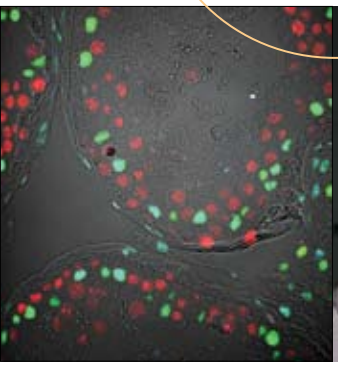

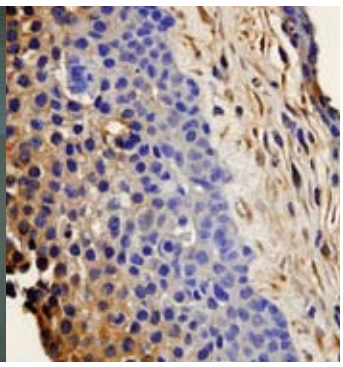
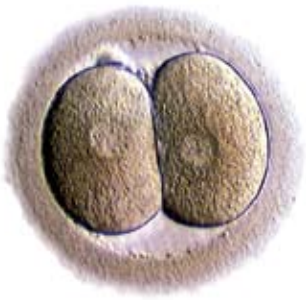
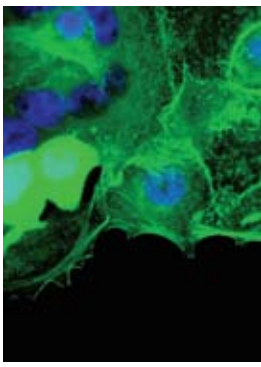

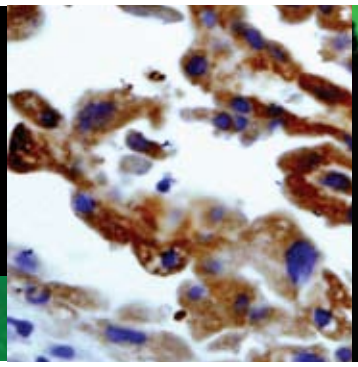
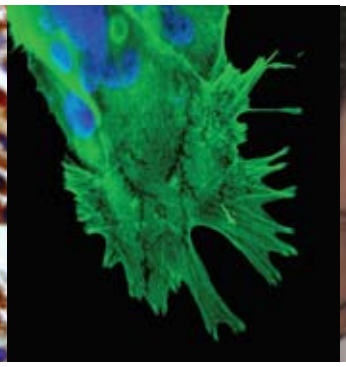

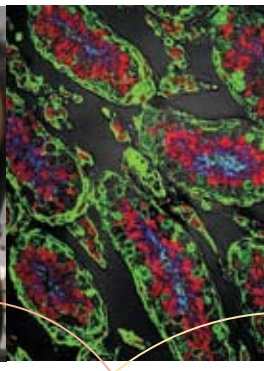

prince henry's institute
2007/08 annual report

phi
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science for better life®

Inside Cover (L- R): Research Officer Dr Ashwini Chand, Endocrine Society Fellow, Dr Izabella Czajka-Oraniec, RD Wright Fellow Dr Colin Clyne, FQRNT Fellow Kristy Brown, Research Officer Dr Kevin Knower and Senior Research Assistant Maria Docanto
Front Cover portraits (top): PHI Director A/Prof Matthew Gillespie; (bottom) PhD Student Gerard Tarulli, Research Assistant Caroline Foo

Annual Report editoral team: David Robertson, Ian Muchamore
Graphic design: Sue Panckridge
Photography: Carla Gottgens

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 Values

- **Quality and integrity** in our research
- **Empathy** for those we help
- **Leadership and excellence**

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

phi
prince henry's institute
science for better life®

Prince Henry's Institute is world renowned for its research into reproductive health and endocrinology, the study of hormones.

For nearly 50 years, the Institute has maintained a reputation for excellence through its first class, internationally competitive research and clinical programs.

Established in 1960 as the Medical Research Centre at Prince Henry's Hospital in South Melbourne, PHI is now an independent Institute based at Monash Medical Centre in Clayton, Melbourne, Australia.

Prince Henry's Institute is:

- an accredited institute of the National Health and Medical Research Council of Australia
- a World Health Organisation Collaborating Centre for Research in Human Reproduction, one of only 10 organisations worldwide and the only Australian organisation with this designation
- an affiliated institute of Southern Health
- an affiliated institute of Monash University
- a partner of the Monash Health Research Precinct
- a member of the Cancer Council of Victoria
- a member of the Victorian Breast Cancer Research Consortium Inc
- an alliance partner with the Ovarian Cancer Research Foundation

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

contents

research highlights 2007/08

PHI researchers are committed to improving the quality of life through the development of disease prevention, early detection tests, diagnostic methods and treatments. In 2007/08 PHI researchers have:

Determining the action of immune cells in bone
- identified that immune cell products regulate bone turnover

New roles for chemokines in embryo implantation
- showed that factors important for leukocyte trafficking are also important for trophoblast migration and act in part by altering the way the trophoblast changes its adhesion as it moves

Proteases and implantation
- showed that only one of a large family of proteases is regulated in the endometrium as it prepares for implantation

Discovering a new role for interleukin 11 in pregnancy
- showed that interleukin 11 can increase trophoblast cell migration as they invade the womb to form the placenta, which has important implications for understanding placental development

Professor Lois Salamonsen, NHMRC Principal Research Fellow and head of the Uterine Biology Group

Understanding the mechanisms of menstruation
- showed that activin A is important for restoration of the endometrium following menstrual breakdown

Defining the proteome of human endometrium
- identified previously unknown proteins that appear as the endometrium becomes receptive for embryo implantation

Understanding the hormone changes in the menopausal transition
- proposed a new classification system for menstrual cycles in the menopausal transition based on changes in serum hormone profiles

Treating abnormal uterine bleeding
- in animal studies, showed that one of the effective treatments for abnormal uterine bleeding in women using implantable progestin-only contraceptives, acts by inducing very rapid repair of the endometrium

Identifying targets for female contraceptives
- showed that a new inhibitor against leukaemia inhibitory factor blocks implantation in mice and thus has potential as a contraceptive for women

Understanding the links between ageing, obesity and breast cancer
- uncovered the mechanisms whereby obesity and ageing increase the risk of breast cancer

Possible drugs for breast cancer therapy
- identified lead compounds which inhibit LRH-1 action and proliferation of breast cancer cells

Preventing menopause-induced obesity
- identified the mechanism of action of Tibolone, a drug used in hormone replacement therapy, to prevent menopause-induced obesity

Understanding Metabolic Syndrome
- developed tissue-specific aromatase 'knock-in' mice to study the role of sex hormones in Metabolic Syndrome

Identifying markers for the detection of ovarian cancer
- developed new methodologies for identifying very low levels of cancer specific proteins in blood

Granulosa cell tumours of the ovary
- identified a role for tyrosine kinases in the pathogenesis of granulosa cell tumours of the ovary and thereby identifying the potential of tyrosine kinase inhibitors as treatment for these tumours

Uncovering the mechanisms of ovarian tumour formation and progression
- demonstrated that loss of betaglycan in ovarian granulosa cells may contribute to the pathogenesis of ovarian granulosa cell cancer

Issues in the management of thyroid cancer
- developed guidelines for the management of thyroid cancer in Southern Health and the characterisation of the strengths and weakness of the thyroglobulin assay used in the follow-up of thyroid cancer

Regulation of the fertility hormone, follicle stimulating hormone
- clarified the mechanisms by which the reproductive hormone, inhibin regulates FSH secretion

Regulation of Sertoli cell junctions
- showed that Sertoli cell tight junctions are hormonally regulated *in vivo*, which is important for understanding male contraception

Androgen-regulated testicular proteins
- used new proteomic technologies to find androgen-regulated proteins in the testis

Discovering a new regulator of foetal Leydig cell/testis development
- demonstrated that the betaglycan gene was essential for proper foetal testis development and endocrine cell function in the foetal testis

Revealing new contraceptive targets in men
- used transcriptional profiling to explore the regulation of genes expressed during spermatogenesis

Developing new technologies to identify markers of male fertility
- applied proteomic technologies to find plasma markers of testicular function, with potential clinical usefulness

Testosterone therapy in older obese men
- examined the role of testosterone therapy in obese older men including its effect on body composition, cardiovascular risk markers and quality of life

Understanding male gender identity
- discovered a genetic link between the androgen receptor and male gender identity

Understanding the functions of sex-determining genes
- identified that SRY has a non-transcriptional function, inhibiting the pro-ovarian factor, β-catenin

Discovery of a new sex-determining gene
- identified FGFR2 as a gene which can lead to sex reversal in mice

Understanding mineralocorticoid receptor signalling
- identified mineralocorticoid receptor signalling in macrophages as an important step in the development of cardiovascular disease

Understanding how high blood pressure develops
- showed that aldosterone signalling in macrophages is a novel mechanism for the development of high blood pressure and cardiac failure

Fundamental mechanisms in cardiovascular disease
- reported interactions of the mineralocorticoid receptor that discriminate between cortisol and aldosterone

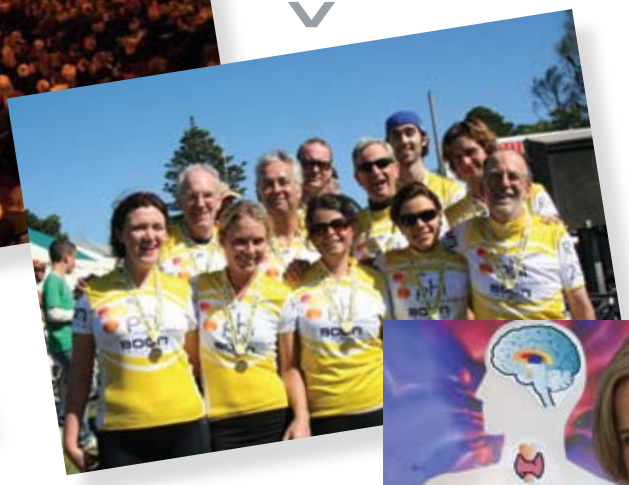
Discovering a key protein in kidney development
- demonstrated that the betaglycan gene was essential for proper nephron formation in foetal kidneys

Professor Rob McLachlan, NHMRC Principal Research Fellow and head of the Male Reproductive Endocrinology and Metabolism Group

phi in the community

From Figaro to Phantom, Melbourne Town Hall

Ride for Reproduction (L-R): Natalie Hannan, Matthew Gillespie, Kathryn Backholer, Vince Harley, Simeon Airey, Michelle Pruyer, Andrew McCallum, Morag Young, Brett Fisher, Peter Wilson, Bruce Watson



Sarah Meachem, Tall Poppy

PHI researchers take an active role in the community, explaining our research and its importance, and engaging with the wider community on the areas where research impacts health and public policy.

Community Support

In January 2008, 120 PHI supporters attended a tennis day as part of the Kooyong Classic Tournament which was sponsored by Davies Collison Cave.

This year a team of 12 PHI cyclists completed a 520 km ride from Echuca to Port Fairy: the annual Murray to Moyne Cycle Relay attracts 1600 cyclists representing over 150 organisations. The PHI team, with support from sponsors and individual donors raised money to support our research into reproductive health and fertility.

In June 2008 over 800 ticket holders attended a gala Prince Henry's Institute concert at Melbourne Town Hall. The event raised public awareness and support for ovarian cancer research. The concert was presented in conjunction with the Rotary Club of Moonee Valley and the Ovarian Cancer Research Foundation. Australian group Pot-Pourri sang popular songs from opera and musical theatre.

Supporting Future Scientists

PHI researchers have a long tradition in promoting medical research as a career in association with the Australian Society for Medical Research (ASMR) which represents Australian health and medical researchers. In June 2008 young PHI scientists Davina Rosairo, Dr Jyotsna Pippal and Dr Ellen Menkhorst hit the highways to talk to students in the ASMR Regional tour of Victorian schools.

Senior Research Officer Dr Sarah Meachem was a recipient of a 2007 Victorian Tall Poppy Award. This is part of a national campaign which promotes greater appreciation of science and medical research.

Media Profile

The media profile of the institute has increased significantly. In the last year more than 1 in 4 PHI researchers have worked with the media to bring health and science stories to life.

Clinical Research Fellow, Dr Carolyn Allan (right) interviewed on Sunrise, Channel 7

L-R: Senior Research Officer Dr Katie Meehan, Mrs Julie Burke, Dr David Burke and Mrs Berwyn Jarrett

Jordan O'Brien, Bendigo Senior Secondary School science teacher and Dr Ellen Menkhorst, Research Officer, PHI

photo: Andrew Perryman, BENDIGO WEEKLY

November 2007 saw nationwide media coverage of the findings from PHI research demonstrating how testosterone supplements in older men can reduce weight gain and potentially lower the risk of heart attack. Dr Carolyn Allan was interviewed on the breakfast television show 'Sunrise'.

Researchers are regularly called upon to provide media comment. PHI experts were asked to comment on media stories about hormone replacement therapy, new developments in IVF, ovarian cancer, endometriosis, male fertility and sex determination.

Early career researchers Tu'uhevaha Kaitu'u-Lino and Louisa Ludbrook were both selected to participate in the prestigious Fresh Scientists scheme. The personalised media training and support they received as part of this program helped create extensive national and international coverage of their work.

Engagement

In November 2007, PHI hosted events celebrating Research Australia's "Thank You" Day, acknowledging Australian medical research achievements. PHI hosted its own "Thank You" Day card, receiving messages of support from the community and VIPs. Many who signed the card had been personally touched by diseases such as breast cancer where PHI researchers are highly active.

PHI can trace its family history back almost 50 years. Over the year we were delighted to welcome members of the family of the late Bill Burke who was Senior Surgeon at Prince Henry's Hospital and a key figure in the establishment of the Medical Research Centre at Prince Henry's Hospital. The memory of Bill's vision lives on through a fellowship to fund a senior researcher at PHI.

chairman's report

The appointment of Matthew Gillespie as the Institute's Director at the beginning of April this year has undoubtedly been the most significant event. Matthew has moved to Prince Henry's after 20 years at St Vincent's Institute, with the last nine years as Associate Director of that Institute. He is an eminent international scientist in the area of bone biology and his work on the role of parathyroid hormone-related protein in breast cancer and its local action in bone is relevant to other breast cancer research being conducted at Prince Henry's. A number of Matthew's research group have moved with him and this cross fertilisation will further enhance the Institute's reputation as an international centre for research excellence, particularly in the role that hormones can play in cancers of the male and female reproductive systems.

Another matter of significance in terms of future direction is the move towards restructuring the Institute as a corporate entity limited by guarantee. To date the Institute has operated under the terms of a Victorian State Charter and as such has been governed under similar regulations to other State enterprises. These regulations have not always been relevant to the operation and governance of a medical research institute and the Victorian Government has encouraged Prince Henry's to pursue an alternative structure. This follows similar moves by other research bodies in the State. The current timetable will see the completion of this restructure before calendar year end.

The Institute has continued to evolve during the past year, with several events helping to reshape the direction of PHI.

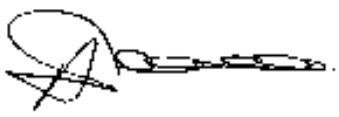
The research activities of the Institute have continued to make good progress and with external funding support through the Ovarian Cancer Research Foundation we are getting tantalisingly close to an effective early detection test for ovarian cancer. A detailed report on progress across the various research activities at Prince Henry's is covered in the body of this report.

The Institute's Board of Management has lost two of its members with resignations during the year from Mrs Ann Ellis and Mr David Pisker. We much appreciated their contributions to Institute governance. Mr Terry Haining, the long serving Financial Services Manager and Board Secretary, has also retired during the year and his role has been taken up by Peter Murray. Terry played an important part in the Institute's administration and his contribution to both the Institute and its Board was highly regarded.

I would also like to take this opportunity to acknowledge the passing of Dr Robert Searls a former Chairman of Prince Henry's, and a long time personal friend.

It will be evident from the obituary in this report that he was a major supporter of the Institute over many years; a man of considerable warmth and integrity who will be greatly missed by all who knew him.

In concluding I would like to acknowledge all those who have supported the Institute during the past year, whether through financial contributions or through giving of their time to the running of Prince Henry's. We will continue to depend on the generous support of members and friends and I encourage those who value the contribution that medical research makes to society to give generously to the important work being conducted at the Institute.



John Robinson
Chairman

director's report

As we approach our fiftieth anniversary, the Institute is in a very strong position to continue its excellence.

The development of anyone's career always has significant milestones – in science it is usually the first scientific presentation, first publication, graduation of your first trainee and I am delighted to add to my personal list as being appointed as Director of Prince Henry's Institute.

The Institute is internationally renowned with an established and proud history in reproductive health, hormone action, sex determination, cancer, obesity and cardiovascular disease. As we approach our fiftieth anniversary, the Institute is in a very strong position to continue its excellence. Integral to its future is the enhancement of our co-operative relationship with our precinct partners of Southern Health and Monash University, particularly through the Clinical School and Monash Institute's of Health. The attainment of a precinct for interactive, developmental and clinical translational research is paramount in the vision of all three parties to ensure a world-class research facility and best health care to Victorians. I am pleased to be working with Ms Shelly Park, CEO of Southern Health, and Professor Steve Wesselingh, Dean of the Faculty of Medicine, Nursing and Health Sciences Monash University, along with Professor John Funder, Director of Research Strategy Southern Health, to realise this strategy.

This year, PHI has been active in community engagement, individual recognition, grant success and training of future scientists all of which are highlighted throughout this annual report.

There have been many personal recognitions and awards made to PHI staff, but I would like to highlight the achievements of a few.

Jock Findlay was appointed an Officer of the Order of Australia in recognition of his achievements in medical research. Along with this award, Jock was also elected to the Board of Directors of the Society for the Study of Reproduction USA, the first non-US person elected to the Board. Sarah Meacham was a recipient of the Victorian Tall Poppy Award, which recognises the achievements of outstanding young investigators. David Robertson, Chen Chen and Guiying Nie were successful in their NHMRC Fellowship renewal or appointments. Training of future scientists was supported by NHMRC Post-graduate Fellowships to Karla Hutt and Amand Sferruzzi-Perri, an NHMRC Training Fellowship to Tu'uhe Kaitu'u-Lino and an NHMRC Post-graduate Scholarship to Jun Yang.

Success of the Institute can also be measured by the awarding of competitive grant funding. Notably, the NHMRC flagship funding award of a Program Grant of $11,822,329 was awarded to Lois Salamonsen, John Aitken, Jock Findlay, Rob McLachlan, David Robertson and Evan Simpson.

Additionally, the endeavours of the research at the Institute were well recognised through Project Grant support; Wah Chin Boon and Malcolm Horne ($595,500); Peter Fuller and Ann Drummond ($552,750); Craig Harrison and David Robertson ($300,000); Evan Simpson, Kristy Brown and Kerry McInnes ($320,000); Morag Young, Colin Clyne, Peter Fuller and Donald McDonald ($470,363). I am assured that funding success through the NHMRC and other agencies will continue.

I would like to thank the Board for their support, and their vote of confidence in me to take stewardship of the Institute into the future.

I am delighted to extend to you this annual report of Prince Henry's Institute, and am indebted to David Robertson, Sue Panckridge, Ian Muchamore and Peter Fuller for its development.

Matthew Gillespie
Director

institute governance

Mr John Robinson
BSc MGSc FAuslmm

Chairman

Chairman, Global Mining Investment Ltd; Monash Health Research Precinct Ltd

Non Executive Director, Perseverance Corporation Ltd; Boom Logistics; PSI Ltd

Mr Richard Amos
BA (Soc/Legal) BA (PR)

Deputy Chairman

Managing Director, Royce Communications

A/Professor Matthew Gillespie
BSc (Hons) PhD

Director (from 1/04/2008)

Ms Carmel Mortell
B Bus ICA EMBA

Partner, KPMG

Treasurer

Mrs Jane Bell
BEc LLB LLM (Lon) FAICD

Treasury Solicitor, Coles Group Ltd

Ms Jay Bonnington
BCom MBA FAICD FCPA

Non Executive Director, St. John of God Healthcare Group, SE Water Ltd, Agriculture Services Victoria and over a portfolio of both government and non-government boards

Mrs Margaret Lothian
BEc LLB (Hons)

Principal Mediator and Senior Member of the Victorian Civil and Administrative Tribunal

Mr Trevor Montgomery
SIPA

Former Senior Investment Advisor, Goldman Sachs JB Were

Professor Nicos Nicola
AO BSc (Hons) PhD

Deputy Director, Walter and Eliza Hall Institute of Medical Research

NHMRC Nominee

Mr Bob Stensholt MP,
BA BD (Hons) MIntLaw Dip Phil

State Member for Burwood

State Minister for Health Nominee

A/Professor Wayne Ramsey
AM CSC MBBS MHA FRACMA

Southern Health Nominee

Executive Director, Medical Services, Southern Health

Company Secretary

Mr Terrence Haining
FCPA GDipAcc&Fin

Financial Services Manager, PHI
Secretary (until 6/12/2007)

Mr Peter Murray
BSc (Econ) FCA

Financial Services Manager, PHI
Secretary (from 6/12/2007)

Retired

Mrs Ann Ellis Dip Ed
(until 6/12/2007)

Dr Jane Glatz
BSc (Hons) PhD MBA

Chief Operating Officer/ Acting CEO, PHI
(until 30/3/2008)

Mr David Pisker
Dip Film Making

Marketing Director, Betfair
(until 6/12/2007)

I, John Robinson, Chair of the Board, certify that Prince Henry's Institute of Medical Research is developing risk management processes consistent with the Australian/New Zealand Risk Management Standard and an internal control system to enable the executive to understand, manage and satisfactorily control risk exposures. The Finance and Audit Committee verifies this assurance and confirms it has been working with management through regular meetings to develop the risk profile of Prince Henry's Institute of Medical Research and to identify and engage resources to enable this profile to be supported by the development of risk management processes.

vale

Bob Searls

Dr Robert J. Searls, AM, LLD, DFC
Born 11th July 1922, died 14th June 2008

Robert (Bob) Searls was an American mining engineer who was born in San Francisco, California, USA and who settled in Melbourne, Australia in 1964. He was an outstanding man - a man of courage, a man of integrity, a community builder, a man intolerant of injustice, generous, supportive and dynamic.

Married a few days short of his 20th birthday, to Ethel Green (known to all as Pixie), he joined the US 15th Strategic Air Force on the Italian Adriatic coast shortly afterwards and served until the end of the war. He flew 50 combat missions in P51 fighters and was awarded the Distinguished Flying Cross, the DFC. He then began his professional career in mining, attending Cornell University to study civil engineering. In May 1957, Bob was diagnosed with thyroid cancer, was treated by radical surgery which was followed by complications for which he required ongoing management. The family moved to the east coast of the USA where Bob joined the Newmont Mining Corporation as an office engineer in 1957. Because of problems of commuting and other considerations, he left the United States and arrived in Melbourne in June 1964. He founded and was a former Chairman of Newmont Holdings which became Newcrest Mining Ltd after 1991. He was also a director of several mining companies and international banks before his retirement in 1985.

Bob had been a Trustee of the Worcester Foundation for Experimental Biology in Worcester, Massachusetts, USA, from 1960 – 1974 and through his connections there got to know the late Professor Bryan Hudson. The latter persuaded Bob to join the Board of the Prince Henry's Hospital Medical Research Centre in 1974 and he became Board Chairman in 1987. He oversaw the incorporation of the Medical Research Centre which was renamed Prince Henry's Institute of Medical Research in 1990. He continued to Chair the Board until 1993 and served for a further two years before retiring in 1995. He was also a member of the Board of Prince Henry's Hospital for 3 years.

His contributions to the Research Centre and to Prince Henry's Institute were recognised by the awards of an Honorary Doctorate of Law, Monash University, in 1992 and Membership of the Order of Australia in 1996.

Bob was an inspirational Chair of the Board who led from the front and by example. His annual Chairman's statements were a revelation in their originality, aptness, conciseness and exhortation to the reader to support the Institute. He was extremely highly regarded by the scientists whom he in turn held in very high regard.

In recognition of his admiration for Hudson Hoagland, a founder of the Worcester Foundation, Bob established a fellowship which enabled the Institute to bring distinguished scientists to Melbourne to lecture and hold research discussions.

Bob attracted several other members to the Board of the Institute including its present Chair, John Robinson.

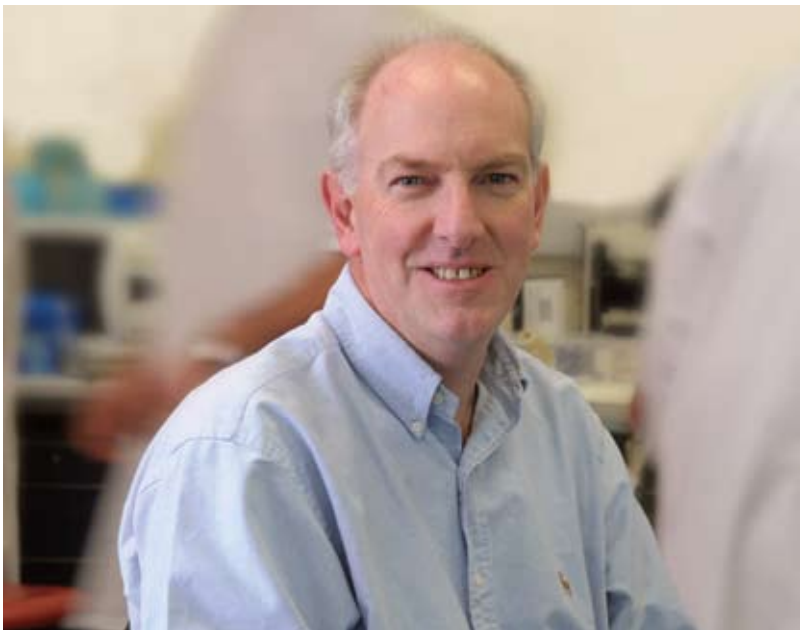
Bob is survived by his wife Pixie, their three children, Jamo, Jesse and Daisy and their families, and by two sisters who live in the United States, Helen and Joyce.

Bob was an inspirational Chair of the Board who led from the front and by example.

research profile

Matthew Gillespie

In December 2007, the Board of Prince Henry's Institute of Medical Research appointed Matthew Gillespie as its fourth Director taking up the appointment in April 2008.



Associate Professor Matthew Gillespie, Director and Group Head, Bone Joint & Cancer

Matthew is a past Monash University graduate, and it was in microbiology that he became fascinated by the prospects of medical research. He undertook Honours and PhD studies under the direction of Professor Ron Skurray within the Department of Microbiology determining how *Staphylococcus aureus* (so called "Golden Staph") acquired resistance to so many antimicrobial agents. This was a period, inspired by genetics and recombinant DNA technology, which provided a strong fundamental laboratory practice for his future.

After obtaining his PhD, his first post doctoral position was with Nick Deacon and Ian McKenzie at the Centre for Cancer and Transplantation at The University of Melbourne. This was an enriching environment and saw his transition from the simple bacteria to multicellular organisms. Like many successful places, the staff and graduate students of that time are now leaders in immunology, cancer biology or commercialisation.

He then joined Professor Jack Martin's group at the Repatriation General Hospital Heidelberg, and subsequently at St. Vincent's Institute of Medical Research when the entire team moved in 1989. This was a period of interest and diversification, examining the cellular communication within bone, how cancers establish and grow in bone, and exploring the interactions of the immune system with the skeleton. These areas remain at the forefront of his research today.

During his post doctoral years, Matthew transitioned through the NHMRC training award and fellowship levels and took leadership roles in the Australian Society for Medical Research (ASMR), the Cancer Council and in the NHMRC on its Research Committee. Matthew has always been committed to develop health and medical research in Australia and will willingly attest to his interest in science and its management for the future; this is reflected in his roles in many funding organisations, professional societies and journals.

Matthew as a past President of ASMR joins John Funder and Jock Findlay at PHI, also past Presidents, as well as Sarah Meachem who will be President of this peak professional society next year. This underlies the commitment that PHI has to fostering Australian medical research.

Finally, PHI welcome's Matthew along with his colleagues to establish a new group at the Institute.

bone, joint & cancer

Our research seeks to identify the pathways that are required to build bone and limit bone destruction.

Our skeleton provides a structural support for our bodies and as a source of nutrients for the blood and immune system. Bone diseases such as osteoporosis, arthritis and most cancers of bone all result in a reduction in bone mass, that can lead to fractures. We seek to identify the pathways that are required to build bone and/or limit bone destruction, and how the cells in the bone microenvironment communicate with each other. Ultimately, we aim to identify new factors or ways to promote bone formation.

Communication between the cells of bone

The internal structure of our skeleton constantly changes as a result of the applied stresses and strains. Extensive bone communication is required between the cells that detect these changes with the cells that destroy (osteoclasts) and rebuild (osteoblasts) bone. The only known therapy that can reliably increase the amount of bone is daily injections of parathyroid hormone (PTH), an expensive treatment.

We are working on new approaches to treatments that build bone. By investigating pathways of PTH action, we have identified new PTH targets and we are investigating their potential in the treatment of osteoporosis.

We have also determined that there is considerable overlap between the skeleton and immune cell function.

Photos: (clockwise from top) Senior Research Officer Vicky Kartsogiannis; PhD students Vanessa Cheung and Ally Chau; Senior Research Officers Steve Bouralexis and Julian Quinn

In particular, many of the cytokines and growth factors required for immune cell differentiation modulate bone formation or bone destruction. This has led to the emergence of a new field of "osteoimmunology" that recognises this pivotal interaction, and aims to determine the interdependence and interrelationships between the immune system and the skeleton.

Cancer

One of the focus areas of the Bone, Joint and Cancer Unit is the spread of primary cancers to other sites in the body that results in secondary cancer.

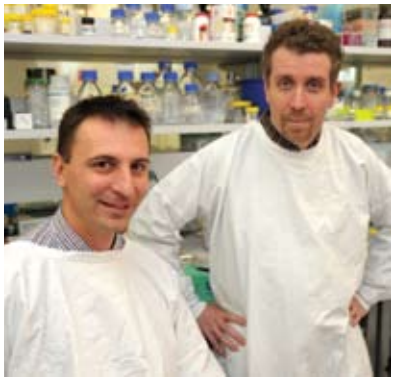
This process, known as metastasis, is a serious and unfortunately common complication of many cancers including breast cancer, which often spreads to bone. We have shown that a protein called osteoprotegerin inhibits the process of bone breakdown. Osteoprotegerin is commonly expressed by the bone forming cells, and we provided some of the first evidence that it is also produced by a number of cancers.

We explored the consequences of regulating osteoprotegerin levels in breast cancers and determined that this factor can regulate tumour growth both in bone and in the breast. This identified a new role for this protein and indicated that high levels of osteoprotegerin in a tumour might be a poor prognostic indicator for patients. We are now determining how this protein affects tumour growth and whether we can counteract its activity.

STAFF

Bone, Joint and Cancer

Steve Bouralexis
Ally Chau
Vanessa Cheung
Matthew Gillespie
Vicky Kartsogiannis
Julian Quinn
Hasnawati Saleh
Melissa Solano



morphogenesis & metastasis

Kaye Stenvers

The regulatory pathways governing cell movement that are utilised during metastasis also shape the testis and ovary during foetal life.

Dr Kaye Stenvers, Senior Research Officer, Female Reproductive Biology Group

Most deaths by cancer are a result of metastasis, or the spread of cancer by malignant cells moving away from the primary tumour site to distant parts of the body.

Understanding how these cells migrate to and invade new sites is essential for early detection, prevention, and treatment of metastasis. One family of multi-functional growth factors, the Transforming Growth Factor-β (TGFβ) family, has been shown to be involved in several aspects of tumour progression. A particular focus of our group is a protein called betaglycan which facilitates the actions of several of these growth factors.

We are pursuing two major lines of investigation in order to understand how betaglycan controls cell migration. The first approach uses human ovarian cancer cells and clinical samples.

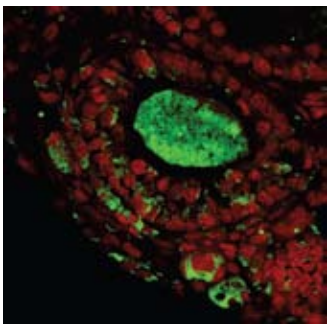


Image: Cross section of an ovary fluorescently stained; red depicting the nuclei and green the cytoplasm. The basic unit of the ovary the follicle, consists of an oocyte (large green structure) surrounded by cuboidal granulosa cells and flattened theca cells.

We have shown that betaglycan is lost from the surface of malignant ovarian cells and that this loss results in cancer cells which exhibit increased motility and invasion.

Reintroduction of betaglycan to cancer cells prevents their spread and may have therapeutic benefits. In order to fully understand the role of betaglycan during cancer progression and metastasis, which represent periods of abnormal cellular growth and migration, we are also studying what this protein does during normal growth, i.e. during gonadal development. By studying gonadal development in tissues depleted of betaglycan, we have shown that betaglycan is essential for the proper formation of the urogenital system, including the ovary, testis and kidney.

Our current work is revealing the detailed mechanisms underlying betaglycan's actions in normal and cancerous cells in order to establish the clinical importance of betaglycan in human reproductive health and to develop therapeutic strategies based on this key protein.

Since joining PHI in 2005, Dr Stenvers' research has focused on the development and functioning of the urogenital system. She has a particular interest in how problems in foetal development impact upon health in adulthood.

female reproductive biology

Our work aims to contribute to the understanding of female reproductive biology and to develop novel contraceptive methods and treatments for infertility and ovarian cancers.

To better understand infertility in women, we are investigating the ovary and the impact of hormones and other secreted factors on ovarian function.

The primary functions of the ovary are to produce eggs (housed within structures called follicles) and hormones, predominantly the sex steroids oestrogen and progesterone and the protein hormone inhibin. Factors produced by the pituitary gland and the ovary are necessary to trigger the growth and development of follicles that culminate in ovulation.

There are a number of processes that impact on fertility in women. For example, the extent to which the ovary successfully develops during the foetal and neonatal time periods is a major determinant of the capacity for reproduction in adulthood. Premature ovarian failure occurs in about 1 in 100 women under the age of 40 leading to reduced reproductive lifespan, and is thought to be due to the poor proliferation or survival of immature eggs during ovarian development.

In addition, folliculogenesis, which is the series of stages a follicle undergoes in the adult ovary in order to produce a mature egg, fails in 10 to 20% of all women, disrupting the generation of viable oocytes. Given the importance of ovarian development and folliculogenesis to ovarian health and function, the focus of our laboratory is to determine the factors which govern these processes.

Hormones produced by the pituitary play important roles in regulating the growth of ovarian follicles and the release of oocytes from the follicles at ovulation. Despite this knowledge, little is known about the factors and mechanisms operating within the ovary that determine how many follicles will form, or which of these will be recruited into the growth phase, or finally which follicles will be selected to ovulate. Understanding these mechanisms are key to identifying new targets for contraceptive development and may also provide insights into premature menopause.

Only by understanding normal ovarian growth and its regulation can we begin to address and treat ovarian disorders.

STAFF

Female Reproductive Biology

Maree Bilandzic
Marissa Bowden
Hui Kheng Chua
Ann Drummond
Ruth Escalona
Paul Farnworth
Jock Findlay
Patty Ho
Ileana Kuyznierewicz
Jason Liew
Davina Rosairo
Mai Sarraj
Kaye Stenvers
Alexandra Umbers
Kenneth Walker
Yao Wang

Above: Dr Mai Sarraj, TM Ramsay Fellow

Left: (L - R) Research Assistant Ruth Escalona, PhD student Jason Liew and Dr Maree Bilandzic. Drs Bilandzic and Sarraj are postdoctoral researchers within the group, working on uncovering the roles of betaglycan in reproductive development and health.

critical requirements for embryo implantation

Guiying Nie

In order to produce a healthy baby, a healthy uterus is required in which the developing embryo can grow. First, the embryo needs to implant into the uterus without being rejected or harming the mother, then a functional placenta must develop to support the embryo.

Dr Guiying Nie, Senior Research Fellow, Uterine Biology Group

A master switch important for implantation

Our research has identified that proprotein convertase 6 (PC6), an important "master switch" responsible for activating other proteins, is tightly controlled in the uterus during its preparation for receptivity and is critical for implantation.

Preventing the production of PC6 in mice causes complete failure of implantation, while blocking PC6 function in human cells inhibits the equivalent critical step for implantation. What makes this discovery more important is that PC6 also plays a critical role in HIV infection through activation of HIV envelope proteins. This makes PC6 an exciting target for preventing pregnancy and HIV infection at the same time.

Our current projects are addressing the following important questions: What is the role of PC6 in making the uterus receptive to embryo implantation?
Can PC6 be used as a diagnostic biomarker for uterine receptivity?
Can PC6 be targeted for the development of a highly effective dual-role female contraceptive that can simultaneously prevent pregnancy and HIV infection?

Discovery of a protein critical for a healthy placenta

Our group has discovered a new factor (HtrA3) which is produced at high levels in the uterus during placental development in mice and humans. We have subsequently shown that HtrA3 is critical for the placenta to function properly - female mice lacking this factor can't produce normal-sized babies.

We are investigating the following questions: What is the role of uterine HtrA3 in making a functional placenta? Can HtrA3 be used as a diagnostic biomarker for early detection of placental malformation and/or malfunction?

Guiying Nie trained as a molecular biologist and biochemist, and received her PhD in 1991 from University of Essex, UK. Dr Nie joined Prince Henry's Institute in 1995 and embarked on research in reproduction in the field of embryo implantation and placental development.
Dr Nie has a strong interest in investigating how the uterus contributes to the success or failure of embryo implantation and placental development.
She was awarded a prestigious NHMRC Senior Research Fellowship in 2007.

implantation research

Scientists at PHI are unlocking the mysteries of early pregnancy by discovering how the uterus implants an embryo to ensure a healthy start to life.

After fertilisation, the embryo must implant into the uterus, the "fertile soil", for further growth; no embryo can survive without implantation.

During most of a woman's monthly cycle, the uterus is hostile to an embryo and implantation will not occur. For successful implantation, the uterus must prepare itself to be receptive; this preparation is crucial as an ill-prepared uterus will reject the embryo. Such implantation failure is a major cause of early pregnancy loss and female infertility: 30% of pregnancies end in spontaneous abortion.

On the other hand, making the uterus non-receptive provides an exciting strategy to stop implantation and thus pregnancy for the development of new contraceptives.

Following implantation, a functional placenta must develop to supply all the nutrients needed by the foetus; the wellbeing of the placenta determines the wellbeing of the foetus.

In addition, the wellbeing of the placenta also determines the wellbeing of the mother during pregnancy. Malformation and malfunction of the placenta is the root causes of a number of pregnancy related disorders, including pre-eclampsia and intra-uterine growth restriction.

How the uterus prepares to be receptive for implantation and how it works to make a healthy placenta is not well understood. We are using a number of strategies to address the following questions:

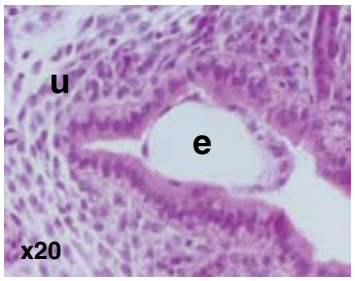
- What makes the uterus receptive for embryo implantation to occur?
- How does the uterus regulate the development of a functional placenta?
- How to translate these research outcomes into clinically useful discoveries?

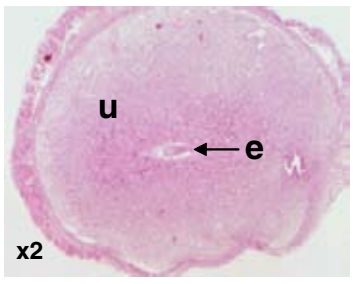
STAFF

Uterine Biology

Neil Borg
Eva Dimitriadis
Natalie Hannan
Judi Hocking
Belinda Hardman
Sophea Heng
Lynette Kilpatrick
Ying Li
Ellen Menkhorst
Guiying Nie
Premila Paiva
Michelle Puryer
Lois Salamonsen
Chelsea Stoikos
Joanne Yap
Jin Zhang

Images: embryo (e) implantation in the uterus (u) at day 4.5 (top) and day 5.5 (below)





Above (L-R): Dr Ellen Menkhorst, Dr Belinda Hardman and Dr Neil Borg, Research Officers, Uterine Biology Group

critical factors for establishing pregnancy

Eva Dimitriadis

There is a growing need for new contraception options for women and our goal is to develop new non-hormonal contraceptives.

Dr Eva Dimitriadis, Senior Research Officer, Uterine Biology Group

My research focuses on the molecular changes in the womb that are critical for establishing pregnancy.

The receptivity of the womb (uterus) to the embryo is critical for establishing pregnancy, and normal development of the placenta is the key to maintaining a healthy pregnancy.

One goal of our research is to identify markers of infertility in women. Our work has shown for the first time that two small regulatory molecules or cytokines, interleukin IL-11 and leukaemia inhibitory factor are important in the earliest stages of implantation, they are also needed later for regulating trophoblast invasion into the uterine lining in women.

These cytokines may be used to identify women who may miscarry early and provide useful markers for a receptive womb to be used during infertility treatments and IVF.

There is also a growing need for new contraception options for women and our goal is to develop new non-hormonal contraceptives.

We are testing some novel inhibitors of leukaemia inhibitory factor and interleukin IL-11 which are critical for implantation in mice. We have now shown that these inhibitors are fully effective at preventing the establishment of pregnancy in mice.

Mice treated with the inhibitor resembles a non-pregnant uterus, while mice not treated with the inhibitor shows that embryo implantation has occurred.

We are currently trialling long acting inhibitors in mice and testing whether they can be administered in a vaginal gel. One exciting possibility is that new non-hormonal contraceptives could be combined with microbicides for women at high risk of sexually transmitted infections, including HIV.

Dr Dimitriadis obtained her PhD in 1997 from Trinity College Dublin, Ireland and joined PHI in 1999. Her research focuses on determining the role of critical uterine factors that lead to infertility and the development of a healthy placenta. Another main focus is the development of new contraceptives that also stop sexually transmitted diseases.

placental research

By understanding how the placenta develops, scientists at PHI hope to improve treatments for pregnancy-related disorders.

Embryo implantation into a receptive endometrium leads to a functional placenta and is critical to human fertility, a successful pregnancy and a healthy start to life.

Infertility affects one in ten couples and about 5% of pregnancies are complicated by preeclampsia (PE) which leads to prematurity and low birth weight babies. PE is caused by insufficient placentation and is a major cause of maternal death.

Abnormalities in placentation affect between 15 and 25% of deliveries in Australia and can have a significant impact on the health and wellbeing of mothers and their children.

A large body of research now shows that the birth weight of babies is an important indicator of health in adulthood and that the uterine environment during pregnancy has profound consequences on health of the offspring, with the effects extending into adult life. A healthy start to life is critical for the future of Australia's next generation of young people.

By understanding how the placenta develops, scientists at PHI hope to improve treatments for pregnancy-related disorders and provide strategies to ensure a healthy start to life.

Investigating how the placenta develops

PHI researchers are undertaking a strategic research program aimed at determining the molecular changes in the placenta that are critical for establishing pregnancy.

Once an embryo has attached to the lining of the womb, it must start to invade through this tissue until the placenta is fully formed. This requires close contact of the cells known as trophoblasts (which come from the embryo and eventually form part of the placenta), with the mother's blood supply, from which the developing foetus will obtain nourishment and oxygen.

Invasion of the trophoblast into the womb is very similar to the way white cells travel from the blood into tissues when needed to counter infection. Our work has shown for the first time that two small regulatory molecules or cytokines, which have been known to be important in the earliest stages of implantation, are also needed slightly later for regulating trophoblast invasion into the uterine lining

Other work has shown that some of the molecules, called chemokines, which are needed for white cells to enter tissues, attract trophoblast cells to the surface of the uterine lining, to change their adhesive properties and to promote their movement into the tissue towards the maternal blood vessels.

Identifying new factors needed to establish a healthy placenta

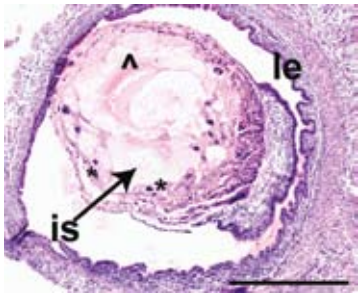
At PHI we are also identifying new factors needed to establish a healthy placenta. Failure to establish a healthy placenta, the organ that delivers oxygen and nutrients to the developing foetus, can lead to miscarriage, pre-eclampsia or impaired growth of the baby in the womb. Even moderately impaired foetal health is associated with a greater risk of contracting diseases in adult life, such as high blood pressure, diabetes, coronary heart disease and obesity. Therefore, a greater understanding of how the placenta is formed is critically important for health, both during infancy and throughout life.

Scientists at PHI have identified a new molecular regulator that appears in the uterus during the very early stages of placental development and is thought to be a novel maternal factor for establishing and maintaining a pregnancy. Research is now focussed on understanding the exact role of this protein in placental development.

STAFF

Uterine Biology

Eva Dimitriadis
Natalie Hannan
Rosemary Keogh
Jaslyn Lee
Ying Li
Ellen Menkhorst
Guiying Nie
Premila Paiva
Michelle Puryer
Lois Salamonsen



Images: (top) Blocking interleukin II signalling in mouse uterus using a novel long acting inhibitor leads to pregnancy failure. Embryo implantation sites at day 10 of pregnancy (top) control treated mice; (bottom) Inhibitor treated mice. e = embryo; l = placental labyrinth; md = maternal decidua; le = luminal epithelium; is = implantation sites containing haemorrhage (^) and giant trophoblast cells (*).

identifying new diagnostic markers of ovarian cancer

Andrew Stephens

Our studies have identified around 100 proteins with potential as diagnostic markers.

Dr Andrew Stephens, Senior Research Officer, Reproductive Hormones Group

Most women with ovarian tumours are diagnosed after the cancer has already metastasised, resulting in one of the highest mortality rates for any of the gynaecological malignancies.

This is because there is no effective way to regularly screen women for early stage disease. A major focus for our research is to identify new biological markers of early stage ovarian cancer from blood, and to develop these for application in the diagnosis, management and treatment of ovarian cancer.

A major challenge in the identification of new cancer markers is their scarcity in blood – typically at least 9 to 12 orders of magnitude lower than other blood proteins. We have developed strategies enabling the analysis of picogram amounts of protein from patient blood samples. Using a combination of affinity chromatography, protein concentration, fluorescent dye labelling techniques and two-dimensional protein separation, we are able to generate protein arrays where up to 2000 blood proteins can be analysed in a single experiment.

Protein array: cancer-specific changes appear as either red (present only in cancer patients) or green (specifically absent from cancer patients).

Cancer-specific changes are then located by comparing arrays from healthy women to those derived from cancer patients. The image below shows an example; cancer-specific changes appear as either red (present only in cancer patients) or green (specifically absent from cancer patients).

We have also established a tissue collection program, where blood and tissue samples are taken at the time of surgery and stored for analysis. Over 200 patients are currently participating in this program.

Thus far our studies have identified around 100 proteins with potential as diagnostic markers. We are now extending our panel of marker proteins using combinations of mass spectrometry and protein labelling technologies. We are also developing a detection system capable of analysing specific combinations of these markers, which will significantly improve the diagnostic accuracy of the marker proteins used.

The ultimate goal of our research is to develop a highly accurate test to detect early stage ovarian cancers, which will contribute significantly to improving patient outcomes.

Dr Stephens joined PHI in 2006, and is the NAB Ovarian Cancer Research Foundation Fellow. He has a keen interest in the application of proteomics technologies to the discovery of disease biomarkers, with a particular emphasis on ovarian cancer and the interaction of ovarian tumours with the immune system.

ovarian cancer research

A major goal of our work is to discover new markers for the early detection of ovarian cancer.

One in 67 women will be diagnosed with ovarian cancer. If the cancer is detected when still confined to the ovary, the five year survival rates are around 90%. However if the diagnosis is made when the cancer has spread to other parts of the body, the five year survival rate is reduced to 30%. Because of its vague symptoms, the disease is very difficult to detect in its early stages. Unfortunately, the majority of women diagnosed with ovarian cancer are already in advanced stages of the disease.
Early detection is the key to surviving ovarian cancer. Unlike breast cancer, there are no screening programs or early detection methods for ovarian cancer, and the five year survival rate for ovarian cancer is much lower than that for breast cancer.

A major goal of our work is to discover new markers for the early detection of ovarian cancer and develop blood tests to detect all types of ovarian cancers in both pre- as well as post-menopausal women.

PHI has set up a state-of-the-art facility, supported by the Ovarian Cancer Research Foundation (OCRF), to detect and identify proteins in blood and tissues. This method is based on the comparison of proteins in blood and ovarian tissue from normal women to those with ovarian cancer. We are seeking proteins that are unique to the cancer that could be used as potential markers for early detection.

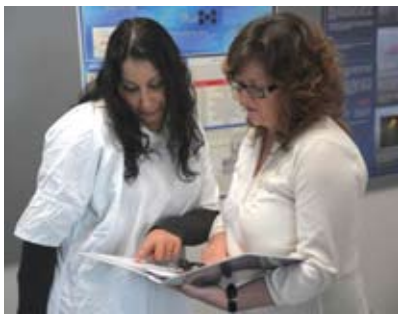
In a complementary approach, we are using a genetic technology, called RNA microarrays, to identify genes that are unique to different types of ovarian cancers and could be used as cancer markers.

Ovarian Health Study

Currently there are no health programs for assessing the health of ovary as there are for the breast and the cervix. The Ovarian Health Study aims to set the parameters for a national health program similar to pap screens for the cervix and mammograms for the breast. This is a collaborative study with Southern Health and Monash University. The study focuses on healthy postmenopausal women who are at increasing risk of developing ovarian cancer. Ovarian health is assessed by a combination of a highly sensitive vaginal ultrasound test and blood tests for ovarian cancer detection including serum inhibin developed by PHI researchers.

Granulosa cell tumours

Granulosa cell tumours account for 5 to 10 per cent of malignant ovarian cancers and they have a unique behaviour requiring specific study. PHI scientists aim to characterise the genes involved in promoting the growth of granulosa cell tumours.



The identification of the changes that cause these tumours will allow the identification of targeted treatments.
PHI is recognised as the leading centre internationally for the study of granulosa cell tumours.

STAFF

Reproductive Hormones

Nicole Fairweather
Samantha Jayasekara
Ming Lee
Enid Pruysers
Adam Rainczuk
David Robertson
Andrew Stephens

Male Reproductive Endocrinology and Metabolism

Peter Stanton

Steroid Receptor Biology

Maria Alexiadis
Sophie Bittinger
Ann Drummond
Peter Fuller
Stacey Jamieson

Above: Witchery Fellow Dr Adam Rainczuk

Left (L-R): MSc Student Davina Rosairo and Senior Research Officer Dr Ann Drummond

a need for new breast cancer therapies

Colin Clyne

We have developed a genetically-modified mouse in which we can manipulate LRH-1 levels specifically in mammary tissue. This will allow us to confirm if the effects we see in cell culture translate to unregulated proliferation and cancer development.

There is an urgent need for new breast cancer therapies. Anti-oestrogen based treatments have been very successful; however not all patients respond to these agents and many of those who do eventually become resistant to therapy. To meet the needs of these underserved women, we are studying a protein related to the oestrogen receptor, known as LRH-1, to determine its potential as a novel target for breast cancer therapy.

We found that LRH-1 protein was present in approximately half of all human breast cancer tissues examined. To understand its effects in these tumours, we produced cell lines in which LRH-1 could be deliberately activated or inhibited. When we activated LRH-1, cells grew more quickly and became more invasive (opposite page, left image); conversely, when LRH-1 was inhibited, we found that cell growth and invasion were markedly reduced (right image).

In an extension of this work, we have developed a genetically-modified mouse in which we can manipulate LRH-1 levels specifically in mammary tissue. This will allow us to confirm if the effects we see in cell culture translate to unregulated proliferation and cancer development in the complex environment of a whole animal.

Based on these encouraging findings, we are working with St Vincent's Institute to identify small molecules that bind to LRH-1 and inhibit its function.

Dr Colin Clyne, NHMRC RD Wright Fellow, Sex Hormone Biology Group

We already have several first-generation compounds and we are currently developing these into more potent and specific analogues. We hope that these molecules will be ready for pre-clinical testing as breast cancer therapeutics within the next 1-2 years.

This work was performed by Kerry Herridge, an honours student, with Dr Ashwini Chand. Our work is funded by the National Breast Cancer Foundation and the Cancer Council of Victoria.

Dr Clyne obtained his PhD in pharmacology from the University of Edinburgh in 1994. Following a postdoctoral position at the University of Texas Southwestern Medical Center in Dallas, he joined PHI in 1998 where his research interests have focused on hormonal aspects of breast cancer. He is currently an NHMRC RD Wright Fellow.

breast cancer research

PHI researchers are working on new treatments for breast cancer by blocking oestrogen within the breast, while still allowing oestrogen action in other important parts of the body, such as the brain and bone.

While the exact cause of breast cancer is unknown, lifetime exposure to the female hormone, oestrogen, is believed to be a major factor in the development of the disease, with 70% of breast cancers being driven by oestrogen.

Current breast cancer treatments work by blocking the action of oestrogen in cells. Newer treatments work by inhibiting the enzyme that produces oestrogen (called aromatase) and thus preventing oestrogen formation. These treatments are helping to improve the quality and length of life in breast cancer sufferers, and are particularly useful in post-menopausal women. However the problem with these inhibitors is that they block aromatase activity elsewhere in the body. Aromatase is important in the brain (particularly for memory), in the liver and in bone for preventing osteoporosis. Our scientists are now identifying factors that uniquely control aromatase production in the breast in an effort to design new, more effective and acceptable breast cancer treatments.

Investigating the role of epigenetics in oestrogen production

Epigenetics describes a trait that is heritable, yet not based upon a change in primary DNA sequence. These epigenetic changes, such as DNA methylation, occur at a higher frequency in cancer than genetic changes, occur at defined regions in a gene, and most importantly are reversible upon treatment with pharmacological agents.

At PHI, we have shown that the aromatase gene may be epigenetically silenced in normal breast tissue, but epigenetically activated in the presence of a breast tumour.

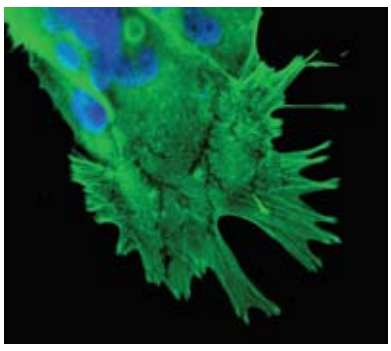
These epigenetic changes reveal an additional layer of regulation of oestrogen synthesis. With the current advances in epigenetic therapeutics, this research will provide additional targets for the treatment of breast cancer.

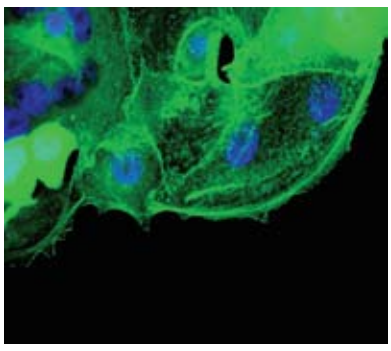
Identifying the link between obesity, aging and breast cancer

Obesity and aging are now recognised to be risk factors for a number of cancers including breast cancer, however the mechanism linking these is unknown. Given the global pandemic of obesity, the prospect that millions more women in their postmenopausal years may contract breast cancer than was previously thought, is very real.

At PHI, we believe that we have discovered the molecular mechanism underlying this causal relationship. Central to this connection is a protein known as LKB1, whose activity we believe to be inhibited in obese as well as ageing individuals.

Microscope images: by activating LRH-1, cells grew more quickly and became more invasive (below); conversely, when LRH-1 was inhibited, we found that cell growth and invasion were markedly reduced (below right).





This protein we have found to inhibit expression of aromatase, the enzyme responsible for oestrogen synthesis in the postmenopausal breast, by stimulating a linkage protein known as AMPK. Thus when LKB1 Is inhibited, as in individuals who are obese and elderly, the net result is that oestrogen formation in the breast is stimulated. Hence the risk of breast cancer is increased. This work suggests that factors which stimulate LKB1 may have therapeutic potential in breast cancer treatment and possibly prevention.

STAFF

Sex Hormone Biology

Kristy Brown
Ashwini Chand
Colin Clyne
Maria Docanto
Nick Fleming
Kerrie Herridge
Kevin Knower
Nirukshi Samarageewa
Evan Simpson
Sarah To

tight junctions & male contraception

Peter Stanton

A focus of our research at PHI has been to study the hormonal regulation of sperm production, termed spermatogenesis, in order to understand how hormonal contraception in men ('the male pill') prevents sperm production.

We have found that the boundaries between cells, or cell junctions, are an important site of hormone action. Tight junctions are a special type of cell junction responsible for providing a seal between adjacent Sertoli cells in the testis, which isolates the special compartment where sperm cells develop from the normal circulation. In animal models and men lacking tight junctions, spermatogenesis ceases, hence these junctions play a vital role.

Sperm production is controlled by the pituitary hormones follicle-stimulating hormone (FSH) and luteinising hormone (LH), with the latter responsible for testosterone production. Male hormonal contraception reduces the amounts of these hormones in the circulation, causing major decreases in sperm production. Our focus has been to find out how FSH and testosterone control tight junctions and their component proteins.

The photomicrograph (facing page, left) shows spermatogenesis in a rodent with normal FSH and testosterone, with tight junctions shown in blue and Sertoli cell nuclei in red. Importantly, the tight junctions are able to prevent a tracer molecule (green) from entering the part of the tubule where sperm are formed, as shown by the black space in the middle of the tubules.

We now know that the boundaries between cells, or cell junctions, are an important site of hormone action. In animal models and men lacking these tight junctions, spermatogenesis ceases, hence these junctions play a vital role.

Dr Peter Stanton, Senior Research Officer, Male Reproductive Endocrinology & Metabolism Group

In animals with low FSH and testosterone (facing page, right), the organisation of the tight junctions proteins (blue) is lost and the green tracer is seen around most cells, showing that tight junctions are no longer working. These photos prove that tight junctions are controlled by FSH and testosterone in rodents. Our current work is examining whether hormonal contraception in men controls tight junctions in a similar manner.

This work formed part of PhD projects recently completed by Gerard Tarulli and Mark McCabe, supervised by Dr Stanton and Dr Meachem.

Dr Stanton joined PHI in 1994, and has been actively researching molecular mechanisms of hormonal male contraception, with a special interest in cell junctions.

male reproductive biology

Scientists at PHI are researching the causes of male infertility in order to discover new treatments and to find strategies to optimise fertility in men.

Investigating the process of sperm production

Scientists at PHI are investigating the complex process of sperm development to better understand the hormonal and genetic factors involved in male fertility. We have identified different, important points in the sperm development pathway for further research.

We are researching how the earliest sperm cells (the spermatogonia) develop, since these cells fail to grow in some infertile men and are particularly prone to damage during cancer treatments. Research is underway to identify the molecules important for the survival of these cells with the aim of finding treatments to stimulate their growth when needed.

As sperm grow, they lie between special nurse cells called Sertoli cells. We research various aspects of Sertoli cell development and function, since problems in Sertoli cells can lead to male infertility. One aspect is the special junctions between Sertoli cells that allow the cells to communicate.
We are studying whether these junctions are affected in infertility and identifying the regulatory factors.

The release of mature sperm from Sertoli cells is vital for the production of large numbers of healthy sperm. This process of sperm release may be a problem in some forms of male infertility; in a significant proportion of men there is an absence of sperm in the semen, yet some sperm are present in the testis. Our current studies are focussed on discovering the molecules involved in sperm release so that we may be able to stimulate this process in order to treat some forms of infertility.

We are also searching for special proteins in the blood that could be used to diagnose different types of infertility by a simple blood test, rather than requiring a biopsy of the testis.

An infertility database

In collaboration with Monash IVF, PHI is working to identify genes that control sperm production and are responsible for poor sperm quality. Patients in affiliated fertility practices are invited to contribute DNA (via a blood sample) along with information about their medical history, physical examination findings, semen quality and hormone levels.

This database is one of the largest in the world for research into the common problem of male infertility.

DNA has also been collected from the children of infertile men who have been conceived by ICSI-assisted IVF, where instead of the egg and sperm fertilising naturally, a sperm is directly injected into each egg. The study of this DNA provides scientists with an insight into which forms of infertility might be inherited and which genes are the cause.

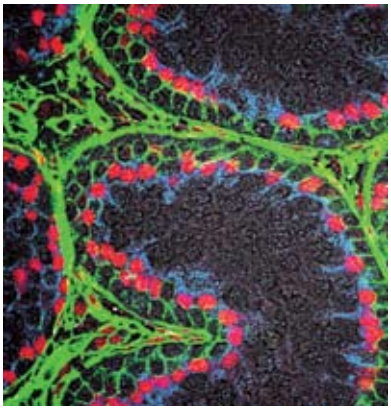
STAFF

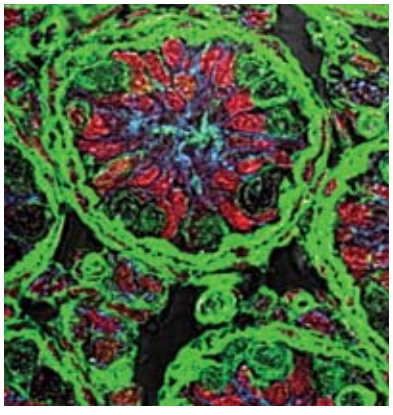
Male Reproductive Endocrinology and Metabolism

Georgia Balourdos
Marina Bashir
Caroline Foo
Mark McCabe
Robert McLachlan
Sarah Meachem
Peter Nicholls
Liza O'Donnell
Kyri Pratis
Ann Reilly
Saleela Ruwanpura
Courtney Simpson
Pavel Sluka
Peter Stanton
Saw Eng Tan
Gerard Tarulli

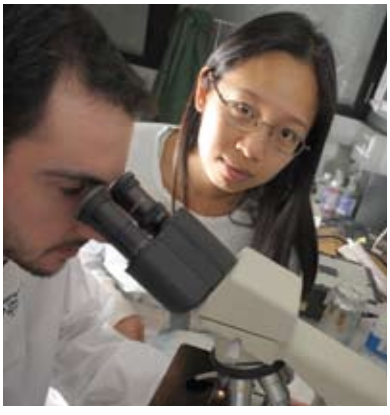
Reproductive Hormones

Ming Lee
David Robertson
Andrew Stephens





Photomicrographs: spermatogenesis



PhD student Gerard Tarulli and Research Assistant Caroline Foo

the endocrinology of inhibin A and B

Craig Harrison

Can a greater understanding of the biology of the hormones, inhibin A and inhibin B, lead to the development of therapeutics to treat reproductive disorders, cancer and osteoporosis?

Since 1999 my research has focussed on understanding the mechanism of action of the reproductive hormones, inhibin A and inhibin B. These hormones play essential roles in mammalian reproduction based on their ability to suppress follicle stimulating hormone (FSH) secretion by the pituitary and sperm and egg production in the gonads. Recent data has also shown that inhibins act as tumour suppressors in reproductive tissues and play important roles in bone remodelling.

I have been fortunate to spend the last 8 years working at the two premier inhibin research centres in the world (PHI in Melbourne and the Salk Institute in California).

During this time, I have been involved in studies that have determined:

- how inhibins are synthesised and secreted by granulosa cells of the ovary and Sertoli cells of the testis.
- that betaglycan, a cell surface receptor, is essential for inhibin activity (see figure, facing page).
- that a naturally occurring mutation of the inhibin gene may cause premature ovarian failure.
- that inhibin A and inhibin B likely play important roles outside reproductive tissues.

The major tools we utilise in our research include:

- site-directed mutagenesis, in which a mutation is created at a defined site in the inhibin molecule.
- bioassays, to monitor the effects of mutations on inhibin A and inhibin B function.
- immunoassays, to monitor the effects of mutations on inhibin A and inhibin B expression.
- immunohistochemistry, to determine which cells/tissues express inhibin receptors and are, therefore, potential target sites for inhibin action.

Identifying the structural elements that mediate the biological activities of inhibin A and B have enabled us to design drugs that may prove effective for modulating fertility, decreasing bone loss and treating certain reproductive cancers.

Dr Harrison joined PHI in 1999 as a TM Ramsay Fellow and continued his postdoctoral training at The Salk Institute. He returned to PHI in 2004 to continue his research and now heads the TGFβ Research Unit. In 2007 he was awarded a NHMRC RD Wright Fellowship.

L - R: Dr Craig Harrison, Peter Nicholls, Courtney Simpson, Karen Chan, Rebecca Crook and Dr Kelly Walton

reproductive hormones

By studying the mechanisms of action of inhibin and activin, our scientists hope to identify new treatment strategies for a range of human conditions.

Investigating inhibin in reproduction

The hormone inhibin plays a key role in the regulation of follicle stimulating hormone (FSH), produced from the pituitary in the brain, which in turn controls sperm production in the testis and egg production in the ovary. When FSH secretion is elevated, the ovary compensates by producing more inhibin. This reduces the secretion of FSH and stabilises its circulating levels, ensuring that only one egg ovulates at a time.

Knowledge about inhibin and how it regulates FSH has a direct impact on natural reproductive processes, including the menopause transition. It is also significant in the treatment of conditions such as premature ovarian failure and infertility. The role of inhibin in the male, while important, is less clearly understood.

Our current research focuses on two circulating forms of inhibins, inhibin A and B, which are believed to have different functions in the body. Inhibin B is found only in the male circulation and in the early stages of follicle and egg development in the ovary in women. Inhibin A, on the other hand, is produced by the dominant follicle in the ovary that is destined to ovulate.

Because of these differing functions, scientists are studying both inhibin forms separately. We have shown that human inhibin A and B differ in their bioactivity and receptor binding properties. Specifically, inhibin A binds to an accessory binding protein called betaglycan to mediate its biological response.

Inhibin B on the other hand uses another, as yet unknown, mechanism which we are currently exploring.

An understanding of the mechanisms involved in inhibin A and B actions will enhance the management/monitoring of reproductive disorders and possibly identify biomarkers with improved sensitivity and specificity.

Researching 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 with premature ovarian failure stop ovulating, their menstrual cycles cease and they experience menopausal-related symptoms of infertility, as well as an increased risk of cardiovascular disease and osteoporosis.

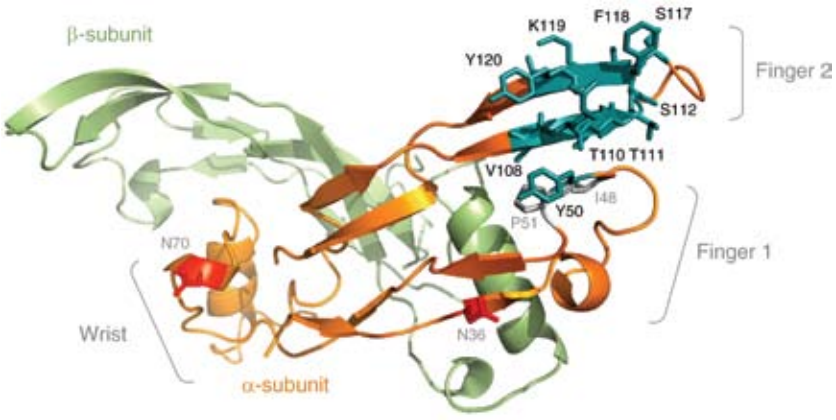
Scientists at Prince Henry's are investigating the possibility that a mutated, less active form of inhibin is present in some women with premature ovarian failure. Because the hormone is less active, it is believed the ovarian supply of eggs diminishes earlier in life, resulting in premature menopause. We hope to gain a better understanding of the cause of this disorder and identify new treatment strategies.

STAFF

Reproductive Hormones

Karen Chan
Jenny Chen
Rebecca Crook
Craig Harrison
Yogeshwar Makanji
Katie Meehan
Peter Nicholls
Irene Papageorgio
Enid Pruysers
David Robertson
Debra Romero
Kelly Walton

Model of inhibin A. The inhibin α-subunit is coloured orange while the inhibin β-subunit is green. Residues that play a role in binding to the co-receptor, betaglycan, are coloured cyan.



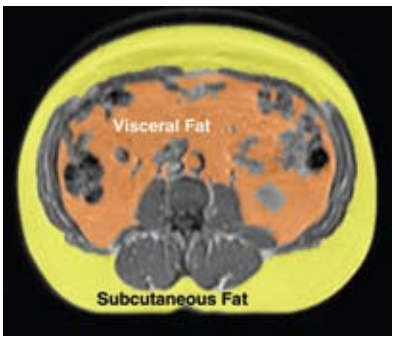
testosterone, obesity & the ageing male

Carolyn Allan

Testosterone, obesity and the ageing male: a conundrum of causality

Testosterone levels decline as a function of age in men beyond the age of 40 years. The ageing male also experiences an increase in body fat and although these two observations have been correlated, causality remains uncertain. Furthermore, the rate and extent of the decline in serum testosterone varies amongst men and is influenced by a number of factors. Increasingly it is recognised that one of the most important determinants of testosterone in the ageing male is obesity.

As part of my research, the effect of obesity on testosterone levels was studied in a group of 223 men aged 55 years and older who were selected because they had symptoms which may be associated with low testosterone levels (loss of energy, fatigue, poor concentration and low libido). Overall, men who were obese were twice as likely to have low testosterone levels as their healthy weight counterparts. The question remains, however, does obesity cause a decline in serum testosterone or do low testosterone levels lead to increasing body fat?



Above: Magnetic Resonance Imaging (MRI): fat deposition in the abdomen

One of the most important determinants of testosterone in the ageing male is obesity.

In order to examine this question in more detail, 62 of the men with low testosterone levels were treated with either a testosterone or a placebo (inactive) skin patch for 12-months. These men were in good physical health and were not overweight. Using computer assisted analysis of Magnetic Resonance Imaging (MRI) studies, the volume of fat in the abdomen at baseline and 12-months was calculated (see MRI image).

By increasing testosterone back to levels typically seen in young men it was possible to prevent these older men gaining intra-abdominal (visceral) fat; it is this type of fat that is linked to diabetes and heart disease.

Our group is now repeating these studies in obese ageing men and comparing the effects of testosterone therapy to those of diet and exercise on body fat and markers of cardiovascular risk such as glucose, insulin and cholesterol. It is hoped that studies such as ours will help to determine the role of testosterone treatment in older men.

Dr Carolyn Allan, Clinical Research Fellow, Male Reproductive Endocrinology and Metabolism Group

Carolyn Allan is an endocrinologist and post-doctoral research fellow who joined PHI in 2000.

hormones & ageing

We are investigating the hormonal changes that occur as men and women age and studying their impact on various health issues in order to help develop strategies to improve the health and wellbeing of ageing people.

Testosterone therapy in ageing men

Although men do not undergo a true "menopause", a form of hormone-replacement therapy (testosterone therapy) is used in some older men to alleviate symptoms associated with ageing.

The use of testosterone therapy remains a controversial issue however, so researchers at PHI are investigating the changes in testosterone levels experienced by some men as they age, and the role played by testosterone therapy. PHI researchers have studied the effects of testosterone treatment on a group of older men who showed a range of symptoms of testosterone deficiency, including tiredness, poor concentration and reduced sex drive. An interesting finding from this study was that administering testosterone to these men for a year prevented the increase in intra-abdominal fat often seen in ageing men (refer to facing page). A number of risk factors for heart disease also showed improvement with this treatment.

We have now commenced a clinical trial examining the effects of testosterone therapy on body fat and markers of heart disease in obese, middle-aged men, as well as studying how lifestyle modification and weight loss affects testosterone production in these men. Finally, our scientists are also working with industrial partners in the development of a new formulation of testosterone that is hoped to be more effective and convenient than existing treatments for testosterone-deficient men. This product is shortly to enter Phase III trials in an international, multi-centre study. They are also participating in studies examining patient response to a new long acting injectable form of testosterone therapy that is available in Australia.

Studies on the menopause transition

The menopause literally means the very last period in a woman's life, and it typically affects women between 45 and 55 years of age. Symptoms of the menopause include hot flushes, low libido and loss of memory.

PHI is involved in several collaborative studies aiming to fully describe the hormonal changes that occur as women age and pass through the menopause. Our researchers are measuring various hormones in women as they approach menopause and during the menopause transition so that we can understand:

– What are the characteristics of menstrual cycle as the menopause approaches?

– What are the cyclic hormonal changes occurring in women before and during the menopause?

– What are the relationships between various hormones and other health measures such as joint, cardiovascular and cognitive function?

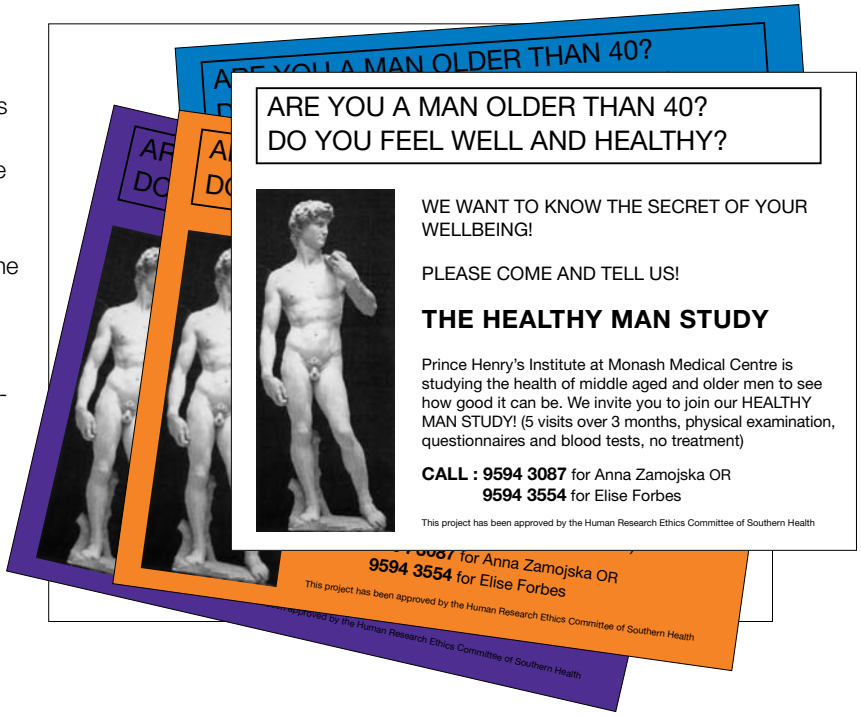
STAFF

Reproductive Hormones

Henry Burger
Enid Pruysers
David Robertson

Male Reproductive Endocrinology and Metabolism groups

Carolyn Allan
Jonathan Cohen
Elise Forbes
Amy Herlihy
Abigail Lewis
Kati Matthiesson
Robert McLachlan
Anna Zamojska



metabolic effects of androgens in women

Anne Corbould

Does androgen excess contribute to insulin resistance in women?

Increased levels of the androgen ('male' hormone), testosterone cause acne and hirsutism in women. Our research has focussed on the question of whether increased levels of androgens in women could also have implications for the risk of metabolic disorders, especially type 2 diabetes. This is an important question because androgen excess is a common problem in women: in reproductive-aged women, polycystic ovary syndrome (PCOS) is the most frequent cause of increased testosterone levels. In addition, we now recognise that obese adolescent girls have significantly elevated circulating testosterone levels in early puberty, and at the other end of the reproductive spectrum, many postmenopausal women, especially those with metabolic syndrome and type 2 diabetes, also have higher-than-normal testosterone levels.

A key abnormality underlying the development of metabolic syndrome and type 2 diabetes is insulin resistance i.e. impaired ability of insulin to stimulate uptake of glucose from the blood stream into skeletal muscle and fat (adipose) tissue. We treated adipose cells of women with testosterone and found that testosterone caused these cells to become insulin resistant. This effect of testosterone was reversed by treating the cells with an androgen receptor antagonist i.e. a drug that blocks androgen action.

Androgen excess is a common problem in women: in reproductive-aged women, polycystic ovary syndrome (PCOS) is the most frequent cause of increased testosterone levels.

Dr Anne Corbould, Clinical Research Fellow, Sex Hormones Biology Group

These preliminary results suggest that increased androgen levels in women may represent a modifiable risk factor for metabolic syndrome/type 2 diabetes. We are currently investigating the mechanisms for this effect of androgens on insulin-mediated glucose metabolism in adipose cells of women.

Anne Corbould is a physician-scientist who joined PHI in 2003 and combines basic laboratory research at PHI with clinical endocrinology at Launceston General Hospital and Monash Medical Centre.

obesity research

PHI researchers are studying hormones in the brain that regulate appetite and metabolism as well as hormones involved in fat accumulation in the body.

Hormones are an important factor in regulating body weight; for example, they control appetite and influence fat deposition in the body. By gaining a better understanding of how these hormones work, we hope to develop treatments for obesity.

The role of oestrogen in obesity and the Metabolic Syndrome

The term, Metabolic Syndrome, is used when a person suffers from obesity, particularly excess fat around the stomach, as well as a combination of other conditions such as insulin resistance, high blood pressure or high cholesterol. People with Metabolic Syndrome are at an increased risk of suffering from various serious conditions including heart disease, stroke, hypertension, type 2 diabetes and kidney failure.

Lack of physical activity, poor diet and a subsequent increase in obesity has resulted in a significant rise in the incidence of the Metabolic Syndrome. This common condition has been estimated to affect 20-30 per cent of the middle-aged population. There is an important, but not yet fully understood, relationship between oestrogen and the development of these conditions. Scientists at PHI are using the ArKO mouse, which is unable to produce oestrogen, in an ongoing series of studies investigating the mechanisms by which oestrogen contributes to maintaining the body's balance of fat tissue, sensitivity to insulin and a healthy heart. We have found that ArKO mice, particularly males, become obese and insulin resistant (see figure).

They also develop fatty liver and cardiovascular and cerebrovascular problems. We have also previously shown that men who are incapable of producing oestrogen, due to a natural mutation, also develop similar problems to the ArKO mice.
This work suggests that oestrogens may be able to prevent the Metabolic Syndrome in both males and females. These studies will give us a better understanding of how oestrogen therapy could best be used in a preventative role.

Metabolic Syndrome and its associated conditions

Researchers at PHI have discovered a potential role for the human gene SOX13 in type 1 diabetes. The SOX13 gene is produced in the developing embryo, particularly in cells that become the insulin-producing beta cells of the pancreas.

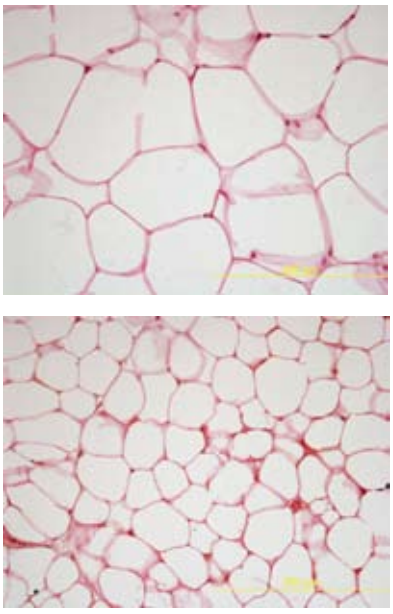
Our studies have shown that SOX13 turns on other genes when it is in the nucleus of the beta cell. Scientists have observed high levels of insulin in those cells containing SOX13 in the nucleus. SOX13 has also been found to form a complex with the SOX9 gene, improving its action. This is important, because humans and mice lacking SOX9 develop diabetes.

Research at PHI is aimed at dissecting the molecular mechanisms by which these two SOX proteins affect insulin production in order to better understand the development of type 1 diabetes.

STAFF

Sex Hormone Biology

Wah Chin Boon
Kristy Brown
Jenny Chow
Anne Corbould
Izabella Czajka-Oraniec
Nirukshi Samarageewa
Michelle Van Sinderen
Evan Simpson
Kenneth Walker



Images: Adipose tissue from Aromatase Knockout mouse (top) and Wild-type mouse (bottom)

the role of mineralocorticoids in heart disease

Morag Young

Mineralocorticoids are steroid hormones normally associated with regulating fluid balance within the body but more recently they have been shown to play an important role in heart function.

To determine the specific cells in the cardiovascular system where mineralocorticoid receptor activation is important for the development of heart disease, we developed a mouse with the mineralocorticoid receptor (MR) specifically deleted from inflammatory cells (monocytes/macrophages). These mice were then used in a model of heart failure to determine if they developed heart disease and hypertension in the same way as normal mice. Surprisingly, they were not only protected from the tissue remodelling processes that lead to fibrosis and heart failure but they were also protected from hypertension. These studies have revealed a novel role for inflammatory cells in the control of blood pressure and a critical role in the development of heart disease. These studies were undertaken with PhD student Amanda Rickard.

The role of high salt intake in models of MR-induced heart failure has remained unanswered for sometime. However, in a second series of studies with PhD student Emily Lam we have shown that specific genes are switched on in the heart by mineralocorticoid hormones when combined with high salt.

Dr Morag Young, Senior Research Officer, Steroid Receptor Biology Group

We have shown that specific genes are switched on in the heart by mineralocorticoid hormones when combined with high salt.

Ongoing studies are investigating the molecular mechanisms whereby high salt changes the way the MR responds to hormone activation.

These studies are designed to identify mechanisms needed to develop tissue-specific drugs, for heart failure and hypertensive heart disease, that provide cardiovascular protection but allow normal MR function in other tissues.

Dr Morag Young is a Senior Research Officer who joined PHI in 2002. Morag has played an active role in the promotion of the importance of medical research to the community, including this year, the challenging role of convenor of Victorian Medical Research Week.

cardiovascular research

Hormones play a key role in the cardiovascular system and in cardiac disease.

Hormones regulate various aspects of the cardiovascular system including the control of blood pressure. High blood pressure, or hypertension, increases the risk of heart disease and stroke. Hormones also act within the heart to regulate the muscle cells and keep the heart functioning normally.

Steroid hormones that control blood pressure

The body's ability to handle salt (sodium chloride) is one of the critical determinants of blood pressure control. The most important factor in the control of salt balance is the adrenal steroid hormone, aldosterone. Steroid hormones communicate with cells through intracellular receptors; for aldosterone, the mineralocorticoid receptor (MR). PHI researchers have identified:
- critical structural differences that distinguish the MR from other steroid receptors
- a novel interaction within the receptor that may enable the MR to distinguish closely related steroids, a proposal that may be exploited for the design of new drugs
- interacting proteins for the MR which will enable cell specific factors to be identified.

Steroid hormones that cause cardiac fibrosis

High levels of aldosterone are a risk factor for cardiovascular disease; drugs that block the MR are a promising treatment for heart failure. Scientists at PHI are investigating the role of aldosterone in the development of cardiac fibrosis, or stiffening of the heart tissue.

Our scientists have pioneered the use of a mouse model of cardiac fibrosis and showed that blocking the MR not only prevents cardiac fibrosis and vascular damage, but can also reverse this process. These beneficial effects also occur in the kidney. Continuing studies in this area aim to better understand the mechanism by which activation of the MR can result in severe cardiac fibrosis.

We hope our studies will aid in the development of future pharmacological interventions and more specific treatments for cardiac fibrosis, heart failure and hypertensive kidney disease.

Peptide hormones and cardiac disease

In the search for treatments for chronic heart failure, scientists at PHI have been exploring the role of the hormone ghrelin in cardiac disease. Ghrelin is produced in the stomach and plays an important role in the heart and heart muscle cells contain high concentrations of a specific receptor for ghrelin.

Our scientists, in a collaborative study, showed that ghrelin's synthetic analogues (called GHRPs) can improve cardiac function and protect heart muscle cells from cell death in a chronic heart failure model. In addition to this protective effect, they have found that GHRPs also reduce cardiac fibrosis.

STAFF

Steroid Receptor Biology

Francine Brennan
Irene Cheung
Peter Fuller
John Funder
Emily Lam
James Morgan
Jyotsna Pippal
Amanda Rickard
Jun Yang
Yishou (Vicki) Yao
Morag Young

Endocrine Cell Biology

Chen Chen
Ruyi Liu
Jyothsna Rao
Qiang Sun
Ernesto Vargas
Kun Wang
Seung-Kwon (Sean) Yang
Yufeng Zhao

Senior Research Officer Dr Morag Young with Group Head Professor Peter Fuller

fgfr2, a new DSD gene

Stefan Bagheri-Fam

One focus of our research is the identification of new genes that cause human Disorders of Sex Development (DSDs) using mouse models.

DSDs, which include conditions such as children born with ambiguous genitalia, occur in approximately four percent of all newborns of which 80% still remain genetically unexplained. The identification of new DSD genes will lead to improved clinical diagnosis of this socially traumatic condition. Identifying the genes responsible for the DSDs will also improve our understanding of the molecular genetic regulatory networks at play during the development of the testis and ovary.

The phenotypic sex (male or female) of an individual is determined in the foetal gonad which has the exceptional feature that it can differentiate into one of two distinct organs, an ovary or a testis.

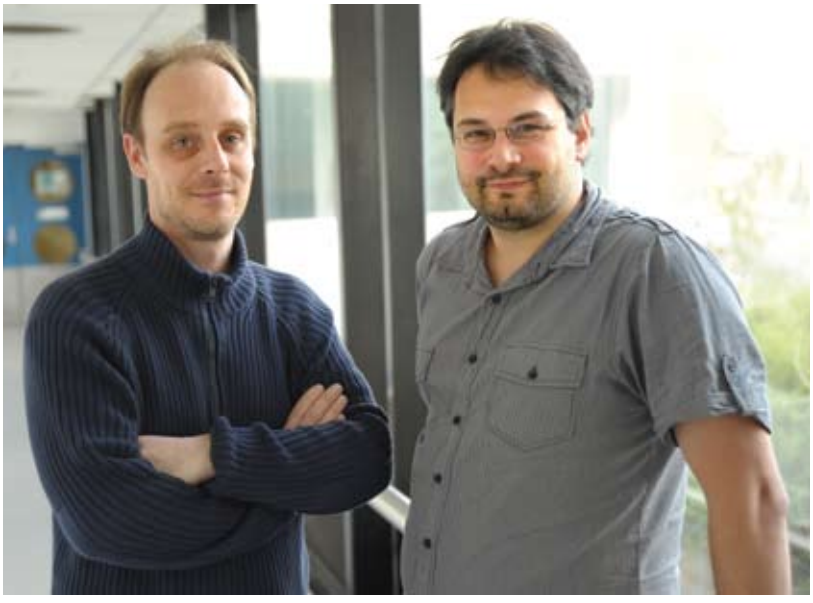
These results indicated that Fgfr2 is important for testis development by acting as the receptor for Fgf9, thereby rendering human FGFR2 a good candidate gene for unsolved disorders of sex development.

In individuals with XY sex chromosomes, the presence of the gene Sry on the Y-chromosome enables the gonad to develop into a testis leading to male development, whereas in XX individuals the gonad will develop into an ovary leading to female development.

A key protein controlled by Sry is fibroblast growth factor 9 (Fgf9) which activates testis growth and differentiation. However it was not known which receptor mediates this process.

We have generated mice lacking Fgf receptor 2 (Fgfr2) and found that these mice show partial XY sex reversal. That is, the gonads form ovotestes which are hermaphroditic gonads containing both ovarian and testicular tissue. An interesting feature of these gonads is that the ovarian and testicular tissues are clearly separated from each other with male-specific marker expression (red) in the centre (figure opposite page, left) and female-specific marker expression (purple) at the poles of the gonad (figure opposite page, right). These and other results indicated that Fgfr2 is important for testis development by acting as the receptor for Fgf9, thereby rendering human FGFR2 a good candidate gene for unsolved DSD cases. Indeed, individuals with terminal deletions of chromosome 10, lacking the FGFR2 gene, show abnormal sex differentiation, from micropenis to partial and complete XY sex reversal.

Dr Stefan Bagheri-Fam joined PHI in 2004, and has been actively researching the molecular mechanisms of male sex determination, focussing on the genes Sox9 and Fgfr2.



L - R: Dr Pascal Bernard, Dr Stefan Bagheri-Fam, Senior Research Officers, Human Molecular Genetics

disorders of sex development

Disorders of sex development (DSDs) can arise if there is a change in one or more of the genes that control gonadal development.

Our sex is determined at conception. Sex development into a male or female foetus is determined by the embryo's genetic make up - by the sex chromosomes (two X chromosomes in females, an X and a Y chromosome in males). Disorders of sex development (DSD; formerly known as intersex conditions) can arise if there is a change in one or more of the genes that control sex development. Such disorders can result in differences in the sexual characteristics of the infant, where the gender of the infant at birth is not clearly male or female, or where the physical sex of the person does not match the sex of their chromosomes (i.e. XY females and XX males). In the majority of sex development disorder cases the underlying genetic changes are unknown. We are now beginning to understand that genes involved in sex determination also affect a wide variety of other processes, such as brain and bone development.

Discovering the genes responsible for disorders of sex development

By identifying new genes responsible for disorders of sex development, we hope to map the 80 per cent of cases that remain unexplained genetically.

To achieve this, several approaches are being taken:

Comparative Genomic Hybridisation

We have collected a number of DNA samples from DSD patients for which the genetic etiology is unexplained. Using human genome microarrays, we are screening for insertions and deletions in DSD patients, expected in about 25% of cases, which represent new DSD causing genes.
Two candidate genes have emerged from two patients, which are being followed up.

Ex vivo culturing of embryonic gonads

Our team has developed mouse gonad culture that replicates the normal gonad development in mice (testis or ovary). This technique has allowed us to manipulate the genes involved in sex determination to evaluate the fate of the gonad. Using this approach we have identified the β-catenin gene as a key player in female gonad development. Stimulating β-catenin gonad function in a male gonad led to the development of a female gonad, indicative of sex-reversal as observed in patients with DSD. We are currently evaluating more genes that could be important for both male and female gonad development using this approach.

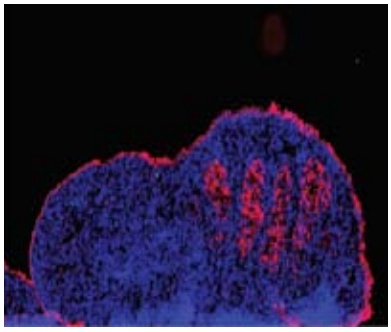
Ethylnitrosourea (ENU) mutagenesis in mice

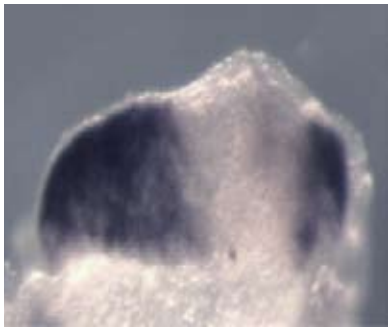
ENU is a powerful method for identifying genes based on function. ENU randomly introduces DNA mutations into the genome some of which affect sex development - these mutations can be tracked and the relevant gene identified. As part of a Monash University Organogenesis Consortium, we are screening for gonadal/reproductive abnormalities in developing mouse embryos. This approach is expected to yield genes important for gonadal development and DSDs.

STAFF

Human Molecular Genetics

Anthony Argentaro
Stefan Bagheri-Fam
Pascal Bernard
Vincent Harley
Suha Hassan
Irumini Jayakody
Sabine Kelly
Louisa Ludbrook
Helena Sim
Paisu Tang





**Images: (right) Expression of the male-specific protein Amh (red) in a section of a foetal XY gonad lacking Fgfr2.
(far right) Expression of the female-specific gene Bmp2 (purple) in a foetal XY gonad lacking Fgfr2.**

oestrogen, brain & behaviour

Wah Chin Boon

It has long been known that men develop compulsive disorders at a younger age and have worse outcomes than women; more boys suffer from Tourette's Syndrome or Autism. These gender biases may be indicative that male and female sex hormones affect behaviour, whether it is normal or pathological, as well as neurodegeneration.

In the brain of both sexes, androgens (male sex hormones) are converted to oestrogens (female sex hormones) by the action of a protein enzyme aromatase. Brain cells also have receptors which respond to oestrogens. Hence, oestrogen produced locally in the brain can influence the function of brain cells.

By studying an oestrogen-deficient mouse model, the aromatase knockout (ArKO) mouse, we have discovered that oestrogens are important for the survival of brain cells, regulating male sexual behaviour and grooming.

The ArKO mouse lacks a functional Cyp19 gene, which encodes aromatase. Hence, ArKO mice are unable to synthesise oestrogen in any body site and are thus a completely oestrogen deficient animal model. We found prominent neuronal cell death (apoptosis) in the hypothalamus of one year-old male, but not female, ArKO mice. This cell death can be prevented by giving oestrogen to the male ArKO mice. Oestrogen protects the brain cells by switching on a set of genes that prevent cell death (anti-apoptotic genes) and switching off a set of genes that cause cell death (pro-apoptotic genes).

Within the hypothalamus a discreet brain region known as the arcuate nucleus contributes to energy balance, such as fat metabolism. Male ArKO mice have fatty livers, which again can be treated by oestrogen replacement.

Dr Wah Chin Boon, Senior Research Officer, Sex Hormone Biology

Another function of the hypothalamus is to regulate grooming, which when in excess has been labelled as an obsessive compulsive disorder trait in animals. Indeed, grooming behaviour was increased in the six month-old male ArKO mice, but not observed in female ArKO mice. Besides excessive grooming, male ArKO mice also run excessively on the running wheel - another compulsive behaviour. All these compulsive behaviours can be ameliorated by oestrogen treatment. The medial preoptic area in the hypothalamus also regulates male sexual behaviour and you would have guessed it – male ArKO mice have an absence of male sexual behaviour. Our observations illustrate the importance of oestrogens in the male brain, hence challenging the traditionally view that oestrogens are solely female sex hormones.

Understanding how oestrogens modulate behaviour has important implications for psychiatry, for better understanding of our society and potentially, for the veterinary industry. This work was mainly performed by Dr Rachel Hill during her PhD candidature under the supervision of Dr Boon and Professor Simpson.

Dr Boon is a molecular biologist who joined the Sex Hormone Biology group in 1998. Even though she has recently set up her own research group at Howard Florey Institute, she remains an active member of PHI with ongoing collaborations. Her main interest is to understand how sex hormones affect brain development and mental health.

neurobiology research

Our studies have provided evidence that male gender identity may be partly mediated through androgens.

Gender Identity

Transsexuals identify with a physical and mental sex opposite to their birth sex. They show differences in the size of certain brain structures and differences in their response to sex hormone odours. Transsexualism can run in families, but the cause is unknown. We undertook a genetic investigation of male-to-female transsexualism, the world's largest. We analysed three genes involved in sex hormone action in 112 male-to-female transsexuals and identified an association with Androgen Receptor. Therefore, this study has provided evidence that male gender identity may be partly mediated through androgens. We are now hoping to extend this research by increasing the number of transsexuals in this study as well as looking at other genes involved in sex hormone action.

Parkinson's Disease

Male and female brains are different and growing evidence highlights the importance of genetic factors. We have shown that SRY, a gene found only in males, is turned on in a brain region called the substantia nigra, and is crucial for controlling voluntary movement. Human SRY protein is produced in the same brain cells that make tyrosine hydroxylase, the enzyme that synthesises the neurotransmitter dopamine.

We demonstrated that by inhibiting SRY function in the substantia nigra, the number of cells that make dopamine is reduced, and movement function is impaired. This suggests that SRY controls dopamine production and we are investigating this at the molecular level using NT2N cells, a human cell line that can be differentiated over 28 days, into dopamine-like neurons. By increasing the level of SRY in NT2N cells, production of tyrosine hydroxylase is increased. Parkinson's disease is caused by the loss of dopamine producing cells in the substantia nigra. We are investigating whether SRY is involved in the male susceptibility to Parkinson's disease in an animal model of Parkinson's disease. The proposed project will provide entirely novel and important insights into the molecular and neurobiological mechanisms of gender differences in Parkinson's disease.

STAFF

Human Molecular Genetics

Daniel Czech
Lauren Hare
Vincent Harley
Joohyung Lee
Rianne Wind

Sex Hormones Biology

Wah Chin Boon
Jenny Chow
Rachel Hill
Evan Simpson
Michelle Van Sinderen

Photo (right) L - R: Dr Anthony Argentaro PhD students Lauren Hare, Louisa Ludbrook, Irumini Jayakody, Daniel Czech

commercialisation, services & core facilities

Intellectual Property and Commercialisation at PHI

Under the Prince Henry's Institute of Medical Research Act 1988, one of the institute's objectives is to commercialise its intellectual property.

To assist achieving this objective, PHI's Intellectual Property (IP) and Commercialisation Committee advises on protection and eventual licensing of IP generated by its scientists and clinicians.

A notable outcome of a recent licensing agreement is the growing royalty stream arising from the inhibin licensing agreement shared between Monash University, St. Vincent's Institute of Medical Research (SVI) and PHI. Since royalties commenced in 2002, PHI's share has amounted to well in excess of $0.5 million.

Achievements during the year under review include the following:

- Two Collaborative Research Agreements were negotiated with SVI regarding a potential cancer therapy and potential fibrosis therapy;
- The institute's IP policy and procedures were reviewed to ensure compliance with current standards of corporate governance and international protocols;
- PHI's Pregnancy Related Enzyme Activity patent application was accepted in Australia. Besides HIV prevention, this I.P. can provide a useful test for uterine fertility;
- PHI's Novel Serine protease patent application was also accepted in Australia. Its prime benefit is as a test for pre-eclampsia. Discussions have commenced with potential commercialisation partners.

PHI / Southern Health Androgen Replacement Service

The Androgen Replacement Service at Monash Medical Centre was developed as a joint venture between PHI and the Southern Health Department of Endocrinology.

Sequencing Centre Manager, Vivien Vasic

Beginning in April 2004, the out-patient clinic now runs twice weekly and is staffed by Endocrinologists/ Andrologists and Clinical Nurse Specialists.

The service was developed to provide improved clinical care to men with androgen deficiency (either as a result of testicular disorders or as a consequence of pituitary disease) who require androgen (testosterone) therapy. Testosterone deficiency is the commonest hormonal disorder in men, affecting approximately 1 in 200 adult males. Individualised, evidence based management plans are established and, where appropriate, shared care protocols with General Practitioners are developed. The service provides educational material (in conjunction with Andrology Australia) for both patients and medical professionals.

The clinic is one of very few such tailored services available through an Australian public hospital. The number of men attending has continued to rise with the clinic now providing care for almost 100 Victorian men. A typical patient will visit the clinic about 4 times per year.

Whilst the service is predominately concerned with the provision of clinical service, it also provides a focus for teaching and research in the field of male reproductive health (andrology). PHI staff, acknowledged as leaders in the clinical and research domains of andrology, are involved in ongoing clinical trials of new formulations of testosterone delivery and are working to develop improved models of care.

Monash Health Research Precinct (MHRP) Core Facility: The Gandel Charitable Trust Sequencing Centre

The Sequencing Centre was established in 1999 from funding provided by the Wellcome Trust after a successful granting submission from MIMR and PHI. The Trust kindly supported purchase of an Applied Biosystems ABIPRISM™ 377 DNA Sequencer and funded running costs for the Centre for 3 years.

In 2005 the Gandel Charitable Trust generously provided funds enabling purchase of the current Applied Biosystems 16 Capillary 3130xl Genetic Analyser that generates sequence read lengths of up to 1000 bases.

notable achievements

Professor Henry Burger AO was the second Director of our Institute and the longest serving. He was Director from 1972 -1990 when Prince Henry's Hospital Medical Research Centre was situated at Prince Henry's Hospital and from 1991-1998 when PHI moved to Monash Medical Centre.

Henry has been a pioneer to the area of reproductive endocrinology contributing both in clinical and basic research. He has received countless accolades for his research which includes the endocrinology and management of the menopause, female and male infertility and the role of the inhibin hormones in ovarian cancer.

Henry is still highly active in PHI research life with 13 publications and 5 invited presentations during 2007. These invitations include the Wyeth Utian Endowed Lecture to the North American Menopause Society and a Symposium presentation at the International Menopause Society meeting in Madrid. In recognition of Henry's considerable scientific contributions, the International Menopause Society recently established the Henry Burger Prize for the Best Published Research on the Menopause in the preceding two years.

Professor John Funder AO was at Prince Henry's Medical Research Centre from 1973 - 1990, when he became Director of the Baker Institute. Upon his 'retirement' in 2001 he became a Senior Fellow at PHI.

PHI congratulates John on his being awarded the 2008 Novartis Prize of the American Heart Association for his contributions to our understanding of hypertension (high blood pressure), and on

his appointment as Director of Research Strategy at Southern Health.

His area of research is the salt-retaining (mineralocorticoid) hormone aldosterone, and the key receptor (mineralocorticoid receptor) into which it fits in organs such as the kidney to do the job. Both hormone and receptor have roles in hypertension and heart failure that have emerged over the past decade, through clinical and basic studies at PHI and elsewhere.

John has served as a link between endocrinology and cardiology, and as the person internationally acknowledged as leading an exciting new era of hitherto unexpected roles for the mineralocorticoid receptors, across a spectrum of disease states.

PHI congratulates Professor Jock Findlay AO, made an Officer of the Order of Australia, in recognition of his achievements as a medical researcher, his contribution to the development of assisted reproductive treatments and also his involvement in national and international health programs.

Jock Findlay joined PHI in 1979 and leads the Female Reproductive Biology Group. A major theme of his research has been in understanding how fertility in women is related to the function of their ovaries, exploring how healthy eggs are stored and released.

Jock has published over 350 research papers and received multiple awards and accolades for his work. He was made a member of the Order of Australia (AM) in 2001.

His research has led to a shift in understanding how hormones have local effects on the body including the production of eggs. Jock's work has also contributed to the development of improved IVF procedures.

The group's current research aims to develop new infertility treatments, better contraceptive choices for women and to provide new leads to understanding and treating ovarian cancer.

awards, fellowships & prizes

Maria Alexiadis
- Kadir-Fatimah Award, 2007

Carolyn Allan
- Henry Burger Clinical Research Award

Anthony Argentaro
- PHI Career Enhancement Award

Pascal Bernard
- PHI Career Enhancement Award

Maree Bilandzic
- Postdoctoral Travel Grant, CASS (Contributing to Australian Scholarship and Science) Foundation

Wah Chin Boon
- US Endocrine Society Travel Award, ENDO 2008

Kristy Brown
- FQRNT Fellow (Le Fonds québécois de la recherche sur la nature et les technologies)
- Travel Grant, Ian Potter Foundation
- Endocrine Trainee Award, Endocrine Society
- Harold Mitchell Foundation travel fellowship

Ashwini Chand
- Burroughs Wellcome Scholarship to attend Frontiers in Reproduction Training Program, Woods Hole, MA, USA
- US Endocrine Society Travel Award to attend a Fellows Careers Workshop and AWE-NovoNordisk New Investigator Travel Grant

Chen Chen
- NHMRC Senior Research Fellowship

Jenny Chow
- Australian Society for the Study of Obesity (ASSO) Scientific Meeting – Best Student Oral Presentation Award
- ASSO Travel Award

Hui Kheng Chua
- Travel award, Endocrine Society of Australia

Colin Clyne
- International Union against Cancer Yamagiwa-Yoshida Memorial International Cancer Study Grant

Izabella Czajka-Oraniec
- Mara E. Liberman Travel Grant
- Ian Potter Foundation Travel Grant

Daniel Czech
- Australian Postgraduate Award

Evdokia Dimitriadis
- Travel Award, Society for Gynecologic Investigation

Jock Findlay
- Appointed as an Officer of the Order of Australia

Tu'uhe Kaitu'u-Lino
- Participant, Fresh Science
- NHMRC Training Fellowship

Kevin Knower
- Cass Foundation Early Career Travel Grant
- Winner, Trainee Poster Competition, US Endocrine Society

Natalie Hannan
- Travel Award, Larry Ewing Training (Society for the Study of Reproduction, USA

Lauren Hare
- Student Poster Prize, Lorne Genome Conference
- Australian Postgraduate Award

Amy Herlihy
- NHMRC Postgraduate Research Scholarship (Public Health)
- SciGen Travel Grant for the Australasian Paediatric Endocrinologists
- Group (APEG) Annual Scientific Meeting

Emily Lam
- Finalist, Royal Society Award for Post Doctoral Scientists
- Travel Award, Heart Foundation Australia
- Travel Award, High Blood Pressure Research Council of Australia
- Travel Award, Women in Endocrinology

Louisa Ludbrook
- Fresh Science Finalist

Sarah Meachem
- Victorian Tall Poppy, Australian Political Science Institute

Ellen Menkhorst
- Cass Foundation Travel Grant
- Harold Mitchell Post-Doctoral Travel Grant Award

Peter Nicholls
- Australian Postgraduate Award

Guiying Nie
- NHMRC Senior Research Fellowship

Sue Panckridge
- John Donges Award, 2007

Jyotsna Pippal
- Ian Potter Foundation Travel Grant

Jyothsna Rama Rao
- Finalist, Novartis Junior Investigator, 2007
- Travel Award, Endocrine Society, 2007
- Monash Postgraduate International Travel Award 2008

David Robertson
- NHMRC Principal Research Fellowship

Amanda Rickard
- US Endocrine Society Scholars Award
- Travel Grant, Heart Foundation Australia
- Travel Grant, US Endocrine Society
- Merit Certificate, Australian Women in Endocrinology
- Quantum award for scientific excellence, PHI
- Travel Grant, High Blood Pressure Council of Australia Meeting

Davina Rosairo
- Finalist, Monash University Higher Degree by Research Student Poster Exhibition

Mai Sarraj
- Travel Grant, Ian Potter Foundation
- 9th Royan International Research Travel Award

Andrew Stephens
- Victorian Cancer Agency Link and Learn Grant
- National Australia Bank Travel Fellowship

Chelsea Stoikos
- RANZCOG Research Foundation Scholarship
- Post-graduate Student Prize, Royal Society of Victoria
- Harold Mitchell PhD student Travel Grant Award
- Finalist Quantum award for scientific excellence, PHI
- Travel Award, Society for Reproductive Biology

Gerard Tarulli
- 1st prize, 2007 Anatomy & Developmental Biology student symposium, Monash University

Kenneth Walker
- National Heart Foundation Postgraduate Biomedical Research Scholarship
- Winner, Faculty of Medicine Research Award, Monash University Higher Degree Research Student Poster Exhibition
- Travel Award, Australian-New Zealand Society of Cell and Developmental Biology (ANZSCDBI) to attend the annual COMBIO conference, Sydney, 2007
- Keith Dixon Prize in Developmental Biology – Best Student Poster Presentation in Developmental Biology, by the Australian and New Zealand Society of Cell and Developmental Biology, ComBio 2007
- 1st Prize in the junior research category – Department of Anatomy and Developmental Biology Student Symposium, Monash University

Yao Wang
- Travel Award, Endocrine Society of Australia

Jun Yang
- RACP (Royal Australasian College of Physicians) Shields Research Entry Scholarship
- NHMRC postgraduate scholarship

service to the scientific community

Carolyn Allan
- Member, Endocrine Society of Australia Program Organising Committee
- Australasian Women in Endocrinology - member of selection panel for travel grants

Anthony Argentaro
- Member, Monash University Internal Biosafety Committee

Pascal Bernard
- Member, Southern Health Human Ethics Committee

Henry Burger
- Member, Infertility Treatment Authority
- Member, Board, Orygen Research Centre, & Chair, Research Committee
- Member, Board, Jean Hailes Foundation for Women's Health & Chair, Research Committee
- Member, Board, Ovarian Cancer Research Foundation
- Faculty Member, Faculty of 1000, Physiology
- Editorial Board, Menopause
- Editorial Board, Climacteric
- Editorial Board, Gynecologic Endocrinology
- Member, Council of Past Presidents, International Menopause Society

Ashwini Chand
- Member, Early Career Innovators Network (ECIN) Committee, Victorian Cancer Agency (VCA)
- Member, Organising Committee: VCA Early Career Development Workshops
- Grant Reviewer, Singapore National Medical Research Council
- Member, Victorian Organising Committee, ASMR Medical Research Week
- Chair, ASMR Careers Sub-Committee
- Member, Editorial Advisory Board, Virtual Endocrine Centre

Colin Clyne
- Member, Editorial Board, Endocrinology
- Member, Editorial Board, Journal of Molecular Endocrinology
- Judge, Best poster, New Investigator Award, US Endocrine Society

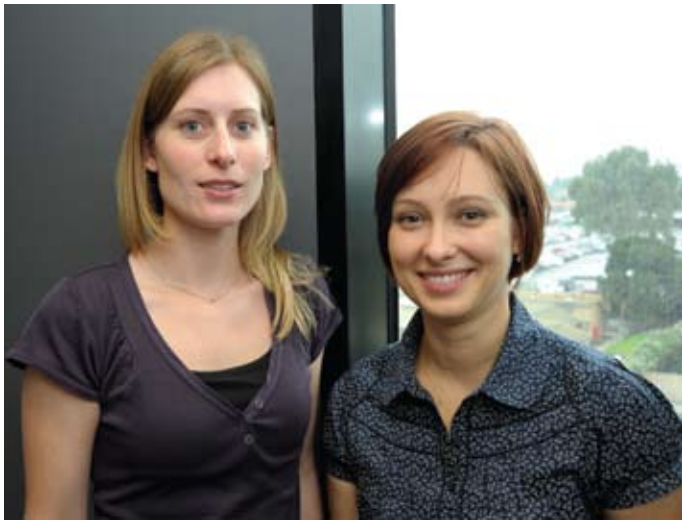
Evdokia Dimitriadis
- Committee Member, Special Interest Group in Endometriosis and the Endometrium (SIGEE), European Society of Human Reproduction and Embryology (ESHRE)
- Member, Program Organising Committee, Annual Scientific Meeting Society for Reproductive Biology (SRB)
- Reviewing Board Member, Journal of Reproductive Immunology

Ann Drummond
- Member, Editorial Board, Reproduction
- Member, Editorial Board, Journal of Endocrinology
- PHI representative, MMC Animal Ethics Committee B
- Coordinator, BMS 3021 Miniprojects for Biochemistry & Molecular Biology

Jock Findlay
- Chair, NHMRC Embryo Research Licensing Committee
- Member, NHMRC Council
- Chair, Infertility Treatment Authority, Victoria
- Member and Chair, Bio21 Scientific Advisory Committee
- Director of Research, Royal Women's Hospital, Melbourne
- Member, Bio21 Hospital Research Directors Committee
- Member, SSR Endowment Sub-Committee
- Co-Director, Ovarian Workshop, USA
- Consultant, University of Adelaide, School of Obstretics, Gyn, Peds.
- Member, Board, Victorian Breast Cancer Research Consortium
- Chair, Scientific Committee, Victorian Breast Cancer Research Consortium
- Member, Board, Bio21 Cluster
- Member, Melbourne Health Biobank Management Committee

Peter Fuller
- Council Member, Cancer Council of Victoria
- Member, Cancer Council of Victoria, Executive Committee
- Member, Cancer Council of Victoria, Venture Grants Committee
- Member, Ministerial Task Force on Cancer, Department of Human Services, Victoria
- Inaugural Member, Victorian Cancer Agency Consultative Council
- NHMRC Representative Board, Howard Florey Institute, Melbourne
- Member, Selection Committee, Pharmacia/Pfizer Foundation Australia, Senior Research Fellowships in Biomedical Science
- Member, Council of the Cabrini Clinical Education and Research Institute, Cabrini Hospital, Melbourne
- Council of Governors, Florey Neurosciences Institutes, Melbourne
- Search Committee, Director of the Florey Neurosciences Institutes
- Co-Editor, Hormone and Metabolic Research
- Section Editor, Endocrine and Metabolic Section, Expert Opinion on Investigational Drugs
- Editorial Board, Steroids
- Editorial Board, Endocrinology
- Faculty Member, Faculty of 1000, Medicine
- Associate Editor, Endocrinology
- Editorial Board, Journal of Molecular Endocrinology

Matthew Gillespie
- Member, Cancer Council of Victoria
- Member, Science Policy Committee of the American Society for Bone and Mineral Society
- Member, Research, Committee of NHMRC
- Member, Audit Committee of NHMRC
- Chair, Project Grants Working Group NHMRC
- Board Member, Australian and New Zealand Bone and Mineral Society
- Board Member, Cancer and Bone Society
- Board Member, International Bone and Mineral Research Society
- Board member, Victorian Breast Cancer Research Consortium
- Editorial Board, Arthritis and Rheumatism



Above L - R: FQRNT Fellow Dr Kristy Brown and Endocrine Society Fellow, Dr Izabella Czajka-Oraniec

- Editorial Board, Bone
- Editorial Board, BoneKey
- Editorial Board, Journal of Bone and Mineral Research
- Editorial Advisory Board, Journal of Oral Biosciences
- Program Chair, Australian and New Zealand Bone and Mineral Society, Melbourne
- Program Committee, 30th Annual Meeting of the American Society for Bone and Mineral Research, Montreal, Canada
- Program Committee, International Bone and Mineral Society and Australian and New Zealand Bone and Mineral Society, Sydney
- Local Organising Committee, International Bone and Mineral Society and Australian and New Zealand Bone and Mineral Society, Sydney
- Program Chair, Cancer and Bone Society, Sydney
- Chair of Membership and Education Committee, International Bone and Mineral Research Society

Vincent Harley

- Member, Monash University International Biosafety Committee
- Editorial Board, Molecular Endocrinology
- Editorial Board, International Journal of Biochemistry and Cell Biology
- Editor/Curator, HUGO Mutation database for sex determining genes and SOX genes, for publication in Human Mutation
- Editorial Board, Sexual Development
- Member of NHMRC GRP Panel
- Vice President and Secretary, Lorne Genome Conference
- Co-organiser, Prince Henry's Institute Minisymposium "Brain sexual dimorphism – genes or hormones?", Monash Medical Centre

Sach Jayasinghe

- Scholar, International Society for Advancement of Cytometry

Tu'uhevaha Kaitu'u-Lino

- Student Representative, Society for Reproductive Biology

Rob McLachlan

- Member, Research on Methods for the Regulation of Male Fertility of the World Health Organisation
- Research Management Committee, Monash University IVF programme

Senior Research Officer Dr Sarah Meachem and Grants & Education Officer Dr Neil Owens

- Secretary, International Society of Andrology
- Associate Editor, International Journal of Andrology
- Associate Editor, International Journal of Andrology
- Associate Editor, Journal of Andrology
- Associate Editor, Journal of Clinical Endocrinology and Metabolism
- Member Organising Committee, International Congress of Andrology
- Member of inaugural Management Committee, Andrology Australia; Director
- Scientific Adviser, Infertility Treatment Authority, Victoria

Sarah Meachem

- President Elect, Australian Society for Medical Research
- Coordinator, Fertility Regulation Unit, Education Program for Reproduction and Developmental Biology
- Member Organising Committee, Endocrine Society of Australia
- Editorial Board, Journal of Endocrinology

Ian Muchamore

- Committee Member, Australian Science Communicators, Victoria Branch

Guiying Nie

- Managing Editorial Board Member, Frontiers in Bioscience
- Reviewing Board Member, Reproductive Biology and Endocrinology

Julian Quinn

- Editorial Board, Bone

David Robertson

- Editor, Women's Health

Davina Rosairo

- PHI Representative, ASMR Regional High School Tours

Lois Salamonsen

- Editorial Board Member, Endocrinology
- Associate Editor (Pacific Region), Reproductive Sciences
- International Advisory Panel, Reproduction, Fertility and Development
- Board of Reviewing Editors, Biology of Reproduction
- Panel Chair, NHMRC Training, Awards Committee
- Member Organising Committee, World Congress of Reproductive Biology, Hawaii

Mai Sarraj

- Speaker: "Careers in Science" to year 5 and 6 school students at Milgate Primary School

Peter Stanton

- Member of the Editorial Board, Journal of Endocrinology

Kaye Stenvers

- Member, Ludwig Institute Institutional Biosafety Committee
- Coordinator, GRS1002, Education Program for Reproductive Biology (EPRB) Monash University
- Organiser, 2008 TGFβ Workshop, MIMR-PHI, Melbourne

Morag Young

- Editorial Board, Endocrinology
- Faculty Member, Faculty of 1000, Physiology
- Judge, Best poster new investigator award, US Endocrine Society
- Victorian Convener, Australian Society for Medical Research (ASMR)
- Chair, Education Sub-Committee, ASMR

students 2007/08

Prince Henry's Institute has a great reputation for postgraduate research and study, combining helpful and encouraging supervision with a high standard of research and expertise.

Our young researchers have achieved great success in 2007-08. Some of the year's highlights include:

Student Symposium
The high caliber of student presentations was again displayed during the 14th Annual PHI Student Symposium in November 2007.

Held over two consecutive days, the Student Symposium provides Postgraduate and Honours students with an opportunity to present their scientific findings to the Institute within a conference setting and provides them with invaluable public speaking experience. The Symposium was supported by Nova Nordisk. Winners of the 2007 PHI Student Symposium: Best Honours/ Masters presentation: **Daniel Czech**

Honours student Daniel Czech, with Novo Nordisk Representative Saras Singam and Adjudicator Dr Padma Murthi (Royal Women's Hospital)

PhD – Best 1st year presentation: **Kenneth Walker**

Novo Nordisk Representative Saras Singam and PhD student Tu'uhevaha Kaitu'u-Lino

PhD – Best overall presentation: **Tu'uhevaha Kaitu'u-Lino**
PhD – Special commendation award: **Natalie Hannan**

Quantum Award for Scientific Excellence

The annual PHI award, proudly sponsored by Quantum Scientific, recognises the best research paper presented by a student at a conference the previous year.

Congratulations to PhD student Amanda Rickard who received the 2007 Quantum Award for Scientific Excellence for her research for her work identifying some of the different factors responsible for inflammation and permanent scarring of the heart. The work of Chelsea Stoikos and Michelle Van Sinderen were highly commended.

Student Committee

The student committee is actively involved in the PHI Student Open Day and Postgraduate Career Seminar Series, held in conjunction with the Monash Careers and Employment Services.

Education Program in Reproduction and Development

The Education Program in Reproduction and Development (EPRD) aims to foster education and research into reproductive biology and embryology for domestic and international postgraduate students. The EPRD program is a joint venture between Prince Henry's Institute and Monash Institute of Medical Research (MIMR), in association with the Monash University Departments of Physiology, Pharmacology, Obstetrics & Gynaecology, Paediatrics and Anatomy & Cell Biology.

The Graduate Diploma & Master of Reproductive Sciences and the Master of Clinical Embryology are run by the EPRD through the MIMR. 36 students, including 29 international students, were enrolled in these courses in 2008. PHI plays a key role in the coordination and teaching of the EPRD program and helps to promote its activities. Many of the Institute's scientists assist in the development of course units, lecture and facilitate practical sessions. PHI researchers also supervise students undertaking research projects in the Master of Reproductive Sciences. For more information on courses and open days telephone: (03) 9594 7100 or visit the website at www.med.monash.edu.au/eprd.

PhD student Amanda Rickard, Quantum Award Winner and Gavin Williams, Quantum Scientific National Sales and Marketing Manager

students
- class of 2007/08

PhD Students

Marissa Bowden BA/BSc (Hons)
'The expression and function of serine protease Htra3 in the ovary'
Supervisors: Professor Jock Findlay; Dr Guiying Nie

Ally Chau BMed&PharmBiotech (Hons)
'Interactions between breast cancer cells and the bone micro environment'
Supervisors: Assoc. Professor Matthew Gillespie; Dr Rachel Mudge

Vanessa Cheung BA/BSc (Hons)
'Role of PTHrP in DNA repair and cellular apoptosis of cancer cells'
Supervisors: Assoc. Professor Matthew Gillespie; Dr Steve Bouralexis

Jenny Chow BBiomedSci (Hons)
'The effect of oestrogen on triglyceride metabolism'
Supervisors: Dr Wah Chin Boon; Professor Evan Simpson

Daniel Czech BSc (Hons)
'The role of SRY in the brain'
Supervisor: Assoc. Professor Vincent Harley

Natalie Hannan BSc (Hons)
'Endometrial proteins in human embryo implantation and their relevance to fertility'
Supervisor: Professor Lois Salamonsen

Lauren Hare BA/BSc (Hons)
'A Genetic Study on Gender Dysphoria and Transsexualism'
Supervisors: Assoc. Professor Vincent Harley; Dr Pascal Bernard

Amy Herlihy BSc GradDipGeneticCounselling
'Population-based genetic screening for Klinefelter's Syndrome: A critical analysis'
Supervisors: Professor Rob McLachlan; Assoc. Professor Jane Halliday; Assoc. Professor Lynn Gillam; Dr Megan Cock

Rachel Hill BSc (Hons)
'Characterisation of the brain of the male Aromatase Knockout (ArKO) mouse'
Supervisors: Dr Wah Chin Boon; Professor Evan Simpson

Sonay Hussein-Fikret BBiomedSci (Hons)
'Steroid receptor coactivators in ovarian granulosa cell tumours'
Supervisor: Professor Peter Fuller

L - R: Premila Paiva, Natalie Hannan, Chelsea Stoikos

Stacey Jamieson BA/BSc (Hons)
'The molecular pathogenesis of the granulosa cell tumour of the ovary'
Supervisor: Professor Peter Fuller

Irumini Jayakody BBiomedSci (Hons)
'Functional analysis of FGFR2 during testis development'
Supervisors: Dr Stefan Bagheri-Fam; Assoc. Professor Vincent Harley

Tu'uhevaha Kaitu'u-Lino BBiomedSci (Hons)
'Understanding endometrial breakdown and repair'
Supervisors: Professor Lois Salamonsen; Dr Naomi Morison

Emily Lam BBiomedSci (Hons)
'Differential regulation of the mineralocorticoid receptor by corticosteroids and salt in the pathology of cardiovascular inflammation and fibrosis'
Supervisor: Dr Morag Young

Jason Liew BBiomedSci (Hons)
'The role of oestrogen in ovarian function'
Supervisors: Professor Jock Findlay; Dr Ann Drummond; Dr Margaret Jones

Louisa Ludbrook BBiomedSci (Hons)
'DAX1 and gonadogenesis'
Supervisor: Assoc. Professor Vincent Harley

Yogeshwar Makanji BAppSci (Hons)
'Biological characterisation of Inhibin A and Inhibin B'
Supervisors: Assoc. Professor David Robertson; Dr Craig Harrison

Mark McCabe BAppBiol/Biotech (Hons)
'Hormonal regulation of the Sertoli cell tight junction'
Supervisors: Dr Peter Stanton; Dr Peter Smooker

Peter Nicholls BBiomedSci (Hons)
'Regulation of spermiation'
Supervisors: Dr Craig Harrison; Dr Peter Stanton

Premila Paiva BSc (Hons)
'Endometrial-placental interactions in human blastocyst implantation: roles for interleukin-11'
Supervisors: Dr Eva Dimitriadis; Professor Lois Salamonsen

Irene Papageorgiou BSc (Hons)
'The role of Cripto in tumourogenesis'
Supervisors: Dr Craig Harrison; Assoc. Professor David Robertson

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

Jyothsna Rama Rao BSc MSc
'Effect of fat hormones on pancreatic beta cells'
Supervisors: Assoc. Professor Chen Chen; Assoc. Professor Helena Parkington

Amanda Rickard BBiomedSci (Hons)
'Mineralocorticoid/salt induced vascular damage and cardiac fibrosis'
Supervisor: Dr Morag Young

Nana Saleh BSc (Hons)
'The influence of lymphocytes on the metabolism of bone'
Supervisors: Assoc. Professor Matthew Gillespie; Dr Julian Quinn

Chelsea Stoikos BSc (Hons)
'Molecular events in the endometrium: implications for infertility'
Supervisors: Dr Eva Dimitriadis; Professor Lois Salamonsen

Qiang Sun MBBS MSc
'Effect of GHS on cardiomyocytes'
Supervisors: Assoc Professor Chen Chen

Paisu Tang BSc (Hons)
'Functional studies on the ATRX protein'
Supervisors: Assoc. Professor Vincent Harley; Professor Jennifer Marshall Graves

Gerard Tarulli BSc (Hons)
'Regulation of Sertoli cell differentiation'
Supervisors: Dr Peter Stanton; Dr Sarah Meachem; Professor John Bertram

Michelle Van Sinderen BSc (Hons)
'Estrogen, adiposity and insulin resistance'
Supervisors: Dr Margaret Jones; Dr Wah Chin Boon; Professor Evan Simpson

Kenneth Walker BSc (Hons)
'Roles of TGF-beta2/betaglycan signalling in the developing kidney'
Supervisors: Professor John Bertram; Dr Kaye Stenvers

Jun Yang MBBS (Hons)
'Mineralocorticoid receptors – mechanisms of ligand- and tissue-specific activation'
Supervisors: Dr Morag Young; Professor Peter Fuller

Sean Yang BSc
'The regulation of growth hormone by secretagogues'
Supervisors: Assoc. Professor Chen Chen; Assoc. Professor Helena Parkington

Masters Students

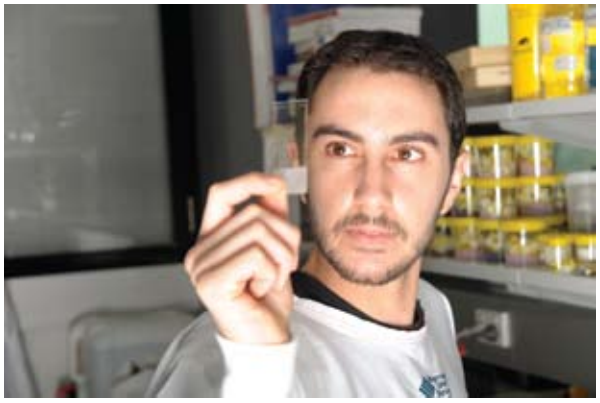
Debora Romero BSc GradDipRSc
'The effects of gonadotrophin treatment on the secretory and cellular proteins of Mouse Leydig cells in vitro'
Supervisors: Assoc. Professor David Robertson; Dr Andrew Stephens

Davina Rosairo BSc GradDipRSc
'Regulation of ovarian follicle development'
Supervisors: Professor Jock Findlay; Dr Ann Drummond

Honours Students

Dimuthu Alankarage BBiomedSci
'Investigating the function of the ADD domain of chromatin remodeling protein, ATRX'
Supervisor: Dr Anthony Argentaro

Marina Bashir BSc
'The role of galectin-1 in spermatogenesis and spermiation'
Supervisors: Dr Kyriakos Pratis; Dr Liza O'Donnell; Dr Peter Stanton



Gerard Tarulli

Irene Cheung BSc
'Characterisation of the MR in zebrafish'
Supervisor: Professor Peter Fuller

Brett Fisher BA/BSc
'Studies on the role of SF1 in gonadal development'
Supervisor: Assoc. Professor Vincent Harley

Suha Hassan BSc
'Mutational analysis of intersex patients'
Supervisors: Dr Pascal Bernard; Assoc. Professor Vincent Harley

Sophy Heng BSc
'Role of PC6 in embryo implantation: identification of PC6 substrates in uterine epithelial cells'
Supervisor: Dr Guiying Nie

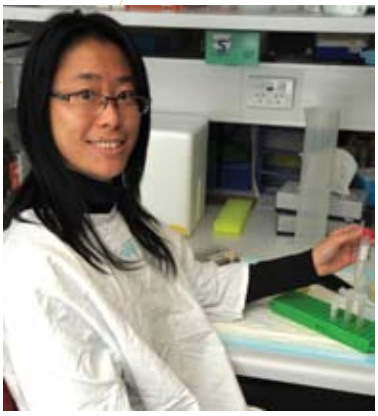
Kerrie Herridge BSc
'Exploring the roles of the orphan nuclear receptor LRH-1 in breast cancer'
Supervisors: Dr Colin Clyne; Dr Ashwini Chand

Pei-yu Ho BSc
'Role of betaglycan in mouse gonadogenesis'
Supervisor: Dr Kaye Stenvers

Jaslyn Lee BBiomedSci
'The role of novel protease HtrA3 in placental development and function'
Supervisor: Dr Guiying Nie

Audrey Lian BBiomedSci
'Oestrogen and the development of obsessive compulsive disorder in mice and men'
Supervisor: Dr Wah Chin Boon

Nadia Sadli BSc
'Regulation of voltage-regulated K+ currents of pancreatic beta-cells by specific somatostatin receptor subtype agonists'
Supervisor: Assoc Professor Chen Chen



Emily Lam

Nirukshi Samarageewa BBiomedSci
'The role of AMPK-related family members in TORC2 co-activation of CREB, and their effect on local aromatase expression in postmenopausal breast cancer'
Supervisor: Dr Kristy Brown

Courtney Simpson BSc
'The role of GDF9 as a modulator of Sertoli cell function'
Supervisors: Dr Peter Stanton; Dr Craig Harrison

Claire Tan BSc
'The oestrogen modulating obsessive disorders circuit/ model'
Supervisor: Dr Wah Chin Boon

Sarah To BSc
'Studies on the epigenetic mechanisms of regulation of the prostanoid receptors EP2 and EP4 in breast cancer'
Supervisor: Dr Kevin Knower

PhD Degrees conferred

Natalie Hannan
Rachel Hill
Sabine Kelly
Tu'uhevaha Kaitu'u-Lino
Saleela Ruwanpura

staff 2007/08

Director
Matthew Gillespie BSc (Hons) PhD

Associate Director
Peter Fuller BMedSci MBBS PhD FRACP, NHMRC Senior Principal Research Fellow (Associate Director from 14/4/08)

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

Senior Fellow
John Funder AO MD BS PhD FRACP

Research Group Heads
Chen Chen MD PhD
NHMRC Senior Research Fellow (until 31/12/07)

Jock Findlay AO PhD DSc
NHMRC Senior Principal Research Fellow; Deputy Director (until 30/9/07)

Vincent Harley PhD NHMRC Senior Research Fellow

Rob McLachlan MBBS FRACP PhD
NHMRC Principal Research Fellow

Guiying Nie PhD,
NHMRC Senior Research Fellow

David Robertson PhD,
NHMRC Principal Research Fellow

Lois Salamonsen PhD,
NHMRC Senior Principal Research Fellow

Evan Simpson PhD
Group Leader, Victorian Breast Cancer Research Consortium

RD Wright Fellows
Colin Clyne PhD
Craig Harrison PhD
Margaret Jones PhD (until 4/1/08)

Honorary Research Associate
Anne Corbould MBBS (Hons) PhD FRACP

FQRNT Fellow (Le Fonds québécois de la recherche sur la nature et les technologies)
Kristy Brown PhD

NAB Ovarian Cancer Research Foundation Research Fellow
Andrew Stephens PhD

Witchery Fellow Ovarian Cancer Research Foundation
Adam Rainczuk PhD

Boylan & Burke Fellow
Jyotsna Pippal BSc MSc MBA Ph

TM Ramsay Fellow
Mai Sarraj MSc PhD

Endocrine Society Fellow
Izabella Czajka-Oraniec MD PhD

Clinical Research Fellows
Carolyn Allan MBBS (Hons) PhD DRCOG(UK) FRACP PhD
Jonathan Cohen MBBS
Kati Matthiesson MBBS FRACP

Visiting Endocrinology Fellow
Siang Chin Lim MD MRCP

VCB Molecular Pathology Fellow
Sophie Bittinger MBBS (until 1/2/08)

Clinical Research Nurses
Nicole Fairweather RN
Elise Forbes RN
Judy Hocking RN
Anna Zamojska RN

Senior Research Officers
Anthony Argentaro PhD
Stefan Bagheri-Fam PhD
Pascal Bernard PhD
Maree Bilandzic PhD
Wah Chin Boon PhD (until 29/2/08)
Eva Dimitriadis PhD
Ann Drummond PhD
Paul Farnworth PhD
Vicky Kartsogiannis PhD
Rosemary Keogh PhD (until 6/6/08)
Joohyung Lee PhD
Sarah Meachem PhD
Katie Meehan PhD
Liza O'Donnell PhD
Kyri Pratis PhD
Julian Quinn MSc D.Phil
Helena Sim PhD
Peter Stanton PhD
Kaye Stenvers PhD
Morag Young PhD

Research Officers
Neil Borg PhD
Steve Bouralexis PhD
Ashwini Chand PhD
Jenny Chen PhD
Nicholas Fleming PhD
Neveen Hanna PhD (until 28/9/07)
Belinda Hardman PhD
Sabine Kelly PhD (until 17/8/07)
Lynette Kilpatrick PhD (until 2/5/08)
Kevin Knower PhD
Kerry McInnes PhD (until 15/2/08)
Ellen Menkhorst BSc (Hons)
Naomi Morison PhD (until 31/12/07)
Pavel Sluka PhD (until 18/1/08)
Ernesto Vargas PhD (until 31/12/07)
Kelly Walton PhD
Yufeng Zhao PhD (until 31/12/07)

Visiting Scholars
Shanaz Aali PhD (until 27/10/07)
Kamran Haidari MSc (until 21/12/07)
Nicole Hunger BSc
Anahita Mehdizadeh (until 24/10/07)
Ruyi Liu MD (until 25/12/07)

Senior Research Assistants
Maria Alexiadis BSc (Hons)
Francine Brennan BSc (Hons)
Maria Docanto BSc (Hons)
Anne Reilly BSc (Hons)
Melissa Solano BSc (Hons)

Research Assistants
Georgia Balourdos BSc (Hons)
Moh'd Banat (until 13/7/07)
Karen Chan BAppSc
Hui Kheng Chua BSc (Hons)
Rebecca Crook BSc (Hons) MSc
Ruth Escalona BSc (Hons) MSc
Caroline Foo BAppSc
Sara Goodman PGDipSc (until 31/10/07)
Natalie Hannan PhD
Kellie-Ann Hardy MSc (until 23/11/07)
Samantha Jayasekara PhD (until 13/6/08)
Ileana Kuyznierewicz BAppSc (Hons)
Ming Yee Lee BBiomedSci, BSc (Hons)
Ying Li BSc GDipMicroBio
Eliane Lin BSc (Hons) (until 17/7/07)
Sivaraja Mahindan BSc, Grad. Cert. in Lab. Tech. (until 14/1/08)
Melinda Marwood BSc (Hons)
James Morgan BSc (Hons)
Devi Ngo BBiomedSci (until 1/2/08)
Michelle Puryer BSc (Hons)
Enid Pruysers
Saw Eng Tan BVet MedTech
Alexandra Umbers BSc (Hons)
Fang Wang MSc (until 1/2/08)
Kun Wang BMed, MMed (until 29/1/08)
Yao Wang BSc
Peter Wilson BSc (Hons)
Yitzou Yao MD
Joanne Yap BSc (Hons)
Jin Zhang MD

Chief Operating Officer
Acting CEO (until 31/3/08)
Jane Glatz PhD MBA

Financial Services Manager
Terry Haining FCPA GDipAcc&Fin (until 30/11/07)
Peter Murray (from 12/11/07)

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

Laboratory & Technical Services Manager
Sach Jayasinghe BSc (Hons)

Grants and Education Officer
Neil Owens PhD

Marketing & Fundraising Manager
Misha Prusa

Human Resources Officer
Christina Matisons MAHRI

OHSE Officers
Elizabeth Klobas (until 2/11/07)
Brett Sargeant (from 27/11/07)

Science Communications Officer
Ian Muchamore BSc (Hons)

Graphic Communications
Sue Panckridge DipArt

Finance Officers
Sheridan Wallington (until 5/10/07)
Lesley Bowyer (from 12/5/08)

Accounts Officer
Jennifer Watson

Facilities Officer
Henry Wos

Purchasing Officer
Peter Wood AIWA (until 6/5/08)

Procurement Analyst
Ibrahim Ziada (until 29/2/08)

Executive Assistant
Diane Yallop

Administrative Officers/ Personal Assistants
Dianne Arnold BSc
Donna Beanland (until 18/7/07)
Jeanette Birtles BSc (Hons)
Sue Elger (until 31/12/07, P/T from 23/6/08)
Janelle Fisher
Abigail Lewis
Susan Smith (until 30/11/07)
Claudette Thiedeman
Jeana Thomas

CORE FACILITIES

Sequencing Manager
The Gandel Charitable Trust Sequencing Centre
Vivien Vasic BSc

Biomedical Engineer
Bruce Watson Dip Mechanical Engineering

Laboratory Technicians
Shelly Lampkin (until 31/1/08)
Robin Leuba BA Dip Ed
Florence Pierre
Susan Taleh BA

PhD Students
Marissa Bowden BA/BSc (Hons)
Ally Chau BMed&PharmBiotech (Hons)
Vanessa Cheung BA/BSc (Hons)
Jenny Chow BBiomedSci (Hons)
Daniel Czech BSc (Hons)
Lauren Hare BA/BSc (Hons)
Amy Herlihy BSc GradDip Genetic Counselling
Rachel Hill BSc (Hons) (until 11/1/08)
Sonay Hussein-Fikret BBiomedSci (Hons)
Stacey Jamieson BA/BSc (Hons)
Irumini Jayakody BBiomedSci (Hons)
Tu'uhevaha Kaitu'u-Lino BBiomedSci (Hons) (until 31/12/07)
Emily Lam BBiomedSci (Hons)
Jason Liew BBiomedSci (Hons)
Louisa Ludbrook BBiomedSci (Hons)
Yogeshwar Makanji BAppSc (Hons)
Mark McCabe BAppBiol/Biotech (Hons)
Peter Nicholls BBiomedSci (Hons)
Premila Paiva BSc (Hons)
Irene Papageorgiou BSc (Hons)
Niroshani Pathirage BSc (Hons) (until 15/2/08)
Jyothsna Rama Rao BSc MSc
Amanda Rickard BBiomedSci (Hons)
Saleela Ruwanpura BBiomedSci (Hons) (until 30/4/08)
Hasnawati Saleh BSc (Hons)
Chelsea Stoikos BSc (Hons)
Qiang Sun MBBS MSc (until 31/12/07)
Paisu Tang BSc (Hons)
Gerard Tarulli BSc (Hons)
Michelle Van Sinderen BSc (Hons)
Kenneth Walker BSc (Hons)
Jun Yang MBBS (Hons)
Sean Yang BSc

Masters Students
Debora Romero BSc GradDip ReprodSci
Davina Rosairo BSc, GradDip Reprod Sci

Honours Students
Dimuthu Alankarage BBiomedSci
Marina Bashir BSc
Irene Cheung BSc
Brett Fisher BA/BSc
Christine Harris BA/BSc (until 1/8/07)
Suha Hassan BSc (until 30/11/07)
Sophy Heng BSc
Kerry Herridge BSc
Pei-yu Ho BSc (until 24/6/08)
Jaslyn Lee BBiomedSci
Audrey Lian BBiomedSci (until 31/12/07)
Nadia Sadli BSc (until 14/11/07)
Nirukshi Samarageewa BBiomedSci
Courtney Simpson BSc
Claire Tan BSc (until 31/12/07)
Sarah To BSc

Undergraduate Research Opportunity Program (UROP)
Chris Ip
Lynsey Marshall

Vacation Students
Irene Cheung
Yaojun He
L Atapattu Mudiyanselage
Kheng Ling Ong
Janelle Ryan
Ramya Sivaanandam

farewells 2007/08

In acknowledgement of long standing and valued service to the Institute.

Professor Chen Chen joined PHI in 1991 having being recruited from the Glaxo Labs in North Carolina. Chen built his Endocrine Cell Biology Group into a highly productive team which has contributed to our understanding of the regulation of growth hormone secretion and more recently, the novel hormone, ghrelin. He has been recruited by the University of Queensland to the Chair of Endocrinology within the Department of Physiology: our loss is very much UQ's gain.

Terry Haining has been a long term Financial Manager of PHI (1997-2007). Terry was a strategic thinker, not only within his own area of expertise, but also more widely within the Institute. Terry's style was unique – a habitual tease, but everyone liked and respected him, both on a personal and professional basis. We wish him well on the golf course.

Sabine Kelly began her career as a research assistant with Vincent Harley in 1996 at the Howard Florey Institute and then undertook her PhD with Vince at PHI. Highlights include papers published in the Journal of Biological Chemistry, Molecular Endocrinology and Current Biology. Sabine has competed her PhD and now works at the Walter and Eliza Hall Research Institute.

Dr Margaret Jones came to PHI in 1997 to work with Evan Simpson where she spearheaded research on the reproductive and metabolic phenotypes of the aromatase knockout mouse. Margaret obtained a NHMRC RD Wright Fellowship in 2003. She and her husband, Russell decided it was time for a life-style change and moved back to Perth from whence she originally came.
We miss her cheerful and competent exuberance.

Sue Smith kept John Funder more or less in line for 25 years, and mentored and gently advised a generation of students and postdocs that passed through his lab. Having moved to Gippsland, at the end of 2007 Sue retired (?) to a much less geographically demanding job at the local Monash campus, and to the delights of grandmotherhood.

Sheridan Wallington commenced her journey with PHI in 1999 and had a fantastic trip. Working with the Financial Manager, Terry Haining, she mastered and maintained a new Arrows Accounting System and provided high levels of service in the areas of Payroll and Superannuation. Her devotion to her cats, the stories she shared and her sense of fun is missed by all.

Peter Wood was our Purchasing Officer for 17 years and one of the last who moved with us from St Kilda Rd. Renowned for his ability to obtain good deals with scientific companies and for his holiday adventure tales about chasing white leghorns. We wish him well.

phi committees

BOARD COMMITTEES

Development Board

The purpose of the Development Board is to provide the Institute with strategic advice and direction for fundraising, and building public and corporate awareness of PHI and its research.

Members:
Richard Amos (Chair)
Ronnie Atlas (from 28/2/08)
Robert Barnes
Jock Findlay AO (until 31/12/07)
Jane Glatz (until 31/3/08)
Janet Hibbins (until 30/4/08)
Joshua Mann (from 28/4/08)
Misha Prusa (Secretary from 28/2/08)
Heath Ruddock (until 31/12/07)
Dylan Simmons (from 28/2/08)

Finance and Audit Committee

The purpose of the Finance and Audit Committee is to assist the board in its oversight of the internal control and compliance, accounting and financial reporting, and risk management processes of PHI by setting the 'tone' for quality financial reporting, sound business risk practices and ethical behaviour.

Members:
Stuart Alford (Chair)
Matthew Gillespie (from 1/4/08)
Jane Glatz (until 31/3/08)
Lisa Hinrichsen (until 18/1/08)
David Linley (until 18/1/08)
Carmel Mortell
John Robinson
Terry Haining (Secretary, until 6/12/07)
Peter Murray (Secretary, from 6/12/07)

Intellectual Property & Commercialisation Committee

The role of the Intellectual Property and Commercialisation Committee is to advise the Board and Director on statutory requirements for corporate governance of commercialisation of the institute's intellectual property and related issues. The Committee also audits whether due diligence has been conducted in relation to any commercial activity contemplated, and expenditure to protect existing and new intellectual property. The Committee comprises up to eleven persons including external experts and members of the Board and staff.

Members:
Margaret Lothian (Chair)
Jane Bell (Deputy Chair)
Jay Bonnington
Peter Chalk
Grant Fisher
Jock Findlay
Matthew Gillespie (from 1/4/08)
Jane Glatz
David Robertson
Lois Salamonsen
Andrew McCallum (Secretary)

INTERNAL COMMITTEES

Occupational Health and Safety & Environment (OHSE) Committee

The OHSE Committee provides a forum for consultation and forms a pivotal role in implementing the Institute's OHSE Management System. The representation by members from each research group allows for ongoing communication and information dissemination across the organisation. The two elected OHSE representatives are also part of the OHSE Committee, and as such, ensure that any safety concerns of PHI employees are at the forefront of committee discussions.

Members:
Jane Glatz (Chair)
Anthony Argentaro
Francine Brennan
Maria Docanto
Caroline Foo
Sach Jayasinghe
Ileana Kuyznierewicz
Vicky Kartsogiannis
Yogesh Makanji
Ellen Menkhorst
Irene Papageorgiou
Jyotsna Pippal
Brett Sargeant
Mai Sarraj

Peer-Review Committee

The role of the Peer-Review Committee at Prince Henry's Institute is to ensure that all experimental data intended for publication is written and stored in a suitable fashion to allow independent access and review. In practice, just prior to manuscript submission to a journal, the responsible author will firstly submit their manuscript to a peer-review process, which checks and records data integrity and storage location, and author contributions. PHI undertakes these requirements as part our responsibility in accepting research grant funds from the NHMRC (Aust).

Members:
Paul Farnworth
Neil Owens
Peter Stanton
Gerard Tarulli (until June 2008)

invited presentations

Maree Bilandzic
- Departmental seminar series, Dept. Anatomy and Developmental Biology, Monash University, Melbourne, June 2008

Kristy Brown
- Invited Speaker, International Association for the Study of Obesity (IASO) Bangkok, Thailand
- Invited Speaker, International Association for the Study of Obesity (IASO) 7th Annual Stock Conference, Bangkok, Thailand, March 30th - April 1st 2008.
- Invited Speaker "Workshop on Epithelial to Mesenchymal Transitions in Breast Cancer" Melbourne

Henry Burger
- Invited Speaker, Hormones, Mood & Sexuality Across the Lifespan, University of Melbourne, Melbourne, Aug 2007
- Invited Speaker, 11th Australasian Menopause Society Congress, Adelaide, Sept 2007
- Invited Speaker, Wulf H. Utian Endowed Lecture, 18th Annual North American Menopause Society Meeting, Dallas, USA, Oct 2007
- Invited Participant, International Menopause, Society Workshop, Zurich, Switzerland, March 2008
- Invited Speaker, 12th World Congress on the Menopause Madrid, Spain, May 2008

Ashwini Chand
- Invited Speaker, US Annual Meeting of the US Endocrine Society (ENDO 2008), San Francisco, USA, June 2008
- Invited Speaker, Endocrine Society of Australia, Annual Scientific Meeting, Christchurch, New Zealand, September 2007

Evdokia Dimitriadis
- Invited Speaker, Contraceptive Research & Development Agency (CONRAD, Washington, USA, Nov 2007

Jock Findlay
- Invited Speaker, Issues in Assisted Reproduction, The Fifth Greek Conference, Kos, Greece, September 2007

L - R: Clinical Research Nurse Nicole Fairweather, NAB Ovarian Cancer Research Foundation Research (OCRF) Fellow Dr Andrew Stephens, Witchery Fellow OCRF Dr Adam Rainczuk, Research Assistant Samantha Jayasekara and Principal Research Fellow A/Prof David Robertson

John Funder
- Invited Speaker, The Japan Endocrine Society, Japan
- Invited Speaker, European Society for Hypertension, Milan, Italy
- Invited Speaker, 2nd International Congress on Low Renin Hypertension, Frascati, Italy
- Invited Speaker, 33rd International Aldosterone Conference, Zermatt, Switzerland, October 2007
- Invited Speaker, Cardiology Grand Rounds, University of Rochester Medical Center, NY, USA
- Invited Speaker, Cardiology Grand Round, Mayo Clinic, Rochester, Minnesota, USA

Peter Fuller
- Invited Chair and Invited Speaker, 33rd International Aldosterone Conference, Zermatt, Switzerland, October 2007
- Invited Chair, Annual Meeting of the US Endocrine Society (ENDO 2008), San Francisco, USA, June 2008

Matthew Gillespie
- Invited Speaker, The Australian and New Zealand Bone and Mineral Society Postgraduate Meeting, Melbourne, April 2008
- Invited Chair and Invited Speaker, The Australian and New Zealand Bone and Mineral Society Postgraduate Meeting, Melbourne, April 2008

Vincent Harley
- Invited Chair and Invited Speaker, IBRO World Congress of Neuroscience, Melbourne, July 2007
- Departmental Seminar Speaker, Monash University Physiology Department, Melbourne, August, 2007
- Departmental Seminar Speaker, University of Melbourne, Department of Anatomy & Cell Biology, Melbourne, 2007
- Departmental Seminar Speaker, University of Adelaide CMGD, Adelaide, September, 2007
- Invited Speaker, CSIRO Molecular & Health Technologies, Melbourne, September, 2007
- 2nd World Congress on Hypospadias and Disorders of Sex Development, Rome, Italy, November 2007

Senior Research Fellow A/Prof Vincent Harley, Human Molecular Genetics Group

- Departmental Seminar Speaker, National Institute of Medical Research, London, United Kingdom, November 2007
- Departmental Seminar Speaker, University College of London, London, United Kingdom, November 2007
- Invited Speaker, Tenth Asian Conference on Transcription (ACT-X), Bangalore, India, January 2008
- 29th Lorne Genome Conference, Lorne, February 2008

Rob McLachlan
- Invited Speaker, Uroscience Meeting, Noosa, Q'land, July 2007
- Invited Speaker, Meet-the-Professor, Endocrine Society of Australia, Christchurch, New Zealand, August 2007
- Invited Speaker, Serono Symposium Preservation of male Fertility, Hobart, September 2007

– Invited Speaker, Fertility Society Annual, Hobart, September 2007
– Invited Speaker, RACOG ASM, Gold Coast
– Invited Speaker, Infertility Treatment Authority, Melbourne
– Invited Speaker, GPCE meeting, Sydney
– Invited Speaker, Australian Chinese Medical Association, Melbourne

Sarah Meachem

– Invited Speaker, Annual Meeting of the US Endocrine Society (ENDO 2008), San Francisco, USA, June 2008
– Invited Speaker, Society for Reproductive Biology, Christchurch, New Zealand, August 2007

Ellen Menkhorst

- Invited Speaker, The Moorhouse School of Medicine in Atlanta, Georgia, USA

Guiying Nie

– Invited Speaker, 13th Int. Federation of Placenta Associations, Kingston, Canada, August 2007
– Invited Speaker, 1st World Congress on Reproductive Biology, Hawaii, USA, May 2008

Julian Quinn

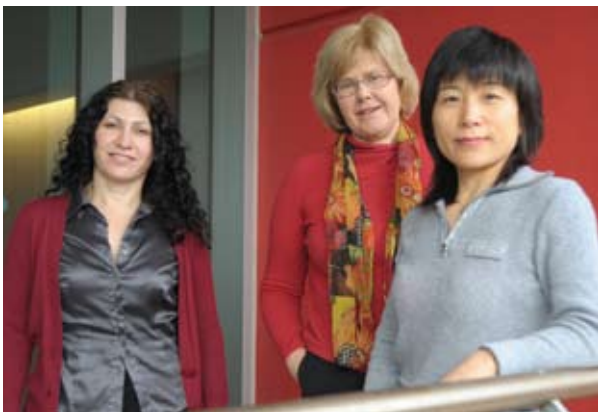
– Invited Speaker, Australian and New Zealand Bone and Mineral Society 17th Annual Scientific Meeting, Rydges Lakeland Resort, Queenstown, New Zealand, September 2007
– Invited Speaker, Brisbane Bone Group meeting, Institute for Molecular Bioscience, University of Queensland, November 2007
– Invited Speaker, The Bone-Joint Interface meeting, Sydney, NSW, June 2008

Lois Salamonsen

– Invited Speaker, 5th Int. Congress on Developmental Origins of Health and Disease, Perth, November 2007
– Invited Speaker, 41st Annual Meeting of the Society for the Study of Reproduction, Hawaii, USA, May 2008
– Invited Speaker, 1st World Congress on Reproductive Biology, Hawaii, USA, May 2008

Mai Sarraj

– Invited Departmental Seminar speaker, Washington State University Pullman, USA, May 2008



L - R: Senior Research Officer Dr Eva Dimitriadis, Senior Principal Research Fellow Prof Lois Salamonsen and Senior Research Fellow Dr Guiying Nie

Kaye Stenvers

– Invited Chair, 'TGF-beta-signalling in development' Symposia, Endrocrinology Society of Australia Annual Meeting, New Zealand, August 2007

Evan Simpson

– Departmental Seminar Speaker, National Institute of Environmental Health Sciences, Research Triangle, North Carolina, USA, July 2007
– Departmental Seminar Speaker, Tele-link seminar, Texas Tech Health Sciences Center - All campuses, Tele-link seminar, Lubbock, Texas, USA, December 2007
– Departmental Seminar Speaker, Center for Reproductive Medicine University of Virginia, Charlottesville, VA, USA, December 2007
– Invited Plenary Speaker, 13th Gynecological Endocrinology Congress, Florence, Italy, February, 2008
– Invited Speaker, 9th Advanced Course on Steroid Enzymes and Cancer, Erice, Italy, May, 2008
– Departmental Seminar Speaker, Westmead Institute, Sydney
– Departmental Seminar Speaker, Institute Molecular Biology, Brisbane, August 2007
– Departmental Seminar Speaker, Hanson Institute, Adelaide, September, 2007
– Speaker and Organiser, Australian Breast Cancer Conference, Melbourne, November, 2007

Sex Hormone Biology Group Leader, Prof Evan Simpson

Morag Young

– Departmental Seminar Speaker, College de France, City, Country, September 2007
– Departmental Seminar Speaker, NIEHS, Research Triangle, North Carolina, USA, October 2007
– Invited Chair and Invited Speaker, 6th International Symposium on "Aldosterone and ENaC: from gene to disease, Zermatt, Switzerland, October 2007
– Departmental Seminar Speaker, Baker IDI Heart and Diabetes Institute, Melbourne, April 2008
– Departmental Seminar Speaker, Department of Pharmacology Monash University, Melbourne, May 2008
– Invited Symposium Speaker, Invited Chair, Annual Meeting of the US Endocrine Society (ENDO 2008), San Francisco, USA, June 2008

visiting speakers

Mr Matias Abregu
GeneWorks
"The Illumina Beadstation microarray platform, and specifics of the analysis platform"

Dr Wah Chin Boon
Howard Florey Institute
"The unexpected effects of estrogen on brain and behaviour"

Dr Georgina (Gina) Caruana
Department of Anatomy and Developmental Biology, Monash University
"Functional genomics of kidney and ureter development"

Dr Timothy J. Cole
Senior Lecturer, Department of Biochemistry & Molecular Biology, Monash University
"Endocrine-regulated pathways in the developing respiratory system"

Dr Jeff Craig & Dr Richard Saffery
Joint Group Leaders, Epigenetics Research Laboratory, The Murdoch Childrens Research Institute
"Epigenetics: you are what your mother ate or your father smoked"

Dr Peter Czabotar
Walter and Eliza Hall Institute
"Structural studies of the Bcl-2 protein family"

Dr Matthias Ernst
NHMRC Senior Research Fellow, Ludwig Institute for Cancer
"Assigning signalling pathways to disease. Genetic dissection of interleukin-6 cytokine biology in the mouse"

Associate Professor Sam El-Osta
Epigenetics in Human Health and Disease Laboratory, Baker Heart Research Institute
"Hyperglycemic variability and the persistence of epigenetic changes associated with gene expression?"

Ms Jennifer Garner
PhD Student, Rice University, Houston, Texas, USA: Intern with Nanotechnology Victoria
"Nanoshell–Assisted Photothermal Tumour Therapy"

Dr Vicki Hammond
Brain development Group, Howard Florey Institute
"The Reelin-signalling pathway and Interneuron Layering in the Mouse Neocortex"

Dr J. Chuck Harrell
University of Colorado Health Sciences Center, Aurora, Colorado, USA
"Dissecting roles of estrogen receptors in breast cancer lymphatic metastasis"

Associate Professor Stuart Hooper
Dept of Physiology, Monash University
"The transition to air-breathing at birth; imaging lung aeration using synchrotron radiation."

Associate Professor Rosemary Horne
NHMRC Senior Research Fellow
Ritchie Centre for Baby Health Research
"25 years of SIDS research: where are we in 2007?"

Dr Rebecca Jones
Maternal and Fetal Health Research Group, University of Manchester, UK
"Endocrine and paracrine regulation of placental function"

Dr Theo Mantamadiotis
Senior Lecturer, Dept Pharmaceutical Biology, Victorian College of Pharmacy, Monash University (Parkville Campus)
"Regulation of gene expression and neural homeostasis by the cAMP Response Element Binding (CREB) protein"

Dr George Mokdsi
Information Services Manager, Griffith-Hack
Training Session: "Performing Patent Searches"

Dr David G. Mottershead
Docent Haartman Institute, Dept of Bacteriology & Immunology, University of Helsinki, Helsinki, Finland
"GDF9, BMP15 and GDF3: Stem Cell Derived TGF-beta Superfamily Members"

Professor George Muscat
Institute for Molecular Bioscience, University of Queensland
"The orphan nuclear receptor ROR alpha regulates lipid homeostasis: insights into the mechanisms involved in resistance to diet induced obesity in staggerer mice"

Professor Michael Parker
Associate Director, Biota Structural Biology Laboratory, St Vincent's Institute
"Structure-based drug discovery at St V's"

Dr John T. Price
Head of Cancer Biology and Metastasis Laboratory, Dept. Biochemistry and Molecular Biology, Monash University
"Stress and Cancer Metastasis: Novel targets and New Insights"

Professor Tony Priestley
Deputy CEO, CRC Water Quality & Treatment
"Assessing Alternative Strategies for the Provision of urban Water"

Dr Danela Rhodes
MRC Laboratory of Molecular Biology, Cambridge, UK
"Structure of the "30nm" chromatin fibre and regulation of its compaction"

Professor Iain Robinson
Division of Molecular Neuroendocrinology, National Institute for Medical Research, London
"Visualising and manipulating the growth hormone axis: tall tales from short tails"

Professor Jonathan R Seckl
Director of Research, College of Medicine and Veterinary Medicine, Endocrinology Unit
Centre for Cardiovascular Science, Edinburgh, UK
"11beta-hydroxysteroid dehydrogenase type 1; from metabolism to memory"

Professor Andrew Sinclair
Director: Early Development & Disease
Murdoch Children's Research Institute
"Testis development: new insights into somatic & germ cell components"

Dr Karen Siu
Physics and Materials Engineering, Monash University
"Medical and biological applications of the synchrotron"

Mr Terry Sunderland
Invitrogen
"Practical demonstration of the E-Gel® CloneWell SYBR Safe™ gels and the E-Gel® iBase™ Power System"

Dr Anne Thompson
Executive Officer, Victorian Cancer Biobank
"Victorian Cancer Biobank: Delivering Biospecimens for Research Outcomes"

Dr Stephen Turner
Pfizer Senior Research Fellow & Senior Lecturer, Department of Microbiology and Immunology, The University of Melbourne
"Acquiring the capacity to kill: Molecular characterisation of virus-specific T cell function"

Associate Professor David Walker
Department of Physiology, Monash University
"Strategies for preventing fetal & neonatal brain damage"

publications
2007

1. Aksglaede L, Andersson AM, Jorgensen N, Jensen TK, Carlsen E, McLachlan RI, Skakkebaek NE, Petersen JH, Juul A 2007 Primary testicular failure in Klinefelter's syndrome: the use of bivariate luteinizing hormone-testosterone reference charts. Clin Endocrinol (Oxf) 66:276-281

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Operating Statement
For The Financial Year Ended 30 June 2008

	2008 $	2007 $
Revenue from operations		
Australian Government Grants	6,291,518	5,956,180
Non-Government Grants	3,570,376	3,387,963
Share of profits from associate using the equity method of accounting	43,798	44,390
Other income	1,841,330	2,112,315
Total revenue from operations	**11,747,022**	**11,500,848**
Expenditure for operations		
Scientific and laboratory expenses	(9,777,736)	(8,669,126)
Administration expenses	(2,055,172)	(2,064,455)
Depreciation expense	(543,093)	(505,943)
Total expenditure for operations	**(12,376,001)**	**(11,239,524)**
Net operating result for the financial year	**(628,979)**	**261,324**

Balance Sheet
As at 30 June 2008

	2008 $	2007 $
Current assets		
Cash and cash equivalents	2,391,351	1,678,314
Receivables	1,380,426	1,751,448
Inventories	-	30,044
Investments in listed companies	7,121,068	9,621,263
Total current assets	**10,892,845**	**13,081,069**
Non-current assets		
Investment in non-listed companies	14,000	14,000
Investments in associate using the equity method of accounting	5,729,825	5,686,027
Property, plant and equipment	1,726,160	1,775,134
Total non-current assets	**7,469,985**	**7,475,161**
Total assets	**18,362,830**	**20,556,230**
Current liabilities		
Payables	2,222,220	1,475,554
Provisions	1,455,587	1,494,437
Total current liabilities	**3,677,807**	**2,969,991**
Non-current liabilities		
Provisions	138,168	163,706
Total non-current liabilities	**138,168**	**163,706**
Total liabilities	**3,815,975**	**3,133,697**
Net assets	**14,546,855**	**17,422,533**
Equity		
Contributed capital	5,711,063	5,711,063
Reserves	1,162,530	3,409,229
Accumulated surplus	7,673,262	8,302,241
Total equity	**14,546,855**	**17,422,533**

Statement of Changes in Equity
For The Financial Year Ended 30 June 2008

	Contributed Capital $	Available-for-sale Revaluation Reserve $	Accumulated Surplus $	Total $
Balance as at 30 June 2006	5,711,063	2,310,034	8,040,917	16,062,014
Movement in fair value of investments in listed companies	-	1,099,195	-	1,099,195
Net result for the financial year	-	-	261,324	261,324
Balance as at 30 June 2007	**5,711,063**	**3,409,229**	**8,302,241**	**17,422,533**
Movement in fair value of investments in listed companies	-	(2,246,699)	-	(2,246,699)
Net result for the financial year	-	-	(628,979)	(628,979)
Balance as at 30 June 2008	**5,711,063**	**1,162,530**	**7,673,262**	**14,546,855**

Cash Flow Statement
For The Financial Year Ended 30 June 2008

	2008 $	2007 $
Cash flows from operating activities		
Receipts from government and other funders	10,232,916	9,984,303
Payments to suppliers and employees	(10,977,507)	(10,586,460)
Goods and Services Tax recovered from the ATO	440,086	864,979
Goods and Services Tax paid to the ATO	(583,165)	(922,956)
Interest received	121,262	100,057
Dividends received	560,740	908,661
Other receipts	1,192,237	691,329
Net cash provided by operating activities	**986,569**	**1,039,913**
Cash flows from investing activities		
Payment for investments	(248,874)	(1,642,587)
Proceeds on sale of investments	502,370	571,826
Payment for property, plant and equipment	(567,873)	(278,102)
Proceeds from sale of property, plant and equipment	40,845	-
Net cash used in investing activities	**(273,532)**	**(1,348,863)**
Net increase / (decrease) in cash held	713,037	(308,950)
Cash and cash equivalents at the beginning of the financial year	1,678,314	1,987,264
Cash and cash equivalents at the end of the financial year	**2,391,351**	**1,678,314**

The summary financial information provided above and on the preceding page, being an Operating Statement, Balance Sheet, Statement of Changes in Equity and Cash Flow Statement, has been extracted from the audited Financial Statements of Prince Henry's Institute. The summary information does not include the notes and other information included in the full set of Financial Statements, which may be obtained from our offices at 246 Clayton Road, Clayton.

The full Financial Statements, from which this summary has been extracted, have been prepared in accordance with the Financial Management Act 1994, applicable Financial Reporting Directions, Australian Accounting Standards, interpretations and other mandatory professional reporting requirements. Australian Accounting Standards include Australian equivalents to International Financial Reporting Standards (IFRS).

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How to contact us

Level 4, Block E, Monash Medical Centre
246 Clayton Road, Clayton, Victoria
T 03 9594 4372
F 03 9594 6125
E reception@princehenrys.org

website www.princehenrys.org

Postal Address
Prince Henry's Institute
PO Box 5152
Clayton VIC 3168, Australia