proteomics system.

The SELDI technology provides a platform for the detailed characterization of the patterns of proteins. By comparing different tissues (ie normal tissue vs cancer) changes in protein expression may provide clues as to why a cancer develops.

We are world leaders in the molecular characterisation of granulosa cell tumours. Granulosa cell tumours of the ovary have a unique behaviour requiring specific study. This is reflected in the ongoing support received for this work from the Granulosa Cell Tumour of the Ovary Foundation, the North American based patient support group. Scientists from Prince Henry's Institute have identified abnormal control of cell growth in these tumours. The genetic changes underlying this behaviour are being sought.

The role of hormones, especially oestrogen, in these tumours is also being investigated. Several potential therapeutic interventions are being tested in human tissue and tissue cells in culture. This molecular understanding will help to predict prognosis (whether the disease will relapse) and to develop specific targeted treatments.

Photo (left): Maria Alexiadis, Witchery Research Assistant and PhD student Simon Chu with the Laser Dissection microscope

Finally, using laser capture microdissection technology scientists are attempting to measure inhibin levels in mucinous tumours, one of the most common types of ovarian cancers.

Australian ovarian health study

Currently there are no health programs for assessing the ovary as there are for the breast and the cervix. An Australian-first study is establishing an ovarian health program for healthy postmenopausal women, who are at risk of developing ovarian cancer.

The study is developing parameters for a health program to be available to postmenopausal women to check their ovaries, in the same way that pap screens and mammograms are available to women wishing to check their cervix or breasts.

Five hundred women, whose last menstrual period was five or more years ago are being recruited for the study. The combined blood test, consisting of CA125 and the hormone inhibin, developed by Prince Henry's Institute and Diagnostic Systems Laboratories Inc, is being tested for the first time in the study.

This study is being jointly funded by the National Australia Bank Ovarian Cancer Research Foundation (OCRF), Diagnostic Systems Laboratories Inc and Inhibin Pty Ltd.

For more information visit www.ocrf.com.au

Funding

National Health and Medical Research Council of Australia
National Australia Bank Ovarian Cancer Research Foundation, Melbourne
Granulosa Cell Tumour of the Ovary Foundation, USA

Collaborators

Inhibin Pty Ltd, Sydney
Monash Institute of Medical Research, Melbourne
Department of Obstetrics and Gynaecology, Monash University, Melbourne
Department of Gynaecology Oncology, Southern Health, Melbourne
Victorian Bioinformatics Consortium, Monash University, Melbourne
Oxford Brookes University, Oxford, UK
Diagnostic Systems Ltd, Houston, USA

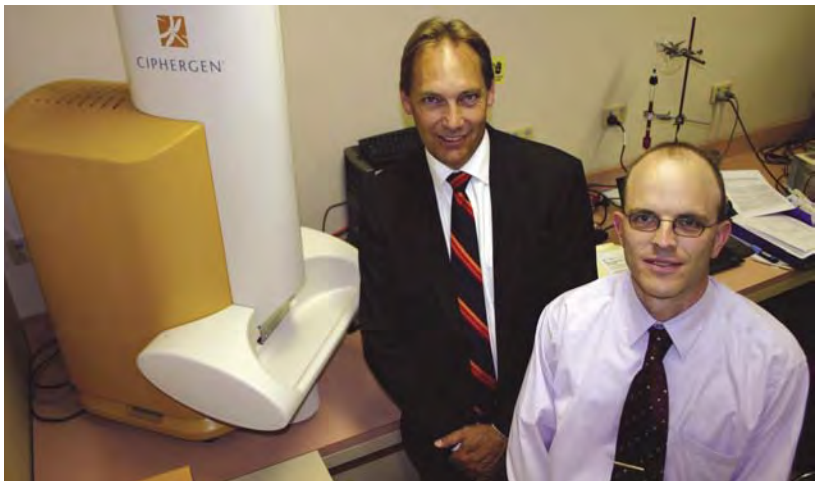


Photo (above): Associate Professor Tom Jobling, Chairman of the NAB Ovarian Cancer Research Foundation, with Dr Martin Oehler with the SELDI Proteomics system

Founding Partner National

ovarian cancer
RESEARCH FOUNDATION
www.ocrf.com.au

In collaboration with the NAB Ovarian Cancer Research Foundation, Scientists at Prince Henry's Institute are working to find an early detection test for ovarian cancer

Ovarian cancer is the sixth most common cancer affecting Australian women. Every year approximately 400 women are diagnosed in Victoria, while across Australia one woman dies every ten hours from this disease.

Although less common than breast cancer, proportionally more women die from ovarian cancer because when diagnosed, the disease is usually well advanced and has often spread to other areas of the body.

The key to improving the survival rate of ovarian cancer is early detection.

The National Australia Bank Ovarian Cancer Research Foundation, in collaboration with Monash Medical Centre and Prince Henry's Institute, is dedicated to continuing research into this insidious disease.

With the support of its founding partner, National Australia Bank, the Foundation has established a Research Fellowship currently held by Dr Martin Oehler (known as the National Australia Bank Research Fellow). The retailer Witchery also supports the Foundation and their support has enabled the appointment of a Research Assistant, Ms Maria Alexiadis (known as the Witchery Research Assistant).

Dr Oehler and Ms Alexiadis are working to progress the development of an early detection program for ovarian cancer in collaboration with Prince Henry's Institute's Professor Peter Fuller and Associate Professor David Robertson.

The Foundation is chaired by Associate Professor Tom Jobling, Head of Gynaecological Oncology at Monash Medical Centre, and was co-founded with Ms Liz Heliotis, Managing Director of the Foundation, in 2000.

For further information about the Ovarian Cancer Research Foundation, please visit www.ocrf.com.au or telephone 03 9296 2040.

Buy a silver ribbon for ovarian cancer research

Every year Ovarian Cancer Research Week is held in the first week of September to raise funds for ovarian cancer research.

Throughout the year, ribbons can be purchased from Witchery stores throughout Australia. The National Australia Bank also sells ribbons in August and September each year during the "Silver Ribbon" campaign.

We urge you to support this worthy cause to help us fund research into an early detection test.

Donations may also be made at any National Australia Bank branch or on-line at www.ocrf.com.au

For further information, please telephone 03 9296 2040

Photo: Maria Alexiadis, Witchery Research Assistant and the Microarray Reader

Female Reproductive Research

Oestrogens are important for fertility. However, the degree to which they are important is still being discovered

Investigating ovulation

Infertility affects one in eight couples with equal contributions from male and female partners. To better understand conditions of infertility in women, we are investigating the ovary and the impact of hormones such as oestrogen and inhibin.

At around birth, the ovary contains the maximum number of eggs it will ever contain. Each egg is in an immature state and incapable of being fertilised. It is housed inside a circle of supporting pre granulosa cells to form a unit called a primordial follicle.

The human ovary has the unique job of looking after the resting eggs in the primordial follicles from birth to menopause some 50 years later. Each day, a group of 20–30 begin

to grow and develop until the pool of primordial follicles is depleted at menopause. Release or ovulation of an egg from a developed follicle does not begin until puberty.

A woman will only ovulate one, and occasionally two, eggs each menstrual cycle. Typically, a Western woman will have 400 menstrual cycles during her reproductive life, so she will ovulate about 400 eggs or 0.1% of the original pool. This means that the vast majority of follicles will never release their eggs. Instead they reach varying stages of maturity before they die by a process called atresia.

Research at the Institute continues to investigate the critical factors in the development of follicular growth, egg production and fertility.

Oestrogen and follicle development

Oestrogens are important for fertility. However, the degree to which they are important is still being discovered.

We have demonstrated that female ArKO mice, deficient in oestrogens, are infertile because the development of their follicles fails at the early antral stage, the time of ovulation.

Photo: Senior Research officers Ann Drummond and Kaye Stenvers

This works shows that oestrogen is not required for survival at birth or for the formation of the reproductive tract that contains the ovary, uterus, cervix and vagina. However, we have discovered that over time that without oestrogen the ovary changes to being more like the tubules in the testicle.

Importantly when the ArKO mice were treated with oestrogen, either as synthetic estradiol or as plant oestrogens in the diet, their ovaries regained a more normal appearance and some of them even ovulated.

These discoveries shed new light on conditions of infertility. In situations where oestrogen levels are very low, follicular development may be inadequate and as a result there is no ovulation.

During the transition to menopause, and at the menopause, oestrogen levels are variable to extremely low, and cells similar to those found in testicles have been described in the ovaries of ageing females. Treatment with oestrogens as part of hormone replacement therapy may reverse this situation.

Inhibin is made in the ovaries, and works on a feedback system from the ovaries to the pituitary which in turn regulates FSH (follicle stimulating hormone) and the reproductive cycle. Mutated inhibin may disturb this process leading to premature loss of follicles in the ovaries. Our work has investigated the function of inhibin in this feedback system, and its role in the regulation of FSH. Further research may provide insight into the cause of this disease.

Funding

National Health and Medical Research Council of Australia

Collaborators

Department of Anatomy, Monash University, Melbourne
Centre for Urological Research, Monash Institute of Medical Research, Melbourne
MRC Human Reproductive Sciences Unit, Edinburgh, UK
Karolinska Institute, Stockholm, Sweden

We would like to acknowledge Australasian Science for allowing us to reprint some of the above information www.control.com.au.

Pregnancy and Menstruation

For just a few days of each woman's cycle, the womb is receptive to pregnancy

Preparing the womb for pregnancy

The receptivity of the womb is critical for establishing pregnancy. There are many biological reasons why women may not be able to sustain a pregnancy and hence will experience miscarriage.

We have developed a substantial program of work to determine molecular changes in the womb that are critical for establishing pregnancy. Over past years, we have discovered a number of factors previously unknown to be important in this situation.

During most of a woman's monthly cycle, the womb is hostile to an embryo and it will reject any embryo that tries to implant. However, for just a few days in each cycle, changes in the lining of the womb make it receptive.

If an embryo enters the uterus at this time, it will attach to this lining and start to invade: this invasion continues until the cells make close contact with the mother's blood supply. It is from the mother's blood that the developing foetus will obtain nourishment and oxygen.

Using a new technology called antisense, our work has identified key factors essential for embryo implantation. In animal studies we have shown that when we blocked certain molecules in the mouse, it failed to establish pregnancy. We have also shown that these factors are present in the womb of women at the time when an embryo would implant and hence are significant targets for investigation.

This work has considerable implications for our understanding of infertility or of inadequate placentation that often leads to miscarriage. It may also assist in improving treatments such as IVF which can be limited by the failure of apparently normal embryos to implant in the womb. Factors known to be important for implantation may provide useful markers for a receptive womb or for identifying women who may miscarriage early.

Abnormal menstrual bleeding

Excessive uterine bleeding impairs the quality of life of many otherwise healthy women. It is the major presenting complaint in women referred to gynaecologists and represents a significant social and medical problem for women, their families and the health services.

Photo: Professor Lois Salamonsen, Uterine Biology group

Hysterectomy is one of the most common major operations: nearly 30% of these are conducted to alleviate heavy menstrual bleeding.

Understanding the mechanisms of normal menstruation, and how the womb lining repairs itself after this, is critical if new treatments are to be developed for abnormal uterine bleeding to supplant the need for hysterectomy.

Our research focuses on how the lining of the womb is shed during each menstrual cycle: it is now clear that it results from a highly controlled inflammatory-type reaction such as seen in pathological situations where tissue is damaged (for example, in joints of rheumatoid arthritis patients). We have shown that the uterus has special control mechanisms to regulate the process.

Menstruation occurs only in women and a few old-world primates. Other animals do not menstruate. Therefore there have been no animal models to use to study the process and this has severely limited scientist's ability to determine the mechanisms. In a major advance, scientists at the Institute have developed a mouse model for menstruation.

In this model most of the known molecular and cellular events of menstruation in women are replicated. These include expression of chemical catalysts (enzymes) that degrade tissues if uncontrolled and influx of white blood cells into the tissue that provide a wealth of mediators of tissue breakdown.

Functional studies are now being carried out to determine the critical factors for menstruation. These are likely to be relevant also to treat abnormal uterine bleeding.

Funding

National Health and Medical Research Council of Australia
WHO Human Reproduction Programme
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CONRAD/CICCR Foundation, USA
Schering AG, Germany
Royal Australian and New Zealand College of Obstetrics and Gynaecology

Collaborators

Department of Obstetrics and Gynaecology, Monash University, Melbourne
Walter and Eliza Hall Institute of Medical Research, Melbourne
Monash IVF, Melbourne
Canberra Fertility Centre, Canberra
Sydney Centre for Reproductive Health Research, Sydney
Women's and Infant's Health, University of Western Australia, Perth
University of Cambridge, UK
Centre for Reproductive Biology, Medical Research Council, Edinburgh, UK

Male Reproductive Research

The Institute has a long standing research program into the complex process of sperm production and the causes of male infertility

Photo: (L-R) Research Officer Jayne Sierens, Senior Research Officer Sarah Meachem and MSc student Gerard Tarulli

Critical phases of sperm production

In Australia it is estimated that one in 20 men are infertile. Our investigation into the complex and timely phases of sperm development hopes to provide insights into some of the hormonal and genetic causes of male infertility.

The hormones follicle stimulating hormone (FSH) and testosterone are of major importance in promoting the production of the earliest sperm cells (the spermatogonia). These cells are particularly prone to damage during cancer treatments and also develop poorly in some men with unexplained infertility. Understanding the hormones and the genes that control spermatogonial replication, survival and maturation is important for the development of new therapeutic targets for male infertility.

Our work has found that FSH plays a key role in spermatogonial survival, not proliferation. A genetic approach to identify genes that underpin the survival response has been initiated.

Later sperm development involves the sperm head and tail development followed by the release of mature sperm into the centre of sperm tubules. This latter process (called spermiation) may be at fault in male infertility but its inhibition by new treatments may also present an opportunity to reversibly interfere with sperm release yielding a new contraceptive.

As sperm grow in the wall of the sperm tubule, they lie between special nurse cells called Sertoli cells. Special connections, called cell junctions, between the sperm and Sertoil cells allow the two cells to communicate and are the subject of our close study. Other junctions between adjacent Sertoli cells are crucial in allowing sperm development to occur in a fully protected and regulated environment.

Further research in this area has shown that hormones control the way in which these junctions work. In particular, that the specific 'glue-like' proteins which form a tight seal between Sertoli cells are controlled by hormones (both FSH and testosterone). We could hypothesize that problems in the ways these junctions operate might shed light on sperm production and infertility. Conversely, these proteins could also be targets for male hormonal contraception.

Infertility database

In a long standing collaboration with Monash Institute of Medical Research, our scientists are determining if genes that control sperm production are responsible for poor sperm quality. Patients in affiliated fertility practices are invited to contribute blood (DNA) samples along with information about their medical history, physical examination findings, semen quality and hormone levels. These patients contribute to one of the largest such databases in the world for research into the common problem of male infertility and forms an essential part of the programs of research at both institutes.

Oestrogens and male infertility

An important discovery has revealed a possible cause of infertility in males. We have found that the protein called LRH-1, a key factor in oestrogen production in females, also regulates oestrogen production in the male testis.

Previous research at the Institute has shown that human male patients unable to synthesize oestrogens are infertile or subfertile. Our work is focussed on investigating the presence of LRH-1 in the male testis to determine its exact function. This involves identifying the genes regulated by LRH-1 and the proteins with which it interacts. These studies may help to identify new genes associated with male infertility and to develop more effective treatments.

Oestrogen linked to sex drive

Loss of libido is a complex problem that can include a mix of lifestyle and hormonal factors. Our research with oestrogen deficient (ArKO) mice has revealed that lack of oestrogen in the male mice caused a total loss of sex drive.

Previous behavioural experiments conducted at the Institute involved placing a male ArKO mouse, deficient in oestrogen, with a responsive normal female mouse. Normal male mice in this situation attempt sex with the receptive female in a matter of seconds. The male ArKO mouse, however, showed no interest in the female whatsoever. Studies investigating the role of oestrogen in the brain reinforced this observation.

Results show that male ArKO mice experienced loss of cells in the medial preoptic area, the region of the brain that controls sex drive. This research paves the way for the development of novel oestrogen treatments for men that enhance libido.

Erectile dysfunction

Erectile dysfunction affects a large number of Australian men and can now often be treated in various ways including tablets. The Institute's work has involved a number of studies investigating the effects of these treatments on relationships and self esteem issues and in the evaluation of new pharmaceutical agents.

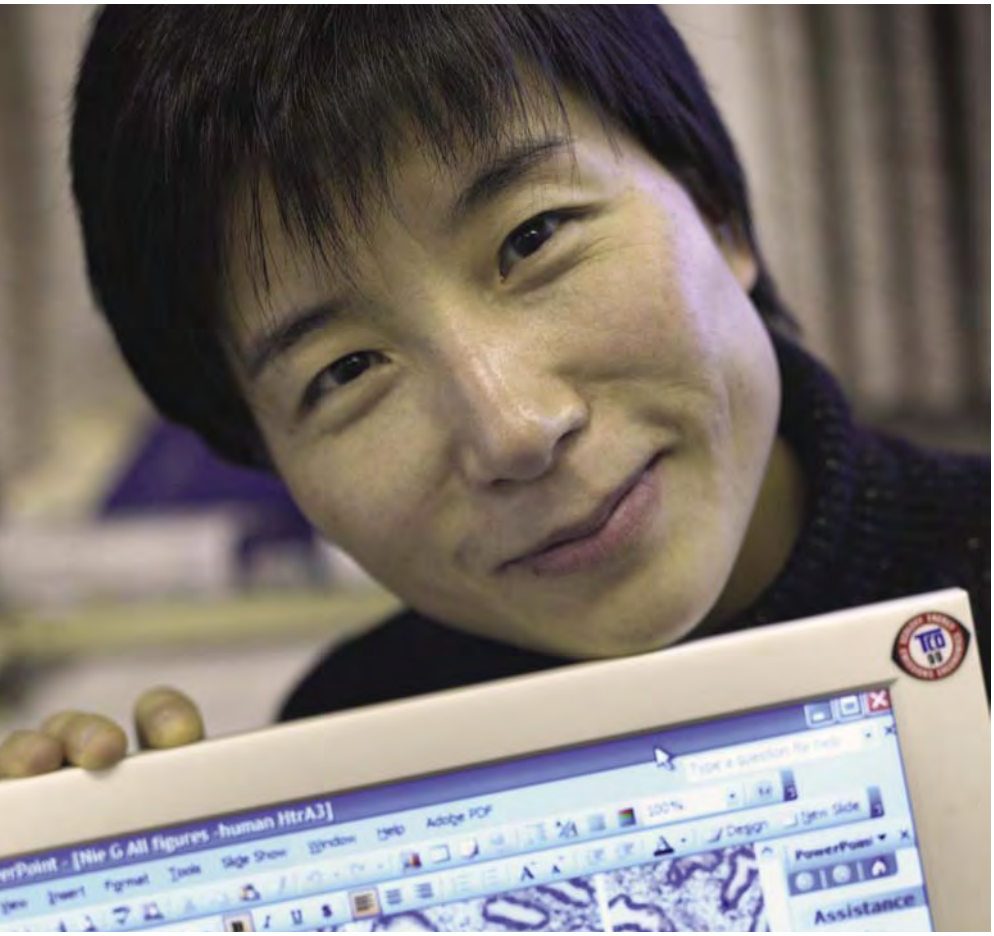
Funding

National Health and Medical Research Council of Australia
Andrology Australia
National Institutes of Health, USA
Schering AG, Germany
Pfizer Pty Ltd
Serono Foundation

Collaborators

Monash Institute of Medical Research, Melbourne
Monash IVF, Melbourne
University of Calabria, Italy
Turku University, Finland
University of Washington, USA
SENDAI University, Tohuko, Japan

New Contraceptive Methods



The exploratory nature of the Institute's research has enabled scientists to discover several targets for new contraceptives for men and women

Photo: Guiying Nie, Senior Research Officer

Male hormonal contraceptive

There is a worldwide need to develop more contraceptive options for men and women. In an ongoing research effort to develop effective male contraceptives, Prince Henry's Institute has undertaken a study to investigate two novel contraceptive agents (acyline and dutasteride) with the University of Washington, Seattle, USA.

The aim of this study is to gain an understanding of the various control points in sperm production in order to reliably block this process.

This work has suggested that sperm production can be suppressed to below a threshold likely to provide excellent contraceptive cover. However there are important differences in the way that men reach this level with a percentage of them remaining resistant to existing treatment approaches. As a result we are using new basic science approaches including microarray analysis to understand the genetic basis for the pre-disposition to respond to contraceptive treatment.

Research has shown that the stage when mature sperm release from the Sertoli cells (called spermiation) is a possible target for hormonal contraception. Agents that effectively block this process may ultimately be used in conjunction with existing contraceptive formulations to allow faster suppression of sperm counts. They may also enable lower doses of contraceptive hormones to be used thus limiting side effects.

Prince Henry's Institute and Monash Institute of Medical Research have continued a Collaborative Research and Licensing Agreement with Schering AG, a leading German pharmaceutical company. This collaborative effort for the next two years will identify and validate novel contraceptive targets within the spermatid release process using sophisticated genomic and proteomic techniques.

Targets for female contraceptives

In developing countries, one in four pregnancies are unwanted and many more are unplanned. There is an identified need for additional contraceptive choices for women as many cannot tolerate hormonally-based contraceptives. Others would prefer contraception that can be used on an occasional basis.

Globally, sexually transmitted diseases cause mortality to millions of women around the world. Therefore, there is a world-wide need for new forms of female contraception particularly those that may have a dual role.

The exploratory nature of the Institute's research has enabled us to discover several genes that are potential targets for new contraceptives.

For the past five years, we have been part of an International WHO-Rockefeller Initiative searching for molecules that are essential for implantation and thus could provide targets for contraception. During 2004, we were invited to join a new initiative by Schering AG, one of the few companies actively involved in contraceptive development. These initiatives are to discover and progress new leads for female contraception not based on the hormones that make many of the current contraceptives unacceptable to women. The Institute also receives funding from the CONRAD/CICCR, a US not-for-profit body, which funds selected research on contraceptive development and which supports our work on other contraceptive leads.

Our research findings have provided a target for a unique female contraceptive. We have discovered that the molecule PC6 (proprotein convertase 6) is a critical maternal factor for embryo implantation in mice. The "proof of principle" established that when the molecule is blocked in the mouse uterus, implantation is prevented.

Importantly the same molecule has been linked with HIV infection. This provides the basis for a unique contraceptive that not only blocks pregnancy but reduces HIV infectivity.

Long acting contraceptives

The World Health Organization estimates that over 20 million women worldwide use progestin-only contraceptives such as Implanon and Depo Provera.

These contraceptives have the advantage of being long-acting. For example, Implanon (a small implant in the arm) provides contraceptive protection for three years or more. However, over 25% of women using these contraceptives discontinue use due to uterine bleeding problems.

The Institute's research investigates the causes of this bleeding, with support from the World Health Organization and the National Institutes of Health in the USA.

We have developed a mouse model in which the mice receive small pieces of the Implanon implants. The uteri of these mice develop many of the same features seen in women using such implants. Studies over the next few years will test how scientists might modify this so that the tissue is not predisposed to bleeding.

The Prince Henry's team is also a co-investigator in a national clinical trial that is testing new short-term treatments for the bleeding problems associated with the use of Implanon. The pilot study from this trial has been extremely encouraging and has enabled the team to devise what they hope will be even more effective treatments for trialling in the second phase of the study. This work is funded by a prestigious grant from the National Institutes of Health in the USA.

Funding

National Health and Medical Research Council of Australia
National Institutes of Health, USA
CONRAD/CICCR Foundation
World Health Organization
Schering AG, Germany

Collaborators

Walter and Eliza Hall Institute of Medical Research, Melbourne
Sydney Centre for Reproductive Health Research, Sydney
Women's and Infant's Health, University of Western Australia, Perth
Royal Women's Hospital, Melbourne
Mater Mother's Hospital, South Brisbane
ANZAC Research Institute, Sydney
University of Bologna, Italy
University of Washington, Seattle, USA
University of Washington, USA

Brain Research

Our research could shed light on why male Obsessive Compulsive Disorder patients suffer a worse fate than women

Hormones drive reproduction

The brain plays an important role in fertility and reproduction because it secretes a special hormone that drives the reproductive process called gonadotropin, releasing hormone (GnRH).

There are many factors that influence the release of GnRH, but these are not wholly understood.

Our researchers have analysed a number of pathways in the brain that regulate GnRH cells and are now studying the function of the different sets of cells in the brain that lead to reproductive centres.

Hormones secreted by the gonads (ovaries and testes) operate a feedback mechanism to the brain and the pituitary gland to regulate the reproductive system.

In addition, other factors such as stress and nutrition are able to alter the brain systems that regulate reproduction. There are defined groups of cells in the brain and pituitary gland that regulate reproduction, and also a set of cells in the brain that regulates stress and another that regulates growth.

The Institute's research is being directed to understanding the processes that are involved in cross communication between these different centres of the brain and the ways in which they interact.

Oestrogen linked to obsessive compulsive disorder

One in 40 people worldwide are affected by Obsessive Compulsive Disorder (OCD) and the exact cause is largely unknown. Symptoms include repetitive and impulsive behaviours such as excessive hand washing, checking or counting.

Several human studies have found that men show an earlier age of onset and have a worse outcome when compared to women sufferers.

Our investigative research has shown that lack of oestrogen is linked to OCD in male mice. The studies revealed that oestrogen deficient male mice displayed obsessive compulsive behaviours such as excessive grooming and running on the tread mill.

Men who suffer OCD often have a genetic deletion of a specific gene called COMT. Our studies found that COMT levels were decreased in the hypothalamus, a region of the brain that impacts grooming, in the oestrogen-deficient male mice.

Treatment of these animals with oestrogen recovered COMT expression levels and behavioural levels to normal. This research could shed light on the phenomenon that male OCD patients suffer a worse outcome than women.

Gender differences start in the brain

In addition to hormones, our studies indicate that sex-specific genes are involved in determining the difference in male and female brains.

For example, we have discovered that the testes-determining gene, SRY, is prominent in the male brain. Using a recently developed probe, our scientists have shown that in the brains of males, SRY is produced in a region of the hypothalamus which resembles the much studied pre-optic area in the rodent associated with sexual behaviour. This finding is significant because females lack the Y chromosome and this area of their brain is smaller.

Our future studies are directed at discovering a direct link between SRY and sexual behaviour and other actions of the gene, SRY, in men's brains.

Photo: (L-R) Alix Rao, Research Assistant and Research Officers Javed Iqbal and Sueli Pompolo, Neuroendocrinology group

Funding

National Health and Medical Research Council of Australia

National Institutes of Health, USA

Endocrine Pharmaceuticals, UK

Collaborators

Howard Florey Institute, Melbourne

Department of Pharmacology, University of Melbourne

Department of Immunology and Pathology, Monash University, Melbourne

Department of Physiology, Monash University, Melbourne

Monash Institute of Medical Research, Melbourne

Garvan Institute, Sydney

AgResearch, New Zealand

University of California, Los Angeles, USA

Mayo Clinic, USA

University of Michigan, USA

LeHigh University, USA

MRC Human Reproductive Sciences Unit, Scotland, UK

Kitsato University, Japan

Research on Ageing

Prince Henry's Institute is involved in vital research to describe the hormonal changes that occur as men and women age

Testosterone Replacement

The use of testosterone replacement therapy in older men is a controversial issue world wide. Prince Henry's Institute research investigates the changes in testosterone levels experienced by some men as they age, and the role played by testosterone replacement therapy

The popular press often features articles and advertisements supporting the idea that the supplementation with testosterone can improve a wide range of symptoms associated with ageing in men. However the effectiveness and safety of such treatment are uncertain.

Dr Carolyn Allan, Clinical Research Fellow and Professor Henry Burger AO, Emeritus Director

The Institute has completed a 12 month study examining the effects of testosterone in a group of older men who presented with a range of such symptoms including tiredness, poor concentration and reduced sex drive. The results of the study include the effects of testosterone on body muscle and fat content, bone density, insulin sensitivity and risks factor for heart disease, such as cholesterol levels and blood clotting factors. A number of questionnaires looking at sexual function and quality of life are also addressed, along with safety issues like prostate health.

Previous research at the Institute has shown that testosterone levels are lower in obese ageing men who often also have symptoms suggestive of testosterone deficiency. Obese men are at an increased risk of several health problems such as heart disease, high blood pressure, diabetes and sleep apnoea.

Over the coming year we plan to undertake new research on obese and diabetic men, and to study the interaction between lifestyle modification and weight loss with testosterone production.

Another area of our research is the recently completed study of the control of testosterone production in ageing men. The data, currently being analysed, is determining whether the age-related decline in testosterone levels is due to reduced activity of the testosterone secreting cells (Leydig cells) of the testis and/or to reduced pituitary hormone stimulation of the testes. This is important in understanding the best diagnostic approach for assessing older men concerned with this aspect of their health.

The menopause

The menopause literally means the very last period in a woman's life. It typically affects women between the ages of 45 and 55 years of age.

The effect of the menopause is significant for some women with symptoms such as hot flushes, low libido and loss of memory. Prince Henry's Institute is providing important scientific input for several collaborative studies that aim to fully describe the hormonal changes that occur as women age and pass through the menopause.

A major collaborative study is with the Melbourne Women's Mid Life Health Project, conducted from the University of Melbourne's Office for Gender and Health.

This study has followed a group of approximately 400 women for 14 years to document their experience of the menopausal transition and the menopause. Hormone levels and markers of cardiovascular risk have also been measured to obtain a representative picture of the health of Australian women at that stage of their lives.

Projects with the Department of Obstetrics and Gynaecology, University of Sydney, and with the Department of Obstetrics and Gynaecology of the Karolinska Institute in Sweden, are clarifying the relationships of hormonal changes to bleeding patterns and the hormonal characteristics of irregular cycles as menopause approaches.

The Institute has been involved in a randomised, placebo controlled trial of a mixture of two herbs given to alleviate the symptoms experienced by peri- and early post-menopausal women, which will be completed later in 2005.

A major study of the relationships between a variety of hormone levels, and aspects of joint, cardiovascular and cognitive function is ongoing, in collaboration with the Jean Hailes Foundation and the Women's Health Program, Monash University

Growth hormone and oestrogen

There are two parallel endocrine changes that occur during the menopause; a reduction in oestrogen and a reduction in growth hormone. In postmenopausal women, growth hormone deficiency contributes to the decline of normal physiological functions in tissues such as the brain and the heart. Our work aims to understand the correlation between oestrogen and growth hormone and the impact on the health of menopausal women.
The oestrogen deficient (ArKO) mouse provides an ideal model to gain insight into the role of oestrogen in the regulation of growth hormone. We have found that growth hormone and its releasing hormone receptors in the pituitary of ArKO mice were significantly decreased. The Institute's research has shown that oestrogen replacement therapy reversed this decline.

Our studies are focussed on creating treatment options for growth hormone deficiency in menopausal women and any other oestrogen-deficient conditions.

Funding

National Health and Medical Research Council of Australia
National Heart Foundation
Pfizer Pty Ltd
Mayne Pharma Pty Ltd
Organon Australia Pty Ltd
Novartis

Collaborators

RMIT University, Melbourne
The Jean Hailes Foundation, Melbourne
Monash University, Melbourne
Southern Health, Melbourne
University of Sydney
Women's and Infant's Health, University of Western Australia, Perth
Baylor College of Medicine, Texas, USA
Tulane University Medical Centre, New Orleans, USA
Merck Research Laboratories, Rahway, New Jersey, USA
National Institute for Medical Research, London, UK
University of Alberta, Canada
Tohoku University, Sendai, Japan
Karolinska Hospital, Stockholm, Sweden
Karolinska Institute, Stockholm, Sweden

Awards & Promotions

AWARDS

Professor Evan Simpson
Roy Greep Award, US Endocrine Society, USA, 2005

Professor Jock Findlay AM
Dale Medal, Society for Endocrinology, UK, 2006

Dr Anne Corbould
Diabetes Australia Research Trust Award, 2005

Dr Anne Reutens
William T Buckland Foundation Award, 2004

Dr Carolyn Allan
The Janet W McArthur Award for Excellence in Clinical Research Women in Endocrinology Abstract Award, Endocrine Society Annual Meeting, USA, 2005

Simon Chu
Servier Young Investigator Award, the Endocrine Society of Australia, 2005

Jenny Chow
Postgraduate Scholarship, Prince Henry's Institute, 2005;
Honours Prize, 11th Student Symposium Presentation, Prince Henry's Institute, 2004
Faculty Postgraduate Research;
Scholarship, Faculty of Medicine, 2005

Agnes Kovacic
Quantum Scientific Award, Prince Henry's Institute Abstract Award, 2004;
Women in Endocrinology Abstract Award, Endocrine Society Annual Meeting, USA, 2005

Claudette Thiedeman
John Donges Administration Award
Prince Henry's Institute, 2004

Maria Hernandez
Kadir-Fatimah Award for Technical Excellence, Prince Henry's Institute, 2004

Yogeshwar Makanji
Graduate Scholarship, Monash University, 2004

Chelsea Stoikos
Postgraduate Scholarship, Prince Henry's Institute, 2005

Pavel Sluka
PhD Prize, 11th Student Symposium Presentation, Prince Henry's Institute, 2004;
First Prize, Postgraduate Research Symposium, Department of Anatomy & Cell Biology, Monash University, 2004

Christine White
Young Scientist of the Year, The Australian and British Council Australia, Sydney, 2005

AWARD NOMINEES

Rachel Hill
Finalist, Junior Novartis Award, Endocrine Society of Australia, 2004

Simon Degen
Finalist, Serono Junior Scientist Award, Society of Reproductive Biology, 2004;
Finalist, Society for Reproductive Biology New Investigator Award, ESA & SRB 35th Annual Scientific Meeting, Sydney, 2004

Christine White
Finalist, Society for Reproductive Biology New Investigator Award, ESA & SRB 35th Annual Scientific Meeting, Sydney, 2004

TRAVEL AWARDS

Dr Helena Sim
International Society of Endocrinology Crown (Takeda) Travel Award, 2004;
International Congress of Endocrinology (ICE), Lisbon, Portugal, 2004

Dr Carolyn Allan
Endocrine Society of Australia, International Congress of Endocrinology Travel Award, 2004;
Monash University Postgraduate Travel Grant, 2004

Dr Morag Young
US Endocrine Society Travel Award, US Endocrine Society, San Diego, USA, 2005;
Ian Potter Foundation Travel Grant, ICE conference, Lisbon, Portugal, 2004

Dr Jiong Zhou
Ian Potter Foundation Travel Grant, US Endocrine Society, San Diego, USA, 2005

Agnes Kovacic
Endocrine Society of Australia International Travel Award, ICE Conference Lisbon, Portugal, 2004;
Monash University International Travel Award, ICE Conference Lisbon, Portugal, 2004;
AWE NovoNordisk New Investigator Travel Award, Australian Women in Endocrinology, 2005

Sonay Hussein-Fikret
Endocrine Society of Australia International Travel Award, ICE Conference Lisbon, Portugal, 2004;
Monash University International Travel Award, ICE Conference Lisbon, Portugal, 2004

Associate Professor Vincent Harley
The Endocrine Society Quest Diagnostics Young Investigator Travel Grant Award, 2004

Kevin Knower
International Congress of Endocrinology Travel Award, ICE Conference, Lisbon, Portugal, 2004

Dr Jayne Sierens
Ian Potter Foundation Travel Grant, Society for the Study of Reproduction, Quebec, Canada, 2005

Dr Eva Dimitriadis
Ian Potter Foundation Travel Grant, Society for the Study of Reproduction, Quebec, Canada, 2005

Dan Dan Feng
Endocrine Society of Australia Travel Award, Sydney, 2004;
Australian Physiological Society Travel Award, 2004;
National Health and Medical Research Council Travel Award, 2004

Nerveen Tawadros
Monash University Travel Grant, 2004;
Endocrine Society of Australia International Travel Award, ICE Conference Lisbon, Portugal, 2004;
Endocrine Society of Australia Travel Award, Sydney, 2004

GOVERNMENT APPOINTMENTS

Professor Peter Fuller
Member, Research Working Group, Ministerial Task Force on Cancer, Department of Human Services, Victoria, 2004;
Member, Ministerial Task Force on Cancer, 2005;
Member, Cabrini Clinical Education and Research Foundation, 2005

UNIVERSITY APPOINTMENTS

Dr Guiying Nie
Honorary Lecturer,
Department of Biochemistry and Molecular Biology
Monash University, 2004

Professor Lois Salamonsen
Honorary Professorship
Department of Obstetrics and Gynaecology, Faculty of Medicine, Nursing and Health Sciences
Monash University, 2004

Associate Professor Chen Chen
Honorary Associate Professor of Physiology
Monash University, 2005

Dr Craig Harrison
Honorary Lecturer
Department of Biochemistry & Molecular Biology, Monash University, 2005

Dr Kerry McInnes
Honorary Assistant Lecturer
Department Anatomy and Cell Biology
Monash University, 2005

APPOINTMENTS - CONFERENCES AND INTERNATIONAL COLLABORATIONS

Professor Henry Burger AO
Representative, Australasian Menopause Society, Melbourne, 2004;
Chairman, International Conference on Hormone Replacement Therapy, Monte Carlo, Monaco, 2004;
Symposium Chair, Amsterdam Menopause Symposium, Amsterdam, Netherlands, 2004;
Chair, Sixth International Novo Nordisk Symposium, Budapest, Hungary, 2005

Professor Evan Simpson
Member, Medical and Scientific Committee Cancer Council Vic, 2004 - 2005/07;
Member, Meetings and Education Programs Committee, US Endocrinology Society, 2004

Professor Peter Fuller
Member, Meetings and Education Programs Committee, US Endocrinology Society, 2004

Professor John Funder AM
Inaugural Chair, International Relations Committee of The Endocrine Society, USA, 2004;
President, International Congress of Endocrinology, Brazil, 2004

Dr Sarah Meachem
Organising Committee, Australian Society for Medical Research, National Scientific Conference, Couran Cove, Queensland, 2004

SOCIETIES

Associate Professor Chen Chen
Executive Committee Member and Education and Learning Committee member, Australian Chinese Association for Biomedical Sciences, 2005

Dr Sarah Meachem
Director, Australian Society for Medical Research, 2004

JOURNAL APPOINTMENTS

Dr Colin Clyne
Scientific Editor, Journal of Molecular Endocrinology, 2004

FELLOWSHIPS

Dr Kara Britt
CJ Martin Fellowship
Institute of Cancer Research, London, 2005

Dr Sarah Meachem
PHIMR Career Development Award
Prince Henry's Institute, 2004

Dr Guiying Nie
PHIMR Fellowship
Prince Henry's Institute, 2005-2006

Dr Carolyn Allan
Novartis Endocrinology Fellowship
Clinical Research Unit, Prince Henry's Institute, Royal Australasian College of Physicians, 2005

Dr Jayne Sierens
Serono Fellowship
Serono Foundation, Geneva, 2004

Dr Colin Clyne
RD Wright Fellowship
National Health and Medical Research Council, 2005

Dr Wah Chin Boon
Faculty of Medicine Fellowship
Monash University, 2005

Dr Morag Young
PHIMR Career Development Award
Prince Henry's Institute, 2005

Dr Haruhiko Hatakeyama
International Society of Hypertension Postdoctoral Visiting Fellowship, High Blood Pressure Research Council of Australia, 2004

ACADEMIC ACHIEVEMENTS

Jenny Chow
Honours, BBiomedSci
Monash University, 2004

Simon Chu
PhD
Monash University, 2005

Hinda Daggag
BSci (Hons)
Monash University, 2004

Simon Degen
MSc
Monash University, 2004

Dan Dan Feng
MSc
Monash University, 2004

Irumini Jakody
Honours, BBiomedSci
Monash University, 2004

Amanda Rickard
Honours, Physiology
Monash University, 2004

Alexandra Umbers
BSc (Hons)
University of Auckland, NZ, 2004

Students 2004/05

Karla Estrada, PhD Student

The following students undertook or continued their studies at the Institute:

Dr Carolyn Allan MBBS FRACP
PhD Student
Testicular function in ageing men
Supervisors: Assoc. Professor Rob McLachlan, Professor Henry Burger AO

Chantacha Anukulkitch MBiomedSci
PhD Student
Influence of photoperiod, testosterone and body composition on changes in gene expression for appetite regulating peptides in the hypothalamus of a seasonal mammal
Supervisor: Professor Iain Clarke

Amanda Beardsley BSc (Hons)
PhD Student
Hormonal regulation of spermiation and spermiation failure
Supervisors: Assoc. Professor David Robertson, Dr Liza O'Donnell

Marissa Bowden BA/BSc (Hons)
PhD Student
The expression and function of mammalian HtrA3 in the ovary
Supervisors: Professor Jock Findlay AM, Dr Guiying Nie

Ashwini Chand BSc MSc
PhD Student
Genetic causes of Premature Ovarian Failure: A candidate gene approach
Supervisors: Assoc. Professor David Robertson, Dr Andrew Shelling

Simon Chu BSc (Hons)
PhD Student
Molecular pathogenisus of ovarian granulosa cell tumours
Supervisor: Professor Peter Fuller

Jenny Chow BBiomedSci (Hons)
PhD Student
The effect of oestrogens and triglycerides homeostasis
Supervisors: Professor Evan Simpson, Dr Wah Chin Boon

Hinda Daggag
Honours Student
Role of SRY interacting protein SIP1 in sex determination
Supervisor: Assoc. Professor Vincent Harley

Simon Degen BSc, MSc
PhD Student
Impact of FSH on Sertoli and germ cell development
Supervisors: Dr Kate Loveland, Dr Sarah Meachem

Karla Estrada BSc (Hons)
PhD Student
Gene expression of neuroeptides believed to be involved in regulating the estrous cycle of the ewe
Supervisor: Professor Iain Clarke

Dan Dan Feng B Med
MSc Student
Effect of free fatty acid on voltage-gated potassium current in rat pancreatic beta cells in vitro
Supervisors: Dr Chen Chen, Dr Ziqiang Luo

Xue Feng Han BMed MSc
PhD Student
Potassium current on GH3 cells
Supervisor: Dr Chen Chen

Natalie Hannan BSc (Hons)
PhD Student
Endometrial proteins in human embryo implantation and their relevance to infertility
Supervisors: Professor Lois Salamonsen, Dr Rebecca Jones

Rachel Hill BSci (Hons)
PhD Student
Characterisation of the brain of the male Aromatose Knockout (ArKO) mouse
Supervisors: Professor Evan Simpson, Dr Wah Chin Boon

Sonay Hussein-Fikret BSc (Biomed) (Hons)
PhD Student
Characterisation of the steroid receptor coactivator family in ovarian tumours
Supervisor: Professor Peter Fuller

Irumini Jakody BBiomedSci (Hons)
PhD Student
Localisation of proteins associated with aromatase expression in the developing testis
Supervisors: Dr Colin Clyne, Dr Sarah Meachem

Tu'uhevaha Kaitu'u BBiomedSci (Hons)
PhD Student
Endometrial breakdown and repair
Supervisors: Professor Lois Salamonsen, Dr Naomi Morison

Sabine Kelly BSc (Hons)
PhD Student
Identification of targets of SOX9 in human sex determination
Supervisor: Assoc. Professor Vincent Harley

Kevin Knower BSci (Hons)
PhD Student
The role of SRY in mammalian sex determination
Supervisor: Assoc. Professor Vincent Harley

Agnes Kovacic BSc (Hons)
PhD Student
Regulation of aromatase by Liver Receptor Homolgue-1 (LRH-1) in pre-adipocytes
Supervisors: Professor Evan Simpson, Dr Colin Clyne

Emily (Yan Mei) Lam BBiomedSci (Hons)
MBiomedSci Student
Do selective 11 beta- Hydroxysteroid Dehydrogenase type 1 inhibitors protect coronary vessel against mineralocorticoid salt induced vascular inflammation?
Supervisor: Dr Morag Young

Riki Lane BA/BSc
Honours Student
SRY in the human brain
Supervisors: Assoc. Professor Vincent Harley, Dr Helena Sim

Jason Liew BBiomedSci (Hons)
PhD Student
The role of oestrogen in ovarian function
Supervisors: Professor Jock Findlay AM, Dr Ann Drummond, Dr Margaret Jones

Louisa Ludbrook BBioMedSci (Hons)
PhD student
DAX1: A regulator of mammalian testis formation
Supervisor: Assoc. Professor Vincent Harley

Yogeshwar Makanji B.AppSc (Hons)
PhD Student
Analysis of the contribution of the Beta A and Beta B subunits to inhibin and activin biological activity
Supervisors: Assoc. Professor David Robertson, Dr Craig Harrison

Dr Kati Matthiesson MBBS FRACP
PhD Student
The regulation of male fertility
Supervisor: Professor Robert McLachlan

Mark McCabe BSci (Hons)
PhD Student
Regulation of inter-Sertoli cell tight junctions
Supervisor: Dr Peter Stanton

Premila Paiva
PhD Student
The role of Interleukin-11 in human implantation
Supervisors: Dr Eva Dimitriadis, Professor Lois Salamonsen

Niroshani Pathirage BSc (Hons)
PhD Student
Regulation of aromatase in endometrial and ovarian cancer
Supervisors: Professor Evan Simpson, Dr Colin Clyne

Suzanne Pietersz BSc
Honours Student
The role of LRH-1 in breast cancer
Supervisors: Professor Evan Simpson, Dr Colin Clyne

Jyothsna Rama Rao
PhD Student
Effect of hormones released by adipocytes on pancreatic beta cells
Supervisors: Dr Chen Chen, Dr Helena Parkington

Amanda Rickard BSc (Hons)
PhD Student
Mineralocorticoid/salt induced cardiac inflammation and fibrosis
Supervisor: Dr Morag Young

Saleela Ruwanpura BBioMedSci (Hons)
PhD Student
The role of FSH in spermatogonial development in rats, mice and men
Supervisors: Dr Rob McLachlan, Dr Sarah Meachem

Pavel Sluka BBioMedSci (Hons)
PhD Student
Hormonal regulation of cell-cell junctions during spermatogenesis
Supervisors: Dr Peter Stanton, Dr Liza O'Donnell, Dr John Bertram

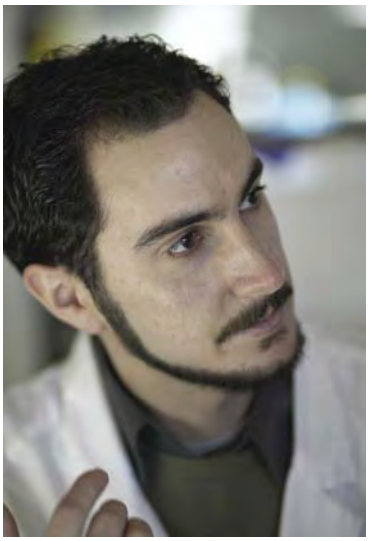
Melissa Stahle
Honours Student
Sexy KRABS: An SRY Affair
Supervisor: Assoc. Professor Vincent Harley

Chelsea Stoikos BSc (Hons)
PhD Student
Activin in the endometrium: implications for infertility and endometriosis
Supervisors: Professor Lois Salamonsen, Dr Eva Dimitriadis

Gerard Tarulli BSci (Hons)
MSc Student
The hormonal regulation of Sertoli cell function
Supervisors: Dr Peter Stanton, Dr Sarah Meachem

Neveen Tawadros BSc
PhD Student
The role of ghrelin in the normal and diseased uterus
Supervisors: Associate Professor Chen Chen, Professor Lois Salamonsen

Yue Qi MD (China) MSc
PhD Student
Interconnections between appetite regulating systems in the hypothalamus and brain stem of the sheep (neuroanatomy and neuroendocrine)
Supervisor: Professor Iain Clarke



Gerard Tarulli, MSc Student

Sean Yang BSc
PhD Student
Regulation of voltage-gated Ca2+ currents of rat somatotropes by somatostatin receptors
Supervisor: Assoc. Professor Chen Chen

Wang Yi MD (China)
PhD Student
Developmental and biochemical studies of SOX13
Supervisors: Dr Vincent Harley, Professor Mary-Jane Gething

Postgraduate Study in Reproductive Biology

The Education Program in Reproductive Biology (EPRB) aims to foster education and research into reproductive biology and embryology for domestic and international postgraduate students.

The Graduate Diploma and the Master of Reproductive Sciences and the Master of Clinical Embryology are offered to postgraduate students. Thirty-seven students were enrolled in these courses in 2004 including eleven international students.

The EPRB program is a joint venture of Prince Henry's Institute (PHI) and Monash Institute of Medical Research (MIMR) in association with the Monash University Departments of Physiology; Paediatrics; Pharmacology; Obstetrics & Gynaecology and Anatomy & Cell Biology.

Prince Henry's Institute plays a key role in the coordination of the EPRB program. Many of the Institute's scientists assist into the development of subjects, give lectures, as well as facilitate the practical sessions.

Associate Professor David Robertson, Head of the Reproductive Hormone Group at PHI is Deputy Director of the program. Dr Sarah Meachem, Senior Research Officer in the Male Reproductive Endocrinology Group is the primary coordinator of the subject Fertility Regulation.
Professor Jock Findlay AM, Deputy Director of the Institute also contributes to this subject.

Prince Henry's Institute is dedicated to the success of the EPRB program and welcomes new students to be involved.

For more information on courses and open days telephone:
03 9594 7100 or visit the website at www.med.monash.edu.au/eprb

Visiting Speakers

2004

Dr David Phillips
Monash Institute of Medical Research: *"Activin A: from sometime reproductive factor to genuine cytokine"*

A/Prof Margaret Morris
Melbourne University: *"Brain changes in obesity - lessons from rodent models"*

Prof Mike Weber
University of Virginia Cancer Center, USA: *"Signal Transduction in Prostate Cancer Progression"*

Dr Graham Lieschke
Ludwig Institute: *"Modeling myeloid cell disorders using genetic approaches in zebrafish"*

Prof Joe Proietto
Melbourne University: *"Stopping the obesity epidemic: identifying the political and biological impediments"*

Dr John Price
St Vincent's Institute: "Novel molecular modulators of breast tumor growth and metastasis"

Prof Shigeaki Kato
Institute of Molecular and Cellular Biosciences, University of Tokyo: *"The function of sex hormone receptors in gene regulations"*

Dr Steve Collins
Melbourne University: *"Creutzfeldt-Jakob disease in Australia - from laboratory bench to national surveillance"*

Prof Warwick Anderson
Monash Physiol: *"Renal resetting of long-term blood pressure - changed vascular and renal structure and reduced nephron number"*

Dr David Nikolic-Paterson
Nephrology, Monash Medical Centre: *"MAPK signaling in renal inflammation and fibrosis"*

Assoc Prof Russ Hovey
Cell and Molecular Biology, University of Vermont, USA
"Endocrine regulation of mammary gland development and morphogenesis"

Dr Michelle Leech
Dept of Medicine, Monash Medical Centre: *"Reciprocal regulation of leukocyte trafficking by glucocorticoid-induced molecules MIF and Annexin-1"*

Dr Caroline Gargett
Dept of Obstetrics & Gynaecology, Monash Medical Centre: *"Stem cells in the uterus - what is the evidence?"*

Dr Nina Wilkins
Acrux Pty, Melbourne: *"Transdermal drug delivery systems"*

Dr Moira O'Bryan
Monash Institute of Medical Research: *"Of snakes and sperm - CRISP proteins"*

2005

Dr Kirsten Robertson
Novum Biosciences
"Insights into the expanding role of the orphan nuclear receptor: LXR"

Professor Diane Keeney
Department of Medicine, Vanderbilt Medical Centre, Vanderbilt University, Texas, USA
"Cytochromes P450, eicasanoids and epithelial squamous differentiation"

Dr Elizabeth Johnson
Bio 21, Melbourne
"The UROP Program"

Dr Mathis Grossmann
Southern Health: *"Human Thyroid-Stimulating Hormone: from molecular mechanisms of action to rational analog design"*

Prof TJ Martin
St Vincent's Institute: *"PTHrP, from cancer hormone to multifunctional protein"*

Prof Yaeta Endo
Professor and Director, Cell-free Science and Technology Research Centre, CellFree Sciences Co., Ltd (Japan)
"Approaching global-wide protein expression with wheat germ cell-free system"

Prof John C Marshall
Health Sciences Centre, University of Virginia Health Sciences Centre, Charlottesville, Virginia, 22908, USA.
"Testosterone, puberty and the etiology of PCOS"

Dr Russell McInnes
Agilent Technologies Inc.:
"The Agilent 2100 Bioanalyzer: A Microfluidics Platform for the Analysis of Nucleic Acids, Proteins and Cells"

Dr Robert Kapsa
National Muscular Dystrophy Research Centre: *"Autologous Genetically Corrected Cells for Neuromuscular Disorders"*

Mr Rafael Goldshmit
Berthold Australia Pty Ltd: *"Fluorescent and Radioisotopic imaging with Fuji film's FLA-5100 Imaging system"*

Scientific Presentations 2004/2005

Advances in Proteomics in Cancer Research, Miami, USA

Advances in Urogenital Research, Victorian College of Pharmacy, Melbourne

American Heart Association Annual Conference, Chicago, USA

American Society of Reproductive Medicine, Philadelphia, USA

Aromatase 2004, Edinburgh, Scotland

Australian Biotechnology Summit Conference, Sydney

Australian Breast Cancer Conference, Melbourne

Australian Health and Medical Research Congress, Sydney

Australian Neuroscience Society Meeting, Melbourne

Australian Proteomics Symposium, Phillip Island

Australian Science Communicators National Conference, Brisbane, Queensland

Australian Society of Immunology Conference, Adelaide

Cancer Genetics and Tumor Suppressor Genes, Cold Spring Harbor, NY

ComBio, Perth

Council for High Blood Pressure Research meeting, Chicago, USA

Department of Human Services Translational Research Workshop, South Australia

Endocrine Society of Australia, Sydney

ENDO 2005 - The Endocrine Society Annual Meeting, San Diego, USA

European Life Sciences Organisation (ELSO) Annual Meeting, Nice, France

FASEB Summer Research Conferences, Tucson, USA

FSA Annual Meeting, Adelaide

Future of Contraception', NIH-sponsored symposium, Seattle, USA

Gordon Research Conference on Reproductive Biology, Connecticut, USA

International Aldosterone Society, Annual Meeting, San Diego, USA

International Congress of Endocrinology, Lisbon, Portugal

International Congress on Endocrinology of Farm Animals, Budapest, Hungary

Japan Endocrine Society Annual Meeting, Kyoto

Keystone Symposia, Colorado, USA

Lorne Genome Conference, Lorne

Mexico General Hospital Centenary Symposium, Mexico City

Monash Institute of Reproduction and Development Symposium, Melbourne

National Institutional Biosafety Committee Forum, Canberra

NIH Investigators Meeting, Sydney

Nuclear Receptors 2004, Stockholm, Sweden

Society for the Study of Reproduction, Vancouver, Canada

Society of Reproductive Biology, Annual Scientific meeting, Sydney

8th Asian Conference on Transcription, Bangkok, Thailand

13th Simpson Symposium and VIIth International Conference on the Extracellular Matrix of the Female Reproductive Tract, "Reproductive Remodelling", Edinburgh, UK

Victorian Breast Cancer Research Consortium, Melbourne

Victorian RNAi Special Interest Group Workshop, Melbourne

WHO Male Contraceptive Meeting, Seattle, USA

XV Ovarian Workshop, Vancouver, Canada

XIXth International Congress of Zoology, Beijing, China

XVIII World Congress of the International Society for Heart Research, Brisbane

Publications 2004

1. Allan CA, McLachlan RI. Age-related changes in testosterone and the role of replacement therapy in older men. *Clin Endocrinol* (Oxf). 2004 Jun;60(6):653-70.

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5. Britt KL, Stanton PG, Misso M, Simpson ER, Findlay JK. The effects of estrogen on the expression of genes underlying the differentiation of somatic cells in the murine gonad. *Endocrinology.* 2004 Aug;145(8):3950-60.

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14. Clyne CD, Kovacic A, Speed CJ, Zhou J, Pezzi V, Simpson ER. Regulation of aromatase expression by the nuclear receptor LRH-1 in adipose tissue. *Mol Cell Endocrinol.* 2004 Feb 27;215(1-2):39-44.

15. Cram D, Lynch M, O'Bryan MK, Salvado C, McLachlan RI, de Kretser DM. Genetic screening of infertile men. *Reprod Fertil Dev.* 2004 Jan 22;16(5):573-580.

16. Dennerstein L, Guthrie JR, Taffe JR, Lehert P, Burger HG. Major findings of the Melbourne Women's Midlife Health Project. Climacteric Medicine – where do we go? Taylor & Francis Ox. On. 2004, 4:27-35.

17. Drummond AE, Findlay JK, Ireland JJ. Animal models of inhibin action. *Semin Reprod Med.* 2004 Aug;22(3):243-52.

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Commercialisation

The objectives of commercialisation activities at the Institute are to identify and negotiate commercial outcomes for intellectual property generated by its scientists. Commercialisation of intellectual property represents a significant opportunity for increasing revenue.

Royalties and Inhibin

Our royalty stream on sales of inhibin products in the USA continues to grow at a pleasing rate and prospects for new markets are very encouraging. In particular, the outlook for sales of the inhibin-based diagnostic test for ovarian cancer is very optimistic even though these are some years off yet.

Antibodies Australia

Our embryonic "Antibodies Australia" activities at Werribee have continued to produce a range of antibodies available for sale to the Australian research market. Several orders have been supplied and customer response has been very positive. Whether there is sufficient market penetration to justify the development of Antibodies Australia into an independent enterprise is being closely monitored.

Two preliminary applications to the Victorian Government's Science, Technology and Innovation Initiative Second Generation Round Three for financial support for Antibodies Australia and a proteomics facility were unsuccessful.

Photo: (L-R) Senior Research Officer Liza O'Donnell, Development & Commercialisation Services Manager Andrew McCallum and PhD student Amanda Beardsley

Intellectual Property

The matter of ownership of Intellectual Property arising from collaborative research arrangements with commercial enterprises in Australia and overseas remains a sticking point in many negotiations. It is pleasing to report some progress in this area with at least some of our prospective partners prepared to concede partial ownership during recent negotiations.

Endometrial Cancer Test

Rights in our jointly held patent for an endometrial cancer diagnostic test were assigned to Diagnotech Pty. Ltd. in exchange for a cash consideration and equity. Further milestone payments are anticipated as this test is commercialised.

Wellcome Trust Sequencing Centre

The Wellcome Trust Sequencing Centre is a joint facility of Prince Henry's Institute and the Monash Institute of Medical Research. The facility was established in 1998 from funding provided by the Wellcome Trust after a successful joint application from each Institute.

The Centre is a core facility of the research precinct at Monash Medical Centre and provides a high quality sequencing service to researchers and clinicians in both Institutes and Southern Health. In addition to the DNA Sequencer instrument, the Centre contains several other major scientific instruments namely, real time PCR instruments and a denaturing high performance liquid chromotography instrument (DHPLC) used for the detection of mutations within DNA.

Sequencing DNA is a crucial step within molecular research because it determines the exact order of the four DNA units A, C, G and T within the gene. Since genes contain the information used by cells to determine their development and function in the body it is essential to determine the sequence of bases within the gene.

DNA sequencing information is essential to identify the role which genes play in the process of disease and help to ensure that more effective treatments and diagnosis are available.

The facility operates under the highest standards and has received accreditation from the National Association of Testing Authorities, Australia (NATA), an Australian government endorsed laboratory accreditor and a leader in accreditation internationally. Accreditation signifies the laboratory's commitment to quality service and compliance to International Standards ISO/IEC 17025-1999.

L-R: Wellcome Trust Sequencing Facility Manager Vivien Vasic, RD Wright Fellow Colin Clyne and Senior Research Officer Michael Lynch

Administration

Excelling in the Business of the Institute

Sound and efficient administration is crucial for the development and maintenance of a strong research program. Prince Henry's Institute administrative team is proud of the Institute's scientific reputation and works to achieve the same level of excellence.

As a public sector organisation, the **Materials & Human Resources** (M&HR) department conducts its activities under the strict guidelines of the State Services Authority. We ensure that all staff are treated with consideration and respect by observation of merit and equity principles. By providing support and guidance, the team helps to shape and achieve the strategic goals of the Institute. This has meant developing and implementing policies that reflect the values of the Institute as well as those of the public sector. M&HR is also responsible for equipment, building matters and other resources including IT.

Highlights include;

- Development of a certified agreement
- Establishment of the PHI staff Intranet
- Establishment of the internal audit overview focusing on legislative requirements of Occupational Health and Safety as well as other risk areas under M&HR.

Development & Commercialisation Services aims to increase funding by fostering relationships with current and future benefactors and donors. Fundraising initiatives provide an avenue for increased funding opportunities. Public relations activities increase community awareness of our research and builds the Institute's national and international profile. Commercialisation protects our intellectual property and generates new sources of income.

Highlights include;

- New marketing format for the annual report
- Introduction of a new Institute logo and image
- Growing membership and initiatives of the Development Board
- Increased royalty payments

Financial Services provides support to research and administration within Prince Henry's while complying with all government requirements and regulations. The department is supported by the Administration Officers and Secretarial Services who provide assistance in many areas including the preparation of grants and payroll. The Purchasing Office handles orders for laboratory equipment and administrative supplies.

Highlights include;

- Transition to implementation of Australian International Financial Reporting Standards
- Coordination of internal audit procedures
- Coordination of risk management policies
- Commencement of governance overview

John Donges Administrative Award

Prince Henry's Institute is proud to announce the winner of the 2004 John Donges Award for administrative excellence. The award is given in recognition of professionalism, courtesy, confidence, accuracy and timeliness. These were attributes of the late John Donges who was the previous treasurer of the Institute. The winner is nominated by the administrative team.

The recipient of the 2004 award is Mrs Claudette Thiedeman. Claudette is the Personal Assistant to Deputy Director, Professor Jock Findlay and Head of Endocrine Genetics, Professor Peter Fuller. She has worked at Prince Henry's Institute since 1992.

Claudette Thiedeman, winner of the 2004 John Donges Administration Award

Staff List

as at June 30th 2005

Sex Hormones in Action

Director and Group Head
Professor Evan Simpson
BSc (Hons), PhD

RD Wright Fellow
Margaret Jones PhD
Colin Clyne PhD

Senior Research Officers
Wah Chin Boon PhD
Souheir Houssami PhD
Jiong Zhou PhD

Peter Doherty Fellow
Anne Reutens MBBS PhD FRACP

Howard Florey Centenary Postdoctoral Fellow
Anne Corbould MBBS (Hons) PhD FRACP

Research Officers
Kara Britt PhD
Kerry McInnes PhD
Jayne Sierens PhD

Research Assistant
Shelley Jacobs BSc

PhD Students
Rachel Hill BSc (Hons)
Agnes Kovacic BSc (Hons)
Niroshani Pathirage BSc (Hons)
Jenny Chow BBiomedSci (Hons)

Honours Student
Suzanne Pietersz BSc

Female Reproductive Biology

Deputy Director, Senior Principal Research Fellow and Group Head
Professor Jock Findlay AM PhD DSc

Senior Research Officers
Ann Drummond PhD
Paul Farnworth PhD
Kaye Stenvers PhD

Research Assistants
Mitzi Dyson BAppSc
Ruth Escalona BSc (Hons) MSc
Yao Wang BSc (Hons)
Alexandra Umbers BSc (Hons)

PhD Students
Marissa Bowden BA BSc (Hons)
Jason Liew BBiomedSci (Hons)

UROP Student
Marnie Sparrow

Neuroendocrinology

Senior Principal Research Fellow and Group Head
Professor Iain Clarke PhD

Senior Research Officer
Sueli Pompolo PhD

Research Officer
Javed Iqbal DVM PhD

Senior Technical Officer
Bruce Doughton DipAgric

Research Assistants
Alexandra Rao BAppSci
Karen Briscoe BSc
Linda Morrish
Alda Pereira BSc

PhD Students
Karla Estrada BSc (Hons)
Chantacha Anukulkitch MD (Thailand)
Qi Yue MD (China) MSc

CJ Martin Fellow
Belinda Henry

Uterine Biology

Principal Research Fellow and Group Head
Professor Lois Salamonsen PhD

Associate Scientist
Professor Jock Findlay AM PhD DSc

Senior Research Officers
Eva Dimitriadis PhD
Gui-ying Nie PhD

Research Officers
Naomi Morison PhD
Lynette Kilpatrick PhD
Claudia Freyer PhD
Kate Hale PhD BEd

Research Assistants
Ying Li BSc GDipMicroBio
Jin Zhang BMed
Premila Paiva BSc (Hons)
Yee Lee Tan BSc (Hons)

Research Nurse
Judy Hocking RN

PhD Students
Natalie Hannan BSc (Hons)
Tu'uhevaha Kaitu'u BBiomed Sci (Hons)
Chelsea Stoikos BSc (Hons)
Christine White BSc (Hons)

Male Reproductive Endocrinology and Metabolism

Principal Research Fellow and Group Head
Professor Rob McLachlan MBBS FRACP PhD

Emeritus Director
Henry Burger AO, FAA, MD BS FRCP FRACP FCP (SA) FRCOG FRANZCOG

Senior Research Officers
Peter Stanton PhD
Sarah Meachem PhD
Michael Lynch PhD
Liza O'Donnell PhD
Kiki Pratis PhD

Clinical Research Nurses
Elise Forbes RN
Joanne McKenzie RN

Research Assistants
Georgia Balourdos BSc (Hons)
Caroline Foo BAppSc
Fiona McLean BSc (Hons)
Michelle Van Sinderen BSc (Hons)
Pavel Sluka BSc (Biomed) (Hons)

Clinical Research Fellows
Carolyn Allan MBBS FRACP
Kati Matthiesson MBBS FRACP

PhD Students
Amanda Beardsley BSc (Hons)
Mark McCabe BSc (Hons)
Saleela Ruwanpura BBioMedSci (Hons)
Gerard Tarulli BSci (Hons)

Reproductive Hormones

Principal Research Fellow and Group Head
Associate Professor David Robertson PhD

Emeritus Director
Henry Burger AO, FAA, MD BS FRCP FRACP FCP (SA) FRCOG FRANZCOG

CJ Martin Fellow
Craig Harrison PhD

Research Officer
Andrew Stephens BSc (Hons) PhD

Research Assistants
Karen Chan BAppSc
Sara Goodman PGDipSc
Enid Pruysers
Eeva Katri Kumpula MSc

PhD Students
Ashwini Chand BSc MSc
Yogeshwar Makanji BAppSc (Hons)

Endocrine Genetics

Senior Principal Research Fellow and Group Head
Professor Peter Fuller BMedSci MBBS PhD FRACP

Senior Research Officer
Morag Young PhD

National Australia Bank Ovarian Cancer Research Foundation Fellow
Martin Oehler MD PhD

International Society of Hypertension Postdoctoral Visiting Fellow
Hurah Hatakeyama PhD

Research Officer
Simon Chu PhD

Witchery Research Assistant
Maria Alexiadis BSc (Hons)

Research Assistants

Yitzou Yao MD (China)
Francine Brennan BSc (Hons)
James Morgan

PhD Students

Sonay Hussein-Fikret BBiomedSci (Hons)
Amanda Rickard BSc (Hons)

Masters Student
Emily Lam BBiomedSci (Hons)

Endocrine Cell Biology

Senior Research Fellow and Group Head
Associate Professor Chen Chen MD PhD

TM Ramsay Fellow
Damien Keating PhD

Research Officer
Ming Yan PhD

Research Assistants

Maria Hernandez BSc (Hons)
Kun Wang BMedMSc
Song Zhang BSc

PhD Students

Neveen Tawadros BSc
Xue Feng Han BMed MSc
Jyothsna Rama Rao BSc (MSc)
Sean Yang BSc

Masters Student
Dan Dan Feng B Med

Human Molecular Genetics

Associate Professor and Group Head
Vincent Harley PhD

Peter Doherty Fellow
Michael Clarkson PhD GDipT

Boylan Burke Fellow
Stefan Bagheri-Fam PhD

Research Officers

Helena Sim PhD
Pascal Bernard PhD

PhD Students

Wang Yi MD (China)
Sabine Kelly BSc (Hons)
Louisa Ludbrook BBiomedSci (Hons)
Kevin Knower BSc (Hons)

Honours Students

Melissa Stahle
Richard Lane

EMERITUS DIRECTOR
Henry Burger AO, FAA, MD BS FRCP FRACP FCP (SA) FRCOG FRANZCOG

SENIOR FELLOW
John Funder AO MD BS PhD FRACP

SENIOR RESEARCH ASSOCIATES

Gordon Baker MD BS PhD FRACP
James Cummins MBBS FRCS FRACS
David de Kretser AO MD BS FRACP
David Healy BMedSci MBBS PhD FRACOG
Sue Davis MBBS PhD FRACP

RESEARCH ASSOCIATES

Emilio Badoer PhD
Nick Balazs BSc FAACB
Dennis Engler MD BS FRACP
Chris Gilfillan MBBS PhD FRACP
Suzanne Silberberg MBBS FRACP
Beverley Vollenhoven MBBS FRACOG
Nigel Wreford PhD
Boyd Strauss MBBS PhD FRACP
Alan Tilbrook PhD
Gabor Kovacs MD FRCOG, FRANZCOG, CREI
Luk Rombauts FRANZCOG, CREI

Administration

Director, Administration
Professor Jock Findlay AM PhD DSc

Financial Services Manager
Terry Haining FCPA GDipAcc&Fin

Purchasing Officer
Peter Wood AIWA

Administrative Officer
Sheridan Wallington

Secretarial/Reception Staff

Dianne Arnold BSc
Jeanette Birtles BSc (Hons)
Pauline Bryant
Sue Elger
Susan Smith
Claudette Thiedeman
Jeana Thomas

Development & Commercialisation Services Manager
Andrew McCallum BE (Met) MEngSc MAICD

Public Relations Coordinator
Rebecca Scott BA Public Relations

Development & Public Relations Officer
Ingelise Jones BA GradDip Communications (PR)

Graphic Communications Coordinator
Sue Panckridge DipArt

Materials & Human Resources Manager
Paul Pearce ARMIT MAppSci GradCertHRM MAHRI

Human Resources Management Officer
Nermeen Tawadros BSc (Med Sci) BCompSci

Materials Resources Officer
Henry Wos

Records Management Assistant
Joan Crane

Maintenance Technician
Bruce Watson

Sequencing Lab Manager
Vivien Vasic BSc

Laboratory Technicians

Robin Leuba BA Dip Ed
Susan Taleh BA

Financial Statements

PRINCE HENRY'S INSTITUTE OF MEDICAL RESEARCH

ANNUAL REPORT 2004/2005

This is the Fourteenth Annual Report of Prince Henry's Institute of Medical Research submitted to the Minister for Industry in accordance with the requirements of the Financial Act 1994.

The Report covers the Institute's financial period, 12 months ended 30th June 2005 and was approved for submission to the Minister at a meeting of the Board of Prince Henry's Institute of Medical Research on 22nd September 2005.

ER Simpson
DIRECTOR

TT Haining
SECRETARY AND FINANCIAL SERVICES MANAGER

PRINCE HENRY'S INSTITUTE OF MEDICAL RESEARCH

STATEMENT OF FINANCIAL PERFORMANCE FOR THE YEAR ENDED 30TH JUNE 2005

	NOTE	2005 $	2004 $
Revenue from Ordinary Activities			
Government Revenue			
Australian Government Grants - Operations	3(a)	4,396,267	3,726,719
Victorian Government Grants	3(b)	1,237,497	1,141,972
Australian Government Grants - Capital	2	1,576,894	3,480,930
Industrial Grants and Contracts	3(c)	149,975	144,191
Other Operating Revenue			
Transfers from Other Institutions	3(d)	213,640	196,753
Revenue from Investments	3(e)	1,210,107	1,853,948
Donations - General	3(f)	311,272	223,463
Donations - Capital	2	344,000	-
Australian Grants & Fellowships	3(g)	1,209,066	798,651
Overseas Grants & Fellowships	3(h)	1,551,167	1,641,711
Proceeds from Sale of Investments	4	1,056,292	548,610
Other Revenue	3(i)	333,707	365,012
Total Revenue from Ordinary Activities		**13,589,884**	**14,121,960**
Expenses from Ordinary Activities			
Scientific Laboratories			
Employee Benefits		5,496,933	5,242,063
Research Support Services		594,899	545,091
Consumable Supplies		1,195,245	1,092,479
Depreciation and Amortisation	7	373,285	374,752
Administration			
Employee Benefits		957,986	841,545
Repairs & Maintenance		53,803	114,902
Travelling & Accommodation		405,168	353,170
Public Relations		168,214	132,626
Cost of Investments Sold	4	1,267,537	1,153,956
Other Expenses		561,274	597,181
Total Expenses from Ordinary Activities		**11,074,344**	**10,447,765**
Net Result for the Reporting Period	4, 9	**2,515,540**	**3,674,195**
Net Increase in Asset Revaluation Reserve	9	**64,761**	**-**
Total Revenues, Expenses and Valuation Adjustments, Recognised Directly in Equity			
Total Changes in Equity Other than those Resulting from Transactions with the Victorian State Government in its Capacity as Owner	9	**2,580,301**	**3,674,195**

The accompanying notes, as set out on pages 70 to 80 form part of these financial statements.

PRINCE HENRY'S INSTITUTE OF MEDICAL RESEARCH

STATEMENT OF FINANCIAL POSITION AS AT 30TH JUNE 2005

	NOTE	2005 $	2004 $
Current Assets			
Cash	10(a)	212,338	111,751
Receivables	5	2,251,796	1,125,621
Inventories		39,366	-
Prepayments		35,156	-
Investments	6	6,286,866	9,600,225
Total Current Assets		**8,825,522**	**10,837,597**
Non-Current Assets			
Investments	6	4,594,469	14,000
Property, Plant and Equipment	7	2,420,034	1,969,075
Other – LSL Grant Recoverable		399,145	410,892
Total Non-Current Assets		**7,413,648**	**2,393,967**
Total Assets		**16,239,170**	**13,231,564**
Current Liabilities			
Payables		1,263,610	1,053,029
Employee Benefits	8	647,465	653,716
Total Current Liabilities		**1,911,075**	**1,706,745**
Non-Current Liabilities			
Employee Benefits	8	1,044,879	821,904
Total Non-Current Liabilities		**1,044,879**	**821,904**
Total Liabilities		**2,955,954**	**2,528,649**
Net Assets		**13,283,216**	**10,702,915**
Equity			
Contributed Capital	1(o) / 9	5,711,063	5,711,063
Asset Revaluation Reserve	1(r) / 9	191,610	126,849
Specific Purpose Reserve	9	12,427	3,629,483
Accumulated Surplus	9	7,368,116	1,235,520
Total Equity		**13,283,216**	**10,702,915**

The accompanying notes, as set out on pages 70 to 80 form part of these financial statements.

PRINCE HENRY'S INSTITUTE OF MEDICAL RESEARCH

STATEMENT OF CASH FLOWS FOR THE YEAR ENDED 30TH JUNE 2005

	NOTE	2005 $	2004 $
Cash Flows from Operating Activities			
Receipts from Granting Bodies		7,573,372	7,417,222
Industrial Grants		149,975	144,191
Grants and Donations for Capital / Specific Purposes		1,888,166	3,704,393
Investment Revenue		1,210,107	1,853,948
Other Receipts		331,783	372,025
GST Recovered		646,719	359,524
Payments to Suppliers & Employees		(9,171,522)	(8,958,622)
GST Paid		(636,108)	(292,144)
Net Cash Flows from Operating Activities	10(b)	**1,992,492**	**4,600,537**
Cash Flows from Investing Activities			
Proceeds from Sale of Assets		41,228	79,710
Proceeds from the Sale of Investments		4,309,456	548,610
Purchase of Investments		(5,861,997)	(4,744,207)
Purchase of Property, Plant and Equipment	7	(454,787)	(447,980)
Net Cash used in Investing Activities		**(1,966,100)**	**(4,563,867)**
Net Increase / (Decrease) in Cash held		**26,392**	**36,670**
Cash at Beginning of the Period		**1,465,003**	**1,428,333**
Cash at the End of the Period	10(a)	**1,491,395**	**1,465,003**

The accompanying notes, as set out on pages 70 to 80 form part of these financial statements.

NOTES TO AND FORMING PART OF THE FINANCIAL STATEMENTS

1. Statement of Significant Accounting Policies

Prince Henry's Institute of Medical Research ("the Institute") is an organisation formed under an Act of the Victorian Parliament, 1988 No 43. The financial report is a general purpose financial report prepared in accordance with the Financial Management Act 1994. The Institute is exempt from income tax under Subdivision 30-BA of the Income Tax Assessment Act 1997.

Accounting policies are selected and applied in a manner, which ensures that the resultant financial information satisfies the concepts of relevance and reliability, thereby, ensuring that the substance of the underlying transactions and other events is reported.

(a) Acquisition of Assets
The cost method of accounting is used for all acquisitions of assets. Cost is measured as the fair value of the asset given up or liabilities undertaken at the date of acquisition plus incidental costs directly attributable to the acquisition.

(b) Property, Plant and Equipment
Items of plant and equipment are recorded at cost less accumulated depreciation.

The following estimated useful lives are used in the calculation of depreciation:

	2005	2004
Plant and Equipment	(2 to 10 years)	(2 to 10 years)
Leasehold Improvements	(21 years)	(21 years)

(c) Revaluation of Non-Current Assets
Assessment of non-current assets recorded at fair value is reviewed with sufficient regularity to ensure that the carrying amount of each asset does not differ materially from its fair value at the reporting date. Revaluations are assessed annually and supplemented by independent assessments, at least every three years. Revaluations are conducted in accordance with the Victorian Government Policy Revaluation of Non-Current Physical Assets.

Revaluation increments are credited directly to the asset revaluation reserve, except that, to the extent that an increment reverses a revaluation decrement in respect of that class of asset previously recognised as an expense in the net result, the increment is recognised immediately as revenue in the net result.

Revaluation decrements are recognised immediately as expenses in the net result, except that, to the extent that a credit balance exists in the asset revaluation reserve in respect of the same class of assets, they are debited directly to the asset revaluation reserve.

Revaluation increments and decrements are offset against one another within a class of non-current assets.

(d) Recoverable amount of Non-Current Assets Valued on a Cost Basis
The carrying amounts of non-current assets valued on a cost basis, are reviewed to determine whether they are in excess of their recoverable amount at reporting date.

If the carrying amount of a non-current asset exceeds its recoverable amount, the asset is written down to the lower amount. The write-down is expensed in the reporting period in which it occurs.

Where a group of assets working together supports the generation of cash inflows, recoverable amount is assessed in relation to that group of assets.

(e) Investments
Investments are recognised at cost. The market value of investments is disclosed at Note 6. Net unrealised market appreciation has not been brought to account.
Managed investments comprise equities and fixed interest investments.

(f) Revenue Recognition
Interest
Interest income is recognised as earned or received.

Dividends
Dividend income is recognised upon receipt. Franking credits from dividends are reimbursed by the Australian Taxation Office and recognised at the time dividends are received.

Grants
Income from grants is recognised at the time the grant is controlled by the Institute.

Sale of Goods and Disposal of Assets
Income from the sale of goods and disposal of other assets is recognised when the Institute has passed control of the goods or other assets to the buyer.

Rendering of Services
Income from a contract to provide services is recognised by reference to the stage of completion of the contract.

Royalties
Royalty income is recognised as earned or received.

Contributions of Assets
Income arising from the contribution of assets, being non-reciprocal transfers, is recognised as the fair value of the equipment donated when the Institute gains control of the contribution.

(g) Foreign Currency Transactions
Foreign currency transactions are translated to Australian currency at the rates of exchange ruling at the dates of the transactions. Amounts receivable and payable in foreign currencies at reporting date are translated at the rates of exchange ruling at that date.

(h) Leases
Finance Leases
A lease asset and a lease liability equal to the present value of the minimum lease payments are recorded at the inception of the lease.

Lease liabilities are reduced by repayments of principal. The interest components of the lease are expenses contingent, rentals are expensed as incurred.

1. Statement of Significant Accounting Policies (cont.)

(h) Leases (cont.)

Operating Leases

Payments made under operating leases are expensed on a straight line basis over the term of the lease, except where an alternative basis is more representative of the pattern of benefits derived from the leased property.

Lease incentives are recognised as liabilities. Lease rental payments are allocated between rental expense and reduction of the liability, on a straight line basis over the period of the incentive.

(i) Receivables

The Institute's policy for settlement of receivables is 30 days from invoice.

Trade receivables and other receivables are recorded at amounts due less any provision for doubtful debts.

Bills of exchange are recorded at amortised cost, with revenue recognised on an effective yield basis.

(j) Inventories

Inventories are measured at the lower of cost and net realisable value.

(k) Payables

The Institute's policy for settlement of payables is 30 days from invoice.

Trade payables and other accounts payable are recognised when the Institute becomes obliged to make future payments resulting from the purchase of goods and services.

(l) Research and Development Costs

Research and development costs are recognised as an expense when incurred, except to the extent that such costs, together with unamortised deferred costs in relation to that project, are expected, beyond any reasonable doubt, to be recoverable.

(m) Goods and Services Tax

Receipts, expenses and assets are recognised net of the amount for goods and services tax (GST) except:

- where the amount of GST incurred is not recoverable from the taxation authority, it is recognised as part of the cost of acquisition of an asset or as part of an item of expense; or
- for receivables and payables which are recognised inclusive of GST.

The net amount of GST recoverable from, or payable to, the taxation authority is included as part of receivables or payables.

(n) Employee Benefits

Long Service Leave

The Parliament of Victoria has enacted the Long Service Leave (Amendment) Act 2005, ("the Act") which amends the Long Service Leave Act 1992. The Act impacts the Long Service Leave provision calculations due to the reduction in the timeframe (vesting period) for an entitlement to a pro-rata long service leave payment on termination from 10 to 7 years. The 2005 Long Service Leave balances reflect the impact of the Act.

The provision for long service leave is made in accordance with AASB1028, "Employee Benefits". The liability for long service leave expected to be settled within 12 months of the reporting date is recognised in the provision for employee benefits as a current liability. The liability for long service leave expected to be settled more than 12 months from the reporting date is recognised in the provision for employee benefits and measured as the present value of expected future payments to be made in respect of services provided by employees up to the reporting date. Consideration is given to expected future wage and salary levels, experience of employee departures and periods of service. Expected future payments are discounted using interest rates on national Government guaranteed securities with terms to maturity that match, as closely as possible, the estimated future cash outflows.

Wages and Salaries and Annual Leave

Liabilities for wages and salaries and annual leave are recognised, and are measured as the amounts expected to be paid when the liabilities are settled.

Sick Leave

An expense for sick leave is recognised as the leave occurs and is measured at rates paid or payable.

Superannuation

The amount charged to the Statement of Financial Performance in respect of superannuation represents the contributions made by the Institute to the superannuation fund during the year. (Refer Note 17)

Employee Benefit On-Costs

Employee benefit on-costs are recognised and included in employee benefit liabilities.

(o) Contributed Capital

Consistent with Urgent Issues Group Abstract 38 "Contributions by Owners Made to Wholly Owned Public Sector Entities" and Financial Reporting Direction 2 "Contributed Capital", transfers that are in the nature of contributions or distributions have been designated as Contributed Capital.

(p) Rounding of amounts

Amounts in the financial statements have been rounded to the nearest dollar.

(q) Specific Purpose Reserve

The Specific Purpose Reserve is used to record funds received by the Institute which remain unspent at year end where the usage of such funds is restricted by the grant funding agreement.

(r) Asset Revaluation Reserve

The asset revaluation reserve is used to record increments and decrements of the revaluation of non-current assets.

NOTES TO AND FORMING PART OF THE FINANCIAL STATEMENTS

1. Statement of Significant Accounting Policies (cont.)

(s) The impact of adopting AASB equivalent to IASB standards

For interim and annual reporting periods ending on or after 30 June 2004, AASB 1047 "Disclosing in the Impacts of Adopting Australian Equivalents to International Financial Reporting Standards (IFRS)" requires an explanation of how the transition process is being managed and a narrative explanation of the key differences in accounting policies that are expected to arise from the transition to AASB equivalents to IASB pronouncements. Further details can be found in Note 19.

2. Grants and Donations – Capital

The following amounts were received in specific support for expenditure on equipment, building projects and the research activities at the Institute being undertaken at the Institute.

	2005 $	2004 $
Australian Government Grants		
NHMRC - Equipment	122,349	121,819
NHMRC - Monash Health Research Precinct Pty Ltd	1,454,545	3,359,111
	1,576,894	**3,480,930**
Donations		
Donation - Equipment in kind	344,000	-
Total	**1,920,894**	**3,480,930**

3. Revenue Analysis

The following has been prepared in support of the items of income shown in the Statement of Financial Performance. Amounts received include amounts receivable but not in hand at 30 June 2005.

	2005 $	2004 $
(a) Australian Government Grants		
Department of Health Housing and Community Services		
National Health and Medical Research Council	3,987,907	3,726,719
National Health and Medical Research Council - Infrastructure Support	408,360	-
Total	**4,396,267**	**3,726,719**
(b) Victorian Government Grants		
Department of Innovation, Industry and Regional Development - Infrastructure Grant	989,652	906,506
Department of Human Services Victoria - Infrastructure Grant	247,845	235,466
Total	**1,237,497**	**1,141,972**

(c) Industrial Grants and Contracts

	2005 $	2004 $
Diagnostic Systems Laboratories	58,500	-
Acrux DDS Pty Ltd	55,197	-
NV Organon (Aust) Pty Ltd	16,700	320
Mayo Clinic College of Medicine	10,032	-
Novo Nordisk Pharmaceuticals	4,779	4,359
Institut fur Zoologie	1,932	-
CIBA Vision Corporation (CV)	1,535	-
Prosearch International Australia	1,300	-
Mayne Pharma Pty Ltd	-	98,470
Eli Lilly Pty Ltd	-	27,127
3T Teahouse	-	8,415
Jurox Pty Ltd	-	5,500
Total	**149,975**	**144,191**

(d) Transfers from Other Institutions

Monash University	164,649	148,993
Southern Health	19,783	-
Walter and Eliza Hall Institute	15,917	-
University of Queensland	4,250	-
The Garvan Institute	3,000	-
University of Melbourne	2,600	5,000
Mercy Hospital	2,141	-
Howard Florey Institute	1,300	-
The Baker Medical Research Institute	-	30,000
University of Adelaide	-	8,852
La Trobe University	-	3,908
Total	**213,640**	**196,753**

(e) Revenue from Investments

Share dividends	1,032,124	1,753,385
Bank deposits at call	177,983	100,563
Total	**1,210,107**	**1,853,948**

(f) Donations

General	**311,272**	**223,463**

(g) Australian Grants and Fellowships

Cancer Council of Victoria	550,000	550,000
Pfizer Australia Pty Ltd	417,533	-
NAB Ovarian Cancer Research Foundation	81,033	89,047
Diabetes Australia	42,500	20,000
Novartis Australia Pty Ltd	40,000	-
Foundation for High Blood Pressure Research	35,000	-
National Heart Foundation	25,000	32,116
The Cancer Institute (NSW)	18,000	-
Australian Research Centre for Complementary and Active Medicine	-	28,769
Acrux DDS Pty Ltd	-	21,695
Royal Australasian College of Physicians	-	18,182
Anzac Health & Research	-	15,677
Glaxo Smith Kline	-	14,100
Ingenix Inc.	-	9,065
Total	**1,209,066**	**798,651**

3. Revenue Analysis (cont.)

(h) Overseas Grants and Fellowships

	2005 $	2004 $
Schering AG	667,772	472,535
Merck & Co Pty Ltd	213,928	82,500
National Institutes of Health	188,815	378,998
CONRAD Program	134,530	185,244
Endocrine Pharmaceuticals UK	83,018	45,175
World Health Organisation	70,062	28,162
Serono Foundation	61,350	-
University of Michigan	51,668	50,564
University of California LA	49,555	45,180
L'Institute Nationale d'Environment	27,986	-
University of Milan	2,094	-
University of Nottingham	389	-
Pfizer Australia	-	284,562
Royal NZ College of Obstetrics & Gynaecology	-	32,737
Mayo Clinic	-	16,216
Pharmacia Upjohn Co	-	14,359
Hamburg University School of Medicine	-	5,479
Total	**1,551,167**	**1,641,711**

(i) Other Revenue

Royalties	214,614	135,182
Travel Support	102,207	123,544
Other	16,886	106,286
Total	**333,707**	**365,012**

4. Results from Ordinary Activities

The following items are included in determining the Net Result for the Reporting Period.

	2005 $	2004 $
Auditors Remuneration		
Audit Services:		
Auditor General - Victoria	10,875	10,600
Employee Benefits		
Long Service Leave	248,851	48,885
Rental Expenses		
Werribee Property/ Monash Medical Centre	2,002	2,002
Sale of Investments		
Proceeds from sale of investments	1,056,292	548,610
Cost of investments sold	(1,267,537)	(1,153,956)
Profit / (Loss) on sale of investments	**(211,245)**	**(605,346)**

The loss on sale of investments resulted from buy back options and was negated from additional dividend and imput tax credits of $544,178 (2004: $1,289,939) included in Revenue from Investments in the Statement of Financial Performance.

Sale of Property, Plant and Equipment

	2005 $	2004 $
Proceeds from sale of assets	41,228	79,710
Written down value of assets sold (Refer Note 7)	(39,304)	(86,727)
Profit / (Loss) on sale of property, plant and equipment	**1,924**	**(7,013)**

5. Receivables

	NOTE	2005 $	2004 $
Current			
Debtors – Ordinary		1,610,528	1,110,621
Debtor – Monash Health Research Precinct	13, 20	602,636	-
Accrued Income		38,632	15,000
Total		**2,251,796**	**1,125,621**

6. Investments

	NOTE	2005 $	2004 $
Current			
Investments at Cost			
Bank deposits at call		1,279,057	1,353,252
Managed Portfolio*		5,007,809	4,648,613
Common Fund – Precinct	20	-	3,598,360
Total		**6,286,866**	**9,600,225**

*The Managed Portfolio consists predominantly of equity securities and fixed interest investments whose Market Value at 30 June 2005 was $6,676,779 (2004 $5,614,493)

Non-Current			
Investments at Cost			
Investments in non-listed companies			
Monash Health Research Precinct Pty Ltd	20	4,580,469	-
Other non-listed companies		14,000	14,000
Total		**4,594,469**	**14,000**
Total Investments		**10,881,326**	**9,614,225**

NOTES TO AND FORMING PART OF THE FINANCIAL STATEMENTS

7. Property, Plant and Equipment

	2005 $	2004 $
At Valuation		
Leasehold Improvements*	710,000	681,000
Less Accumulated Amortisation	-	(35,761)
	710,000	**645,239**
At Cost		
Plant and Equipment	5,578,876	4,854,982
Less Accumulated Depreciation	(3,868,842)	(3,531,146)
	1,710,034	**1,323,836**
Total		
Property, Plant & Equipment	6,288,876	5,535,982
Less Accumulated Depreciation & Amortisation	(3,868,842)	(3,566,907)
Total Property, Plant and Equipment	**2,420,034**	**1,969,075**

* A valuation of leasehold improvements was undertaken for the 30 June 2005 Financial Statements by an agent of the Valuer General – Victoria. The valuation was conducted to assess the fair value of the property and was undertaken in accordance with the Financial Management Act 1994 and other relevant accounting policies and pronouncements.

The recoverable amount of the assets is its fair value less costs to sell or its value in use.

Reconciliations of the carrying amounts of each class of property, plant and equipment at the beginning and end of the current financial reporting period are set below.

	Leasehold Improvements $	Plant & Equipment $	Total $
2005			
Carrying amount at 1 July 2004	645,239	1,323,836	1,969,075
Additions at Cost	-	454,787	454,787
Donation - Equipment in-kind (Refer Note 2)	-	344,000	344,000
Disposals	-	(39,304)	(39,304)
Revaluation increment	64,761	-	64,761
Depreciation	-	(373,285)	(373,285)
Carrying amount at 30 June 2005	**710,000**	**1,710,034**	**2,420,034**

8. Employee Benefits

	2005 $	2004 $
Current		
Accrued Salaries & Wages	210,202	178,880
Long Service Leave*	119,339	91,323
Annual Leave	317,924	383,513
	647,465	**653,716**
Non-Current		
Annual Leave	108,125	-
Long Service Leave*	936,754	821,904
	1,044,879	**821,904**
Total Employee Benefits	**1,692,344**	**1,475,620**
Movement in Long Service Leave		
Balance 1 July 2004	913,227	899,629
Provision made during the reporting period	248,851	48,885
Settlement made during the reporting period	(105,985)	(35,287)
Balance 30 June 2005	**1,056,093**	**913,227**
Employee numbers working at 30 June	134	131

* The following assumptions were adopted in measuring the present value of long service leave:

- A wage indexation factor has been applied to the current salary base to estimate wage growth. In 2005 the factor was 4.5% (2004: 4.50%).
- Bond rates have been applied to the estimated future value of the liability in order to estimate the present value. In 2005 the rates were between 5.26% to 5.91% from years 1 to 12 (2004: 5.23% to 5.94% years 1 to 12).

9. Equity & Reserves

	2005 $	2004 $
Contributed Capital		
Balance at the beginning of the reporting period	5,711,063	5,711,063
Balance at the end of the reporting period	**5,711,063**	**5,711,063**
Reserves		
Asset Revaluation Reserve *		
Balance at the beginning of the reporting period	126,849	126,849
Increase of Leasehold Improvements during the reporting period	64,761	-
Balance at the end of the reporting period	**191,610**	**126,849**
**Specific Purpose Reserve ** **		
Balance at the beginning of the reporting period	3,629,483	248,409
Transfers (to)/from accumulated surplus	(3,617,056)	3,381,074
Balance at the end of the reporting period	**12,427**	**3,629,483**
Accumulated Surplus		
Balance at the beginning of the reporting period	1,235,520	942,399
Net Result for the reporting period	2,515,540	3,674,195
Transfer from/(to) Specific Purpose Reserve	3,617,056	(3,381,074)
Balance at the end of the reporting period	**7,368,116**	**1,235,520**
Total Equity		
Balance at the beginning of the reporting period	10,702,915	7,028,720
Total changes in equity recognised in the Statement of Financial Performance	2,580,301	3,674,195
Total equity at the end of the reporting period	**13,283,216**	**10,702,915**

* An independent valuation of the property was conducted for the purpose of the Financial Statements as at the 30 June 2005. The effect of this valuation was to increase the value of property by $64,761, this amount is now reflected in the Asset Revaluation Reserve.

** The Specific Purpose Reserve represents funds received from NHMRC for the purpose of constructing a building for the Monash Health Research Precinct.

10. Notes to The Statement of Cash Flows

(a) Reconciliation of Cash

For the purposes of the Statement of Cash Flows, cash includes cash on hand and in banks and investments in money market instruments, net of outstanding bank overdrafts.

Cash Assets at the end of the financial year as shown in the Statement of Cash Flows is reconciled to the related items in the Statement of Financial Position as follows:

	2005 $	2004 $
Cash Assets	212,338	111,751
Deposits at Call (Refer Note 6)	1,279,057	1,353,252
	1,491,395	**1,465,003**

(b) Reconciliation of Net Result for Reporting Period to Net Cash Provided by Operating Activities

	2005 $	2004 $
Net Result for the Reporting Period	2,551,301	3,674,195
Add/(less) non-cash items:		
(Profit)/Loss on sale of non current assets	(1,924)	7,013
(Profit)/Loss on sales of investments	211,245	605,346
Add/(less) items classified as investing activities:		
Depreciation	337,524	374,752
Capital donations in kind	(344,000)	-
Add/(less) changes in assets and liabilities:		
(Increase)/Decrease in receivables	(1,126,184)	(139,343)
(Increase)/Decrease in inventories	(39,366)	-
(Increase)/Decrease in prepayments	(35,156)	-
(Increase)/Decrease in long service leave grant recoverable	11,747	15,049
Increase/(Decrease) in payables	210,581	(32,375)
Increase/(Decrease) provision for employee entitlements	216,724	95,900
Net Cash Flows from Operating Activities	**1,992,492**	**4,600,537**

11. Responsible Persons Disclosures

(a) Responsible Minister
The Hon. J. Brumby in his capacity as Minister for Innovation.

(b) Directors

The Directors of the Institute during the year were:
John Robinson *(Chair)*
Evan R. Simpson *(Institute Director)*
Russell J. Fynmore AO *(Deputy Chair)*
Lisa Hinrichsen *(Honorary Treasurer)*
Jane Bell
Anne Ellis
Margaret Lothian
Trevor J. Montgomery
Nicos Nicola AO
Bob Stensholt MP
Edward Byrne
Linda Sorrell (appointed 5 August 2004)
Michael Burn (appointed 5 August 2004)
David Pisker (appointed 5 August 2004)

	2005 $	2004 $
(c) Remuneration of Directors		
Remuneration received or due and receivable by Non-executive Directors	-	-
Insurance to indemnify liabilities whilst acting as a Director	20,410	19,346
Retirement benefits to Non-executive Directors	-	-
Loans to Non-executive Directors	-	-
Transactions to Non-executive Directors	-	-
Superannuation paid for Non-executive Directors	-	-

Remuneration to the Institute Director is included in Executive Officer Remuneration Note 11(d)

(d) Executive Officer Remuneration	**No.**	**No.**
Income received or due and receivable by executive officers whose income is:		
$100,000 - $110,000	2	-
$110,001 - $120,000	-	1
$120,001 - $130,000	1	1
$130,001 - $140,000	1	1
$140,001 - $150,000	1	1
$160,001 - $170,000	-	1
$190,001 - $200,000 (Refer note 11(c))	1	-
$200,001 - $210,000 #	1	-

Including termination payment of $101,342 comprising long service leave and annual leave entitlements.

Total Remuneration for Period	**$1,289,575**	**$964,379**

12. Lease Liabilities

Aggregate lease expenditure contracted at balance date

	2005 $	2004 $
Operating Lease – Werribee Property:		
Not later than one year	2,000	2,000
Later than one year but not later than five years	8,000	8,000
Later than five years	12,000	14,000
	22,000	**26,000**

The Institute has entered into a lease agreement for the provision of laboratory facilities at the Monash Health Research Precinct. Provisions of the lease require a per annum lease payment of $289,300, increasing at the rate of 3% per annum. The lease commenced on 1 September 2005.

Operating Lease – Monash Health Research Precinct:		
Not longer than 1 year	241,083	-
longer than 1 year but not longer than 2 years	296,533	-
longer than 2 years but no longer than 5 years	944,049	-
longer than 5 years	6,814,442	-
	8,296,107	**-**

13. Contingent Assets and Liabilities

As at 30 June 2005 there were no Contingent Assets or Liabilities (2004: $Nil) other than in Note 20.

14. Economic Dependency

The Institute is reliant upon grants from the National Health and Medical Research Council for approximately 40% of operating expenditure and the Victorian Government for approximately 11% of operating expenditure for support of its basic research activities.

15. Financial Instruments

(a) Significant Accounting Policies
Details of the significant accounting policies and methods adopted, including the criteria for recognition, the basis of measurement and the basis on which revenues and expenses are recognised, in respect of each class of financial assets, financial liability and equity instruments are disclosed in Note 1 to the financial statements.

(b) Significant Terms, Conditions and Objectives of Derivative Financial Instruments
The Institute does not enter into or trade complex derivative financial instruments.

15. Financial Instruments (cont.)

(c) Credit Risk

The Institute has adopted the policy of only dealing with creditworthy counterparties and obtaining sufficient collateral or other security where appropriate, as a means of mitigating the risk of financial losses from defaults.

The Institute does not have any significant credit risk exposure to any single counterparty or any group of counterparties having similar characteristics. The carrying amount of financial assets recorded in the Statement of Financial Position, net of any provision for losses, represents the Institute's maximum exposure to credit risk.

(d) Interest Rate Risk

The following table details the Institute's exposure to interest rate risk as at the reporting date.

	Weighted Average Interest Rate	Variable Interest Rate $	Fixed Interest Rate Maturity Less than 1 Year $	Fixed Interest Rate Maturity 1 to 5 Years $	Non Interest Bearing $	At 30 June Total 2005 $	At 30 June Total 2004 $
Financial Assets							
Cash	-	-	-	-	212,338	212,338	111,751
Receivables	-	-	-	-	2,251,796	2,251,796	1,125,621
Investments	5.14%	1,279,057	-	-	9,602,278	10,881,335	9,614,225
		1,279,057	**-**	**-**	**12,066,412**	**13,345,469**	**10,851,597**
Financial Liabilities							
Payables	-	-	-	-	1,263,610	1,263,610	1,053,029
		-	**-**	**-**	**1,263,610**	**1,263,610**	**1,053,029**

(e) Net Fair Value of Financial Assets and Liabilities

The net fair value of cash and cash equivalents and non-interest bearing monetary financial assets and financial liabilities of the Institute approximates their carrying amounts.

The net fair value of other monetary financial assets and financial liabilities is based upon market prices where a market exists or by discounting the expected future cash flows by the current interest rates for assets and liabilities with similar risk profiles.

For non-traded equity investments the net fair value is based upon the underlying net assets, future maintainable earnings and any special circumstances pertaining to a particular investment.

The carrying amounts and net fair values of financial assets and liabilities at reporting date are:

	2005		2004	
	Carrying Amount $	Net Fair Value $	Carrying Amount $	Net Fair Value $
Financial Assets				
Cash and cash equivalent	212,338	212,338	111,751	111,751
Receivables	2,251,796	2,251,796	1,125,621	1,125,621
Investments	10,881,335	12,550,305	9,614,225	10,580,105
	13,345,469	**15,014,439**	**10,851,597**	**11,817,477**
Financial Liabilities				
Payables	1,263,610	1,263,610	1,053,029	1,053,029
	1,263,610	**1,263,610**	**1,053,029**	**1,053,029**

16. Capital Commitments

	2005 $	2004 $
Commitments for capital expenditure not provided for in the accounts		
Plant and equipment	-	-
Not later than one year	-	-

17. Superannuation

The majority of employees of the Institute are members of VicSuper Pty Ltd, which is a defined contribution fund. The Scheme is fully funded as at 30 June 2005. Institute contributions are calculated at rates of a minimum of 9% to a maximum of 17% of the employee's salary.

	2005 $	2004 $
Employer Contributions		
VicSuper Pty Ltd	603,146	570,315
Uni Super Management Pty Ltd	46,415	28,152
Other	24,072	10,257
	673,633	**608,724**
Outstanding employer contributions		
VicSuper Pty Ltd	-	-
Uni Super Management Pty Ltd	-	-
Other	-	-
	-	-

18. Related Party Transactions

Transactions between affiliated entities are on normal commercial terms and conditions no more favourable than those available to other parties.

	2005 $	2004 $
Other Transactions of responsible persons and their related entities		
Ms Linda Sorrell (Director) – Chief Executive of Southern Health Southern Health has provided services for several years on normal commercial terms and conditions.		
Consumables, Telephone and Diagnostic Services	223,128	257,927
The Institute has provided services to Southern Health for several years on normal commercial terms and conditions.		
Medical and Nursing Services	32,350	32,917

18. Related Party Transactions (cont.)

	2005 $	2004 $
Professor E. Byrne (Director) – Dean Faculty of Medicine Monash University Monash has provided services for many years on normal commercial terms and conditions.		
Animal Services, Maintenance, Network and Training Services	662,845	430,728
The Institute has provided services to Monash University for several years on normal commercial terms and conditions		
Research and Animal Services	744,334	492,397
Mr T. Montgomery (Director) – Employed at Goldman Sachs J B Were, who are the Institute's Stockbrokers. Goldman Sachs J B Were has provided services for several years on normal commercial terms and conditions.		
Purchase and Sale of Investments - Brokerage Fees Paid	10,342	15,129
Donations received by the Institute from the Goldman Sachs J B Were Charitable Fund	-	5,000

19. AASB 1047 Guidance Disclosure: Impacts of adopting Australian equivalents to International Financial Reporting Standards

For the financial year commencing 1 July 2004 the Institute must comply with Australian equivalents to International Financial Reporting Standards ("AIFRS") as issued by the Australian Accounting Standards Board. This financial report has been prepared in accordance with Australian accounting standards and other financial reporting requirements ("AGAAP") applicable for reporting periods ended 30 June 2005. The Institute will report for the first time in compliance with AIFRS when results for the financial year ended 30 June 2006 are released.

It should be noted that under AIFRS, there are requirements that apply specifically to not-for-profit entities. The Institute was established to achieve the objectives of government in providing services free of charge or at prices significantly below their cost of production for the collective consumption by the community, which is incompatible with generating profit as a principal objective. Consequently, where appropriate, the Institute applies those paragraphs in accounting standards applicable to not-for-profit entities.

19. AASB 1047 Guidance Disclosure: Impacts of adopting Australian equivalents to International Financial Reporting Standards (cont.)

An AIFRS compliant financial report will comprise a new statement of changes in equity in addition to the three existing financial statements, which will all be renamed. The Statement of Financial Performance will be renamed as the Operating Statement, the Statement of Financial Position will revert to its previous title as the Balance Sheet and the Statement of Cash Flows will be simplified as the Cash Flow Statement. However, for the purpose of disclosing the impact of adopting AIFRS in the 2004/05 financial report, existing titles and terminologies will be retained.

With certain exceptions, an entity that has adopted AIFRS must record transactions that are reported in the financial report as though AIFRS had always applied. This requirement also extends to any comparative information included within the financial report. Most accounting policy adjustments to apply AIFRS retrospectively will be made against accumulated funds at the 1 July 2004 opening balance sheet date for the comparative period. The exceptions include deferral until 1 July 2005 of the application and adjustments for:

- AASB 132 Financial Instruments: Disclosure and Presentation; and
- AASB 139 Financial Instruments: Recognition and Measurement.

The comparative information for transactions affected by these standards will be accounted for in accordance with existing accounting standards.

The Institute has taken the following steps in managing the transition to AIFRS and has achieved the following scheduled milestones:

- established a steering committee to oversee the transition to and implementation of the AIFRS;
- established an AIFRS project team to review the new accounting standards to identify key issues and the likely impacts resulting from the adoption of AIFRS and any relevant Financial Reporting Directions as issued by the Minister for Finance;
- participated in an education and training process to raise awareness of the changes in reporting requirements and the processes to be undertaken; and
- initiated reconfiguration and testing of user systems and processes to meet new requirements.

A number of differences between AGAAP and AIFRS have been identified as potentially having a significant impact on the financial position and financial performance of the Institute following the adoption of AIFRS. These differences and their potential impacts are outlined below. The estimates disclosed represent the best estimate of the quantitative impact of the changes as at the date of preparing the 30 June financial reports. The actual effects of transition to AIFRS may differ from the estimates disclosed due to:

- changes in facts and circumstances;
- ongoing work being undertaken by the AIFRS project team;
- potential amendments to AIFRS and Interpretations; and
- emerging accepted practice in the interpretation and application of AIFRS and UIG Interpretations.

Employee Benefits

Under existing Australian accounting standards, employee benefits such as wages and salaries, annual leave and sick leave are required to be measured at their nominal amount regardless of whether they are expected to be settled within 12 months of the reporting date. On adoption of AIFRS, a distinction is made between short-term and long-term employee benefits. AASB 119 Employee Benefits requires liabilities for short-term employee benefits to be measured at nominal amounts and liabilities for long-term employee benefits to be measured at present value. AASB 119 defines short-term employee benefits as those that fall due wholly within twelve months after the end of the period in which the employee renders the related service. Therefore, liabilities for employee benefits such as wages and salaries, annual leave and sick leave are required to be measured at present value where they are not expected to be settled within 12 months of the reporting date.

The effect of the above requirement on the Statement of Financial Position as at 1 July 2004 is an estimated decrease in the employee benefits liability and a corresponding increase in the Accumulated Surplus of $11,875. For the year ended 30 June 2005, employee benefits expense is also expected to decrease by $43,281 and the 30 June 2005 employee benefits liability is expected to decrease by $43,281.

Financial instruments

The Institute has elected to apply the first-time adoption exemption available under AASB 1 First-time adoption of Australian Equivalent to International Financial Reporting Standard to defer the date of transition of AASB 139 Financial Instruments: Recognition and Measurement until 1 July 2005. Accordingly, there will be no quantitative impacts on the financial positions as at 1 July 2004 and 30 June 2005 or on the financial performance for the year ended 30 June 2005.

From 1 July 2005 the Institute's managed investment portfolio will be recorded at its market value and the increment in the portfolio's carrying value will be taken to the Asset Revaluation Reserve.

20. Monash Health Research Precinct

In 2002 Prince Henry's Institute of Medical Research ("Institute") entered into an agreement with the Commonwealth Government of Australia, acting through and represented by the Department of Health and Ageing, in which the Government agreed to fund the construction of research laboratories for the Institute at the Monash Health Research Precinct ("Precinct") located at the Monash Medical Centre campus of Southern Health. In accordance with the Agreement the Commonwealth is to provide funding of $4,500,000 over a period of 3 years towards the construction of a building to house the research laboratories with a further $1,000,000 being available to complete the fit-out of those laboratories.

These funds are being pooled with other grant funds and bank loans to enable the construction of a new research facility to accommodate not only the Institute, but also certain activities of Monash University represented by Monash Institute of Medical Research ("MIMR") and the Monash Institute of Health Services Research ("MIHSR").

Monash Health Research Precinct Pty Ltd ("MHRP") was established to facilitate the above and specifically for the purpose of the following:

- constructing a new research facility at the Precinct:
- managing the Precinct to ensure its efficient and effective of location of space to each shareholder and to other users; and
- allocating to the shareholders the costs and expenses of any shared resources and facilities of the Precinct.

Southern Health, Monash University and Prince Henry's Institute of Medical Research are each shareholders of MHRP. As at 30 June 2005, the issued capital of MHRP totalled 13,690,229 shares of $1.00 each. These shares were held by the following entities:

- Monash University holds 5,991,570 Shares (44%);
- Prince Henry's Institute of Medical Research holds 4,580,469 Shares (33%); and
- Southern Health holds 3,118,190 Shares (23%).

During June 2005 the Institute entered into a 21 year lease with MHRP commencing 1 September 2005, for the use of the laboratories. (Refer Note 12).

As at 30 June 2005 an amount of $602,636 is included in receivables in regard to MHRP and consists of:

	$
Commonwealth grants received	5,054,545
Interest earned to 30 June 2005	128,560
Total funds provided to MHRP	**5,183,105**
Purchase of shares in MHRP (Refer Note 6)	(4,580,469)
Debtor - MHRP (Refer Note 5)	**602,636**

Contingent Asset

A grant of $445,454 in respect of the (MHRP) development is due from the Commonwealth Government. Release of these funds is conditional upon receipt of satisfactory final reports from MHRP and a certificate of occupancy. Upon receipt of the funds the MHRP will issue 1,048,090 $1.00 shares to the Institute.

Contingent Liabilities

The Institute will release a payment of $445,454 to the MHRP upon receipt of the final development grant due from the Government, as described in the Contingent Assets note above.

21. Events Occurring After Balance Date

There were no significant events after balance date.

PRINCE HENRY'S INSTITUTE OF MEDICAL RESEARCH

STATEMENT OF OPERATIONS FOR THE YEAR ENDED 30TH JUNE 2005

GENERAL INFORMATION

a) Establishment
The Institute is established by the Prince Henry's Institute of Medical Research Act 1988 (the Act). The responsible Minister is the Minister for Innovation.

b) Objectives
The objectives, powers and functions of the Institute as described in Section 5 of the Act are set out below:

1) The objectives of the Institute are:

a) to operate as a charitable scientific organisation; and
b) to further knowledge in the field of medicine, particularly human medicine and biotechnology, by the conducting and carrying out of research including research
   (i) to discover the nature and causes of human diseases and afflictions; and
   (ii) to improve the methods of preventing, diagnosing and treating diseases; and
c) to develop commercially, exploit and market industrial and intellectual property rights developed by or on behalf of the Institute; and
d) to provide services in the fields of human and animal medicine; and
e) to provide, and aid in the provision of, educational programs relating to the subject of research conducted by the Institute; and
f) to publish information relating to the work of the Institute.

2) The Institute shall have the following powers:

a) To enter into contracts, agreements or arrangements;
b) To hold industrial and intellectual property rights relating to inventions or discoveries made by or on behalf of the Institute;
c) To hold money raised, or received by way of grants, subsidies, subscriptions, gifts, bequests or in any other manner;
d) To borrow or otherwise obtain financial accommodation and charge all or any part of its real and personal property as security for the repayment of any liability in accordance with this Act and
e) To create and issue debentures in accordance with this Act and
f) To invest and from time to time vary the investment of any of its money in accordance with this Act.

c) Services
The Institute is dedicated to research in the field of endocrinology - the study of hormones and their role in health and disease, including cancer. In addition, the Institute is affiliated with Monash University and as such, provides teaching services to undergraduates and postgraduates and is associated with Southern Health.

d) Implementation of Government policy
The Institute is not responsible for implementing Government policy.

e) Administrative Structure

i) Members of the Board of Management

Mr John Robinson BSc, MGSc, FIMM
Chairman, Member of the Institute appointed by the Board

Mr Russell Fynmore AO, FCPA
Deputy Chairman
Member of the Institute appointed by the Board

Ms Lisa Hinrichsen B.Bus, BA, CA
Honorary Treasurer
Member of the Institute appointed by the Board

Professor Evan R Simpson BSc (Hons), PhD
Director

Mrs Jane Bell BEc, LLB, LLM (Lon), GAICD
Member of the Institute appointed by the Board

Mr Michael Burn B.Comm
Member of the Institute appointed by the Board

Professor Edward Byrne B.Med.Sci, MBBS (1st Class Hons) Dipl. Clin Sci., FRACP, MD, D.Sc, FRCP (UK), Exec MBA
Nominated to the Board by Monash University

Mrs Ann Ellis DipEd
Member of the Institute appointed by the Board

Ms Margaret Lothian BEc, LLB (Hons)
Member of the Institute appointed by the Board

Mr Trevor Montgomery SIPA
Member of the Institute appointed by the Board

Professor Nic Nicola AO BSc (Hons), PhD
Nominated to the Board by the National Health and Medical Research Council

Mr David Pisker Dip. Film Making
Member of the Institute appointed by the Board

Ms Linda Sorrell MHA, B.Hlth.Services Management, Grad. Cert Casemix
Nominated to the Board by Southern Health

Mr Bob Stensholt MP, BA, BD (Hons) MIntLaw Dip Phil
Nominated to the Board by the Minister for Health and Ageing

ii) Office Bearers

Chairman: Mr J Robinson
Deputy Chairman: Mr R J Fynmore AO
Hon. Treasurer: Ms L Hinrichsen
Director: Professor E R Simpson
Deputy Director: Professor J K Findlay AM
Public Officer and Secretary: Mr T T Haining

iii) Organisation Chart (please see page 16)

PRINCE HENRY'S INSTITUTE OF MEDICAL RESEARCH

STATEMENT OF OPERATIONS FOR THE YEAR ENDED 30TH JUNE 2005

iv) Postal address:

PO Box 5152, Clayton, Vic 3168, Australia

Courier address:
Clinical Research & Services, Level 3, Block E
246 Clayton Road, Clayton, Vic 3168, Australia

Administration & Laboratories:
Level 4, Block E, Monash Medical Centre
246 Clayton Road, Clayton, Vic 3168, Australia

Biological Resources Facility:
Biotechnology Precinct, VIAS
Werribee, Victoria

Telephone: (03) 9594 4372
Facsimile: (03) 9594 6125
Home Page: http://www.princehenrys.org

f) Information
Information about the powers, functions and duties of the Institute can be found in the Prince Henry's Institute of Medical Research Act 1988.

Reports of the activities of the Institute can be found on its website and in the Annual Report of its operations, available from the Institute, reports to funding bodies such as the National Health and Medical Research Council of Australia, The Cancer Council of Victoria, the World Health Organization and other private foundations, and publications in learned scientific and medical journals, theses and reviews available in biomedical libraries.

g) Subsidiaries
The Institute does not have subsidiaries, and has a Joint Venture with Monash University for Australia Taxation Office (Goods and Services Tax) purposes related to the Monash Health Research Precinct.

REVIEW OF OPERATIONS

a) Operational Objectives
The operational objectives of the Institute for the 12 months ended 30th June 2005 were to further medical knowledge by conducting research in the field of endocrinology, to disseminate new information by publication in learned scientific journals and presentations at scientific and clinical meetings, to apply, where possible, the new information to clinical practice, to develop commercially intellectual property rights, and to provide educational programs particularly relating to the research interests of the Institute.

The Institute is a member of the Monash Health Research Precinct. Stage 1 of the new building development for the precinct has commenced. This development will enhance the facilities available for the Institute to meet its objectives.

b) External Influences
There were no legislative or other factors that substantially affected achievement of the operational objectives of the Institute.

c) Changes to Objectives
There were no major changes to the powers or functions of the Institute or to its organisational structure or methods of operation during the 12 month period under review.

d) External Reviews
No external review of the objectives, functions, powers or duties of the Institute were carried out.

e) Summary of Operations
The major research and development activities, and the clinical services and teaching programs of the Institute are summarized in the Annual Report for 12 months ended June 2005.

f) Promotional Activities
Community awareness of the Institute and the services it provides has been developed by circulating newsletters to Members and benefactors of the Institute, distributing the Annual Report to donors and interested parties, including Foundations, Trusts, Companies, and other research and teaching institutions. Community awareness has also been established by the participation of senior members of the Institute in public and professional education programs as well as many of the Institute's activities being reported in the media.

g) Legislative Responsibilities
The Institute had no responsibility for the administration of other Acts of legislation, and was not affected by any judicial decisions during the financial year.

h) Regulations
The Institute has 10 By-Laws, made under Section 19 of the Prince Henry's Institute of Medical Research Act 1988. It is the opinion of the Board that these regulations are too numerous to summarise, and a list can be obtained from the Institute.

i) Employees
There were 108 full-time, part-time and casual employees on 30th June 2005 and 108 on 30th June 2004. These figures do not include postgraduate scholars studying at the Institute during the 12 months ended 30th June 2004.

j) Pecuniary Interests
Members of the Board have made declarations of interest under Section 14 of Prince Henry's Institute of Medical Research Act 1988.

k) Overseas Visits
All overseas visits undertaken on behalf of or paid for by the Institute were for technical purposes.

STATEMENT OF OPERATIONS FOR THE YEAR ENDED 30TH JUNE 2005

l) Occupational Health and Safety
The Institute's staff is its greatest asset and hence OH&S is a key issue. A Safety Committee comprising of representatives from all groups and management is constituted as per the Victorian OH&S Act 2004. One staff member is designated Safety Manager under the jurisdiction as listed under the Act and this person represents PHIMR on the Southern Health Safety Representative group. We also have extensive liaison with Monash University in OH&S. The Safety Manager (Materials & Human Resources Manager) chairs four safety meetings per annum and undertakes the overseeing of orientation and training as well as development of safety policy. The Safety Manager also sits on the Southern Health Radiation Safety Committee. During 2005 a comprehensive audit of safety was undertaken with a favourable outcome. The GAP analysis did highlight areas where more attention was needed and these are currently under development as is a review of policy on responsibilities under the new OH&S act.

m) Environmental Regulations
The Institute complies with the Environmental Protection Act in respect of its operations. Discharges to air and water are below specific levels of contaminants and solid waste is disposed of in an appropriate manner. Biomedical waste and sharps are disposed of through appropriately licensed contractors.

n) Industrial Relations
The Institute largely follows the guidelines of the Public Sector and Monash University with respect to matters of industrial relations, except where provisions are laid down by the National Health and Medical Research Council. There was no time lost due to industrial accidents and disputes during the year.

o) Freedom of Information
There were no requests made directly to the Institute under the Freedom of Information Act 1982.

p) External Committees
No external committees dealing with public policy matters were set up during the financial year.

q) Consultants
Wyndarra Consulting – Risk Management and Internal Audit Consultancy.

r) Performance Statistics: The financial statistics are summarised in the financial statements which accompany this statement of Operations. Other statistics are summarised in the following table.

TABLE 1

	2005	2004
Scientific papers published or accepted for publication	89*	92**
Postgraduate Students:		
Total number of students	37	46
Enrolled for Ph.D	32	28
Enrolled for Masters, Honours and BMedSci	5	18
Number Graduating:		
Ph.D	6	5
Masters, Honours and BMedSci	12	8

Institute Staff:

	2005		2004	
	Number	**EFT**	**Number**	**EFT**
Research Staff	110	72.95	109	73.67
Laboratory Support	2	.52	2	.47
Buildings/Facilities Operations	1	.50	1	.50
Management/ Administrative Staff	21	16.11	19	14.82
TOTAL	**134**	**90.08**	**130**	**89.46**

* Denotes calender year 2004
**Denotes calender year 2003

PRINCE HENRY'S INSTITUTE OF MEDICAL RESEARCH

DIRECTOR'S DECLARATION

We hereby certify that the Financial Statements and notes as set out on pages 70 to 83 for Prince Henry's Institute of Medical Research have been prepared in accordance with part 4.2 of the Standing Directions of the Minister for Finance under the Financial Management Act 1994, applicable Financial Reporting Directions, Australian Accounting Standards and other mandatory professional requirements.

In our opinion, the Financial Statements present fairly the financial transactions during the year ended 30 June 2005 and the financial position of Prince Henry's Institute of Medical Research as at 30 June 2005.

At the date of signing the Financial Statements, we are not aware of any circumstances which would render any particulars included in the Statements to be misleading or inaccurate.

T.T. Haining
Principal Accounting Officer

R. Fynmore AO
Deputy Chairman

Dated at Melbourne the 22nd day of September 2005

AUDITOR GENERAL
VICTORIA

INDEPENDENT AUDIT REPORT

Prince Henry's Institute of Medical Research

To the Members of the Parliament of Victoria and Members of the Board of the Institute

Matters Relating to the Electronic Presentation of the Audited Financial Report

This audit report for the financial year ended 30 June 2005 relates to the financial report of Prince Henry's Institute of Medical Research included on its web site. The Members of the Board of Prince Henry's Institute of Medical Research are responsible for the integrity of the web site. I have not been engaged to report on the integrity of the web site. The audit report refers only to the statements named below. An opinion is not provided on any other information which may have been hyperlinked to or from these statements. If users of this report are concerned with the inherent risks arising from electronic data communications they are advised to refer to the hard copy of the audited financial report to confirm the information included in the audited financial report presented on this web site.

Scope

The Financial Report

The accompanying financial report for the year ended 30 June 2005 of Prince Henry's Institute of Medical Research consists of the statement of financial performance, statement of financial position, statement of cash flows, notes to and forming part of the financial report, and the supporting declaration.

Members' Responsibility

The Members of the Board of Prince Henry's Institute of Medical Research are responsible for:

- the preparation and presentation of the financial report and the information it contains, including accounting policies and accounting estimates
- the maintenance of adequate accounting records and internal controls that are designed to record its transactions and affairs, and prevent and detect fraud and errors.

Audit Approach

As required by the *Audit Act 1994*, an independent audit has been carried out in order to express an opinion on the financial report. The audit has been conducted in accordance with Australian Auditing Standards to provide reasonable assurance as to whether the financial report is free of material misstatement.

The audit procedures included:

- examining information on a test basis to provide evidence supporting the amounts and disclosures in the financial report
- assessing the appropriateness of the accounting policies and disclosures used, and the reasonableness of significant accounting estimates made by the members
- obtaining written confirmation regarding the material representations made in conjunction with the audit
- reviewing the overall presentation of information in the financial report.

Victorian Auditor-General's Office Level 34, 140 William Street, Melbourne Victoria 3000
Telephone (03) 8601 7000 Facsimile (03) 8601 7010 Email comments@audit vic gov au Website www audit vic gov au

Independent Audit Report (continued)

These procedures have been undertaken to form an opinion as to whether the financial report is presented in all material respects fairly in accordance with Accounting Standards and other mandatory professional reporting requirements in Australia, and the financial reporting requirements of the *Financial Management Act* 1994, so as to present a view which is consistent with my understanding of the Institute's financial position, and its financial performance and cash flows.

The audit opinion expressed in this report has been formed on the above basis.

Independence

The Auditor-General's independence is established by the *Constitution Act 1975*. The Auditor-General is not subject to direction by any person about the way in which his powers are to be exercised. The Auditor-General and his staff and delegates comply with all applicable independence requirements of the Australian accounting profession.

Audit Opinion

In my opinion, the financial report presents fairly in accordance with applicable Accounting Standards and other mandatory professional reporting requirements in Australia, and the financial reporting requirements of the *Financial Management Act* 1994, the financial position of Prince Henry's Institute of Medical Research as at 30 June 2005 and its financial performance and cash flows for the year then ended.

MELBOURNE
22 September 2005

for JW CAMERON
Auditor-General

Victorian Auditor-General's Office Level 34, 140 William Street, Melbourne Victoria 3000
Telephone (03) 8601 7000 Facsimile (03) 8601 7010 Email comments@audit.vic.gov.au Website www.audit.vic.gov.au

Community Support & Donations

Your support inspires our research

Photo: Natalie Hannan, PhD Student, Uterine Biology group

Community Support & Donations

Prince Henry's Institute depends heavily on the financial generosity of community donations to support its research initiatives.

Named Funds

Donors may request to set up a capital donation in the name of a loved one. These named funds are permanently invested, with the income from these investments applied in accordance with the wishes of the donor/s. These Funds may be allocated as a fellowship, scholarship or award. The Funds are included in the Financial Statements as a Note to the Balance Sheet.

The TM Ramsay Fellowship

Lady Ramsay generously established the TM Ramsay Fellowship as a perpetual memorial to her late husband, Sir Thomas Ramsay. The TM Ramsay Fellowship is awarded every 2 years, enabling Prince Henry's Institute to assist young postdoctoral scientists to establish their careers in medical research.

Photo: Sue Elger, Personal Assistant (left) with RD Wright Fellow Margaret Jones and daughter Elizabeth

Dr Damien Keating, part of Prince Henry's Endocrine Cell Biology Group was awarded the TM Ramsay Fellow in April 2004.

Dr Keating has been working on finding possible links between obesity and the onset of type 2 diabetes. Specifically, he is investigating whether certain hormones secreted from fat cells cause the reduced levels of insulin release from the pancreas that occurs in this disease.

The Fred Boylan & Bill Burke Fellowship

Mr Fred Boylan was the Institute's first Chairman. The Boylan/ Burke Fellowship was established following a bequest from his wife, the late Mrs June Boylan.

Dr Stefan Bagheri-Fam was awarded the Boylan/Burke Fellowship in 2004. He joined Prince Henry's Human Molecular Genetics Group in May 2004 from the University of Freiberg, Germany. Dr Bagheri-Fam is investigating the role the FGFR2 protein plays in sex determination and whether it is essential for male development. This will provide a better understanding of how the fate of male development is decided.

Prince Henry's Institute Postgraduate Scholarship Fund

Prince Henry's Institute has been able to use funds from donations and investments to form a scholarship fund for PhD students. Students are invited to apply for the 4 year scholarships, with recipients selected by the Research Management Group at the Institute. The Institute congratulates the following 5 students currently studying on a Postgraduate Scholarship: Sonay Hussein-Fikret (2002); Saleela Ruwanpura (2004); Natalie Hannan (2004); Jenny Chow (2005); Chelsea Stoikos (2005).

The John Donges Administration Award

The Donges family set up this fund in 2003 in honour of the late Mr John Donges, former Treasurer of Prince Henry's Institute. Each year, a member of Administration is rewarded for their professionalism, courtesy, confidence, accuracy and timeliness. Claudette Thiedemen received the award for 2004.

Kadir-Fatimah Award

The Kadir Fatimah Fund was set up by Khalid bin Abdul Kadir, who studied for his Doctorate of Philosophy at the Institute 1980-1982. On his departure, he kindly made a donation to start the Fund in honour of his parents, which awards Research Assistants for technical excellence. The 2004 recipient was Maria Hernandez.

Prince Henry's Hospital Memorial Scholarship Fund

This perpetual fund was established from the Estate of the late Alex Ogilvy who was a past Member and Chairman of the Board. The fund is a memorial to the service provided by Prince Henry's Hospital to the people of Victoria for more than 100 years. Donations are invited to this Fund so that the income from the permanently invested capital will provide urgently needed funds to support postgraduate students.

The Hudson Hoagland Fund

Dr Robert Searls, past Chairman of the Board of the Institute, established this fund some years ago as a memorial to his friend, Hudson Hoagland, co-founder of the Worcester Foundation for Experimental Biology, Shrewsbury, Mass. USA. Each year, we invite an eminent scientist from overseas or select a promising younger scientist from the Institute to be the Hudson Hoagland Fellow. Income generated by the Fund enables travel from or to an overseas institution, which fosters links and promotes scientific interchange.

Volunteer Support

Prince Henry's Institute would like to thank the following people and organisations for volunteering their professional services to the Institute:

David Pisker, Tribal DDB
Heath Rudduck, Tribal DDB
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Livia Montalto, DDB Rapp Collins
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Darrell Tiemens, Royce
Alicia Kegele, Vic Super
Fiona Van Der Poel, Vic Super
Keith Nathan, Phillips Fox

Community Support & Donations

Donations to special appeals provide Prince Henry's with physical facilities such as buildings and major items of equipment, all necessary for research work. Prince Henry's Institute particularly pays tribute to the individuals, Trustees and Directors of the following Trusts, Foundations and Corporations for their generous response to our requests for assistance:

Corporate Donations

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Members of Prince Henry's Institute contribute to the ongoing wellbeing of the Institute by providing links with the community, with business and with government. We value their advice, their personal generosity, their leadership and direction.

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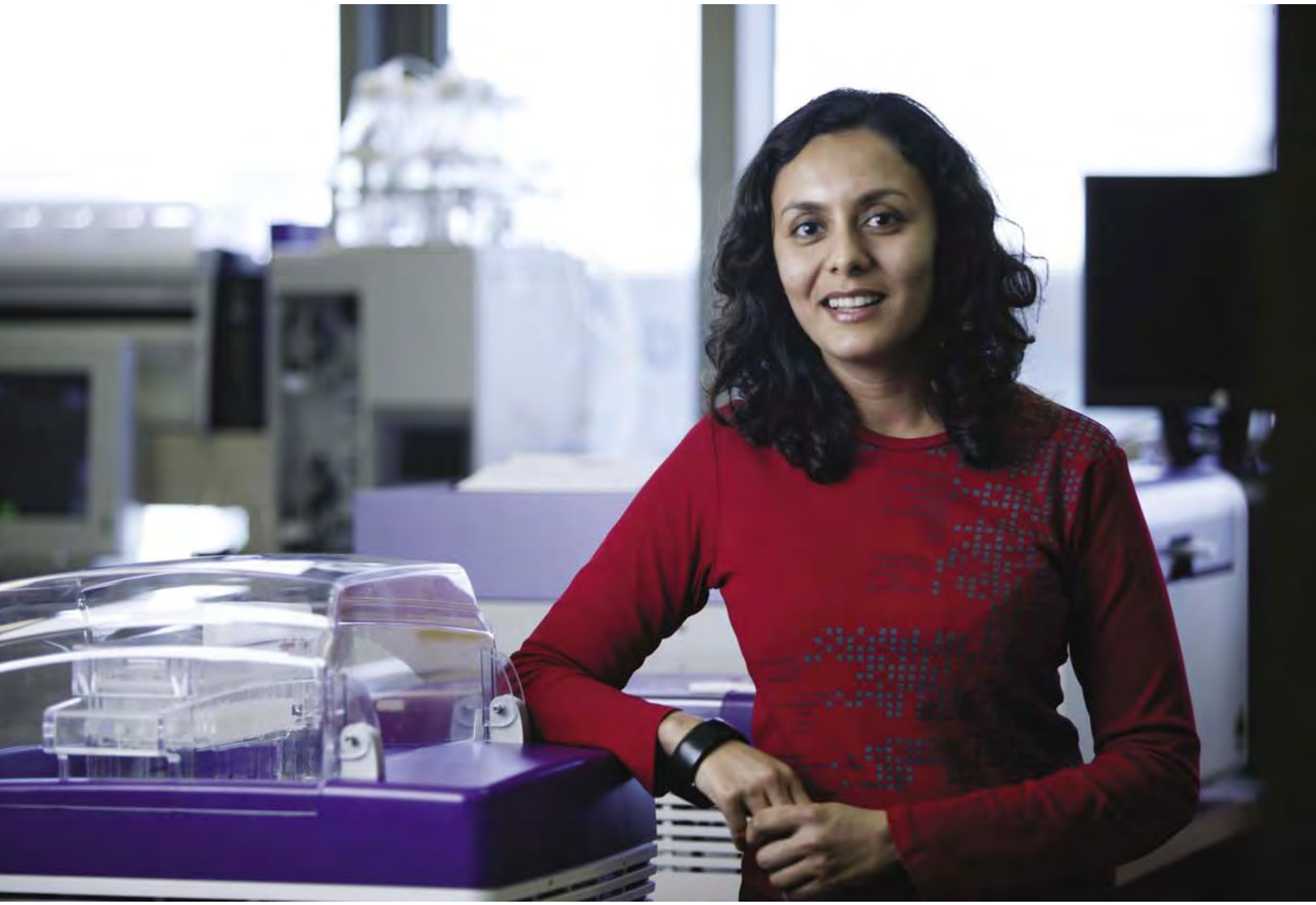
Your support inspires our research



Our achievements are made possible only by the continuing generosity of our supporters

Our pursuit for excellence in medical research continues to attract significant research grants from Australian & overseas organisations.

Your donations, however big or small, contribute to the upgrading of technology, the education of our

Photo: Ashwini Chand, PhD student, Reproductive Hormones

students, and to the investigation of hormones in health and disease. Our staff and students greatly appreciate and acknowledge your support.

Donations

Individual donations to the Institute contribute to much needed funding for research. Donations over $2 are tax deductible.

Bequests

A Bequest is a simple way to support medical research beyond your lifetime.

When considering including Prince Henry's Institute in your Will, we recommend that you seek professional advice from a solicitor, accountant or other consultant with respect to taxation and financial matters.

Our staff will be happy to discuss your Bequest with you. A conventional bequest could be worded as follows:

"I give to Prince Henry's Institute of Medical Research….. [insert the sum of money, percentage of estate or description of property]….. free of State and Federal duties and declare that the receipt of the Director, or other proper officer of the Institute, shall be a full discharge to my Executors for this bequest."

Named Funds

Investing in a Named Fund is a special way to acknowledge a friend or loved one. This can be either a single gift or installments from a capital donation.
A capital donation generates income through permanently invested funds. These funds are applied according to the wishes of the donor/s. Some of our named funds form fellowships, scholarships & awards.

Corporate Support

Corporate support can involve funding research, scholarships or fellowships, sponsoring equipment or events, or offering professional services.

Celebration Gift

Celebrate birthdays, weddings & anniversaries by donating a monetary gift on behalf of friends or family.

Memorial Gift

Sending a monetary gift in memory of a friend or loved one is a unique and thoughtful way to donate to the Institute.

For more information please contact:
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Prince Henry's Institute
PO Box 5152
Clayton VIC 3168
Ph: (03) 9594 4372
Fax: (03) 9594 6125
Email:
andrew.mccallum@princehenrys.org

Photo: Ashwini Chand, PhD student, Reproductive Hormones

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Ramsay Fellow Damien Keating, with daughter Gracie

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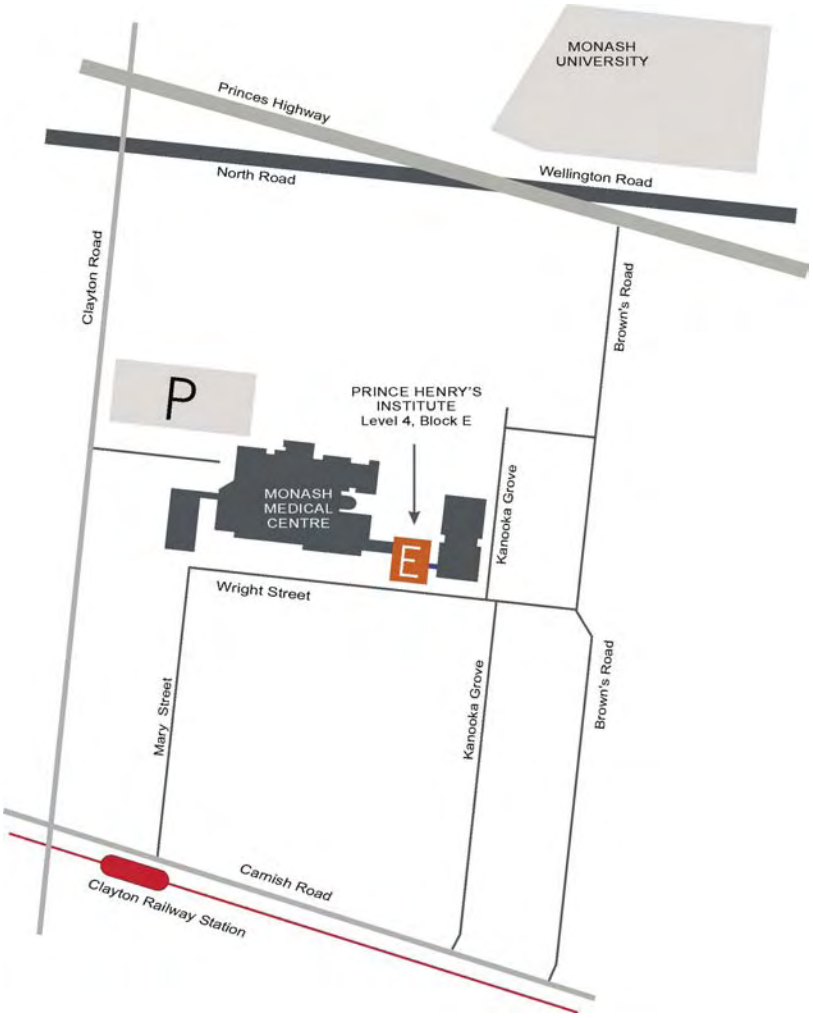

Prince Henry's Institute

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