prince henry's institute
2008/09 scientific report

phi
prince henry's institute
science for better life®

CONTENTS

ABOUT US

Prince Henry's Institute is a not-for-profit medical research institute located at Monash Medical Centre Clayton in Victoria, Australia.

PHI has over 160 staff and students and our vision is to improve quality of life through the investigation of hormones in the fields of reproductive health, cancer, obesity, bone health and cardiovascular disease.

Since its inception in 1960 as the Medical Research Centre at the former Prince Henry's Hospital, we have made significant contributions to health and medicine. The past five decades have seen major discoveries, impacting the lives of tens of millions of people across the globe. Some highlights include:

- New technologies developed by PHI researchers to detect common hormone deficiencies.
- We were part of a team of researchers that, after several decades of intensive research, discovered the reproductive hormone inhibin. This hormone was later used by PHI researchers to produce the first blood test for ovarian cancer.
- PHI research played a key part in the development of a brand new class of drugs to treat breast cancer - aromatase inhibitors.
- PHI studies have proven how the aromatase gene plays an essential role in breast cancer development, sperm formation and the metabolism of body fat.
- PHI jointly developed and commercialised a biochemical test for the detection of endometrial cancer.
- PHI studies have led to a new hormonal method of contraception for men which has shown this can be an effective approach. We are now leading the Australian arm of a major international late-stage clinical trial of male contraception.

Prince Henry's Institute is:

- a partner of the Monash Health Translation Precinct (MHTP)
- an affiliated institute of Southern Health
- an affiliated institute of Monash University
- a member of the Cancer Council Victoria
- a member of the Victorian Breast Cancer Research Consortium Inc.
- an alliance partner with the Ovarian Cancer Research Foundation
- an accredited institute of the National Health and Medical Research Council
- supported by the Victorian Government's Operational Infrastructure Support Program

RESEARCH OVERVIEW

PHI specialises in medical research that improves the detection, diagnosis and treatment of serious health conditions that are controlled by hormones.

Hormones are made by almost every organ of the body and play a significant role in a person's health and wellbeing. Our primary research areas are: Cancer, Cardiovascular disease, Reproductive Health and Positive start to life and healthy ageing

Cancer

Breast cancer

Breast cancer is one of the leading causes of cancer related death in Australian women, with one in 12 women diagnosed with breast cancer before 75.

We have uncovered how certain factors drive breast cancer growth, which is paving the way towards new targeted breast cancer treatments that block cancer growth with fewer side-effects than current approaches.

PHI researchers are also working to identify why cancers such as breast cancer spread to bone and determine ways to limit this growth.

Ovarian cancer

While ovarian cancer isn't the most common cancer, it is one of the most frightening – because most women who are diagnosed with ovarian cancer survive less than five years.

Unlike cancers such as breast cancer, there are no self-examination techniques or discernible symptoms of ovarian cancer and there is no conclusive way to make a diagnosis without surgery. Sadly the result is a very high proportion of late stage diagnoses, meaning the cancer is well advanced and has often spread to other parts of the body.

If ovarian cancer is detected and treated early survival rates increase from less than 30% to 90%.

We are committed to reducing the number of women dying from ovarian cancer by conducting research to find an early detection test for the disease.

Endometrial cancer (cancer of the uterus)

Endometrial cancer is the most common gynaecological cancer. We have identified factors that may affect the progression of this disease and are determining the success of blocking these factors as a form of treatment. We are also working on an early diagnostic test for those at high risk of developing endometrial cancer.

Reproductive health

Fertility

Approximately 15% of Australian couples of reproductive age have problems with fertility. PHI researchers are working to understand the role of hormones in fertility and the changes with age.

We are also working to understand factors regulating sperm production and why this fails, causing infertility and conversely how it can be used for contraception when reversed and suppressed.

Contraception

Between 1995 and 2000 more than 700,000 women, most in the developing world, died due to causes associated with unintended pregnancies. As a result the World Health Organization has identified a critical need to increase contraceptive options for women.

For many women, existing contraceptives are not acceptable or not available. We are investigating new ways to prevent pregnancy as well as block sexually transmitted diseases, including HIV.

We are also studying male hormone contraception, how it affects sperm production and action and whether there are new opportunities to translate discoveries into effective contraception methods.

Pre-eclampsia

Pre-eclampsia is a life threatening condition experienced during pregnancy, which often causes multi-organ failure in the mother and can result in death for both mother and baby. Onset of pre-eclampsia is sudden and as there is no cure the only treatment is pre-term delivery.

Pre-eclampsia is associated with intrauterine growth retardation and babies of low birth weight, which can increase the chance of long-term health problems such as heart disease, hypertension and diabetes in adulthood.

We are endeavouring to develop a test to predict high risk pregnancies for pre-eclampsia, allowing for better management of the condition and reducing life threatening risks to mother and baby.

Cardiovascular disease

Cardiovascular disease (heart, stroke and blood vessel disease) is the leading cause of death in Australia, killing one Australian every ten minutes. In 2006, 46,000 people died as a result of cardiovascular disease, representing a staggering 34% of all deaths.

Around 3.67 million Australians are affected by cardiovascular diseases with 1.10 million Australians disabled long-term as a result. Sadly, over the past decade, the prevalence of heart, stroke and vascular conditions in Australia has increased by 18.2%*.

We are looking at the effects of hormones on the cardiovascular system in order to develop drugs that are better targeted to prevent cardiac failure and treating cardiac problems such as hypertension.

* Statistics sourced from Heart Foundation

Positive start to life and healthy ageing

Disorders of Sex Development

One percent of babies are born with a disorder that affects their sex development, meaning their testes or ovaries have not developed correctly, their genitalia may not be distinctly male or female, the development of their sex anatomy may be incomplete or they may have chromosome abnormalities.

Our aim is to identify the genes that cause disorders of sex development and the mechanisms underlying the formation of testes and ovaries in an embryo.

Neurological Disorders

Chromosomal differences between men (XY) and women (XX), is a key area of investigation for PHI researchers who are especially interested in the SRY or 'male only' gene.

We are unravelling the genetic factors that underlie gender differences in susceptibility to neurological disorders such as Parkinson's disease, schizophrenia and drug addiction.

Bone health

Osteoporosis and other conditions that affect the skeleton, such as orthopaedic implant failure and cancer-induced and inflammatory bone loss, are an enormous health cost burden to Australia.

Whilst there are several therapies available to stop the breakdown of bone, the same is not true for therapies that build new bone.

We are working on new approaches to treatments that build bone and investigating possible treatments for osteoporosis.

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RESEARCH HIGHLIGHTS 2008/09

2008

Older men testosterone boost

A clinical study led by researchers at Prince Henry's Institute provided strong evidence that a testosterone boost could have the benefits for some older men.

Allan CA, Strauss BJ, Burger HG, Forbes EA & McLachlan RI. (2008). Testosterone therapy prevents gain in visceral adipose tissue and loss of skeletal muscle in nonobese aging men. Journal of Clinical and Endocrinology and Metabolism 93, 139-146.

Sex reversal gene

A gene has been identified that is important for male sex determination and the finding may help explain unexplained cases of Disorders of Sex Development.

Bagheri-Fam S, Sim H, Bernard P, Jayakody I, Taketo MM, Scherer G & Harley VR. (2008). Loss of Fgfr2 leads to partial XY sex reversal. Developmental Biology 314, 71-83

Hormone changes in menopausal transition

A series of studies have shown how hormones produced by the ovary are involved with the decline in eggs during late reproductive life.

Robertson DM, Hale GE, Fraser IS, Hughes CL & Burger HG. (2008). A proposed classification system for menstrual cycles in the menopause transition based on changes in serum hormone profiles. Menopause 15, 1139-1144

Development of the ovary

A study has shown that transforming growth factor-beta inhibits follicle development by increasing the rate of follicle death.

Rosairo D, Kuyznierewicz I, Findlay J & Drummond A. (2008). Transforming growth factor-beta: its role in ovarian follicle development. Reproduction 136, 799-809.

2009

Breast cancer, hormones and obesity link

A new molecular link was discovered that helps account for the increased incidence of breast cancer in obese older women.

Brown KA, McInnes KJ, Hunger NI, Oakhill JS, Steinberg GR & Simpson ER. (2009). Subcellular localization of cyclic AMP-responsive element binding protein-regulated transcription coactivator 2 provides a link between obesity and breast cancer in postmenopausal women. Cancer Research 69, 5392-5399.

Study links enzyme to family breast cancer

A study showed that some women, known to be at high family risk of breast cancer, have higher levels than other women of a key enzyme, aromotase, in their breast tissues.

Chand AL, Simpson ER & Clyne CD. (2009). Aromatase expression is increased in BRCA1 mutation carriers. BMC Cancer 9, 148.

Gene link gender identity

The largest ever genetic study of male to female transsexuals found a significant genetic link between gender identity and a gene involved in testosterone action.

Hare L, Bernard P, Sanchez FJ, Baird PN, Vilain E, Kennedy T & Harley VR. (2009). Androgen receptor repeat length polymorphism associated with male-to-female transsexualism. Biological Psychiatry 65, 93-96.

Endometrial repair and activin

In a study that may lead to new treatments of abnormal uterine bleeding problems it was shown that endometrial repair is controlled by the action of activin.

Kaitu'u-Lino TJ, Phillips DJ, Morison NB & Salamonsen LA. (2009). A new role for activin in endometrial repair after menses. Endocrinology 150, 1904-1911.

Sticky proteins required for pregnancy

Research, which may explain why some women have fertility problems, revealed how two proteins are needed for the embryo to successfully attach to the inside of the uterus.

Marwood M, Visser K, Salamonsen LA & Dimitriadis E. (2009). Interleukin-11 and leukemia inhibitory factor regulate the adhesion of endometrial epithelial cells: implications in fertility regulation. Endocrinology 150, 2915-2923.

3D view of sperm development pathway

PHI research has provided a 3D view of how genes and hormones interact in diverse ways during sperm production. This understanding may also lead to novel approaches to male contraception.

O'Donnell L, Pratis K, Wagenfeld A, Gottwald U, Muller J, Leder G, McLachlan RI & Stanton PG. (2009). Transcriptional profiling of the hormone-responsive stages of spermatogenesis reveals cell-, stage-, and hormone-specific events. Endocrinology 150, 5074-5084.

Bone loss mechanisms

A study found that an experimental drug with potential as a diabetes treatment causes rapid loss of bone.

Quinn JM, Tam S, Sims NA, Saleh H, McGregor NE, Poulton IJ, et al. Germline deletion of AMP-activated protein kinase {beta} subunits reduces bone mass without altering osteoclast differentiation or function. FASEB J. 2009 Sep 2.

Proteomics and establishing pregnancy

Proteomics technology has been used to identify novel proteins key to establishing pregnancy. The study showed how the enzyme PC6 is regulated in the uterus.

Kilpatrick LM, Stephens AN, Hardman BM, Salamonsen LA, Li Y, Stanton PG, et al. Proteomic identification of caldesmon as a physiological substrate of proprotein convertase 6 in human uterine decidual cells essential for pregnancy establishment. J Proteome Res. 2009 Nov;8(11):4983-92.

Identification of a protein which inhibits the spread of cancer

A study showed how the molecule betaglycan may affect cell behaviours including the ability of ovarian cancer cells to metastasise.

Bilandzic M, Chu S, Farnworth P, Harrison CA, Nicholls P, Wang Y, Escalona RM, Fuller PJ, Findlay JK, Stenvers KL. 2009. Loss of betaglycan contributes to the malignant properties of human granulosa tumor cells. Mol Endocrinol. 23(4): 539-548.

Ageing and female hormones

A detailed study has helped unpick the complex relationships between several female hormones involved in the menstrual cycle and how these alter in later life.

Robertson DM, Hale GE, Jolley D, Fraser IS, Hughes CL & Burger HG. (2009). Interrelationships between ovarian and pituitary hormones in ovulatory menstrual cycles across reproductive age. Journal of Clinical Endocrinology & Metabolism 94, 138-144.

Immune cells and hypertension

This research has demonstrated an important, unexpected role for the mineralocorticoid receptor in macrophage function and of the macrophage in determining the inflammation in cardiac fibrosis and high blood pressure.

Rickard AJ, Morgan J, Tesch G, Funder JW, Fuller PJ & Young MJ. (2009). Deletion of mineralocorticoid receptors from macrophages protects against deoxycorticosterone/salt-induced cardiac fibrosis and increased blood pressure. Hypertension 54, 537-543.

PHI IN THE COMMUNITY

Medical research should never simply begin and end in the laboratory. Central to research are the benefits it provides to the broader community. PHI embraces the multiple opportunities to engage with the wider community, to share how our discoveries are bringing science to life. The support and generosity of the community also further enhances our capacity to undertake research and for that we are very thankful.

Raising awareness and public support for ovarian cancer

In partnership with the Ovarian Cancer Research Foundation, our researchers have provided scientific expertise at dozens of major community, education, fundraising campaigns such as the NAB Silver Ribbon Appeal and other social events such as L'Oréal Melbourne International Fashion Week.

Media engagement

PHI research discoveries are promoted through local, state, national and international media.

Major coverage in 2009 included our research trial of male contraception, endometriosis research and the discovery of a molecular link between breast cancer and obesity, which was featured nationally on ABC TV news.

Reliable health information for Victorians

Institute researchers provide scientific expertise and editorial content for multiple community health factsheets which are available through the Victorian Government's website Better Health Channel.

PHI on the Internet

In 2009 the Institute developed and launched a brand new "community friendly" web site. New social media initiatives such as Twitter and Facebook also broadened the online opportunities to promote the Institute's latest discoveries.

Community support of clinical research

Hundreds of non-scientists play an essential role in the Institute's research by supporting our research in a very special fashion. These are research participants in clinical studies and trials who are generous enough to give us some of their time.

Hundreds of Victorian women have actively supported our sample collection for ovarian cancer research. Also, during 2009, participant recruitment commenced for the Melbourne arm of a major international study of a new male contraceptive method. The male contraception study is supported by the World Health Organization.

Researchers in the community

Many PHI researchers are active in school education initiatives which promote careers in medical research and innovation. Some researchers have been matched with local schools through the CSIRO's Scientists in Schools scheme. They have developed ongoing partnerships with teachers and these special relationships broaden school students' experiences in their science studies.

Other researchers have gone on the road with the Australian Society for Medical Research (ASMR) to visit schools through country Victoria. The ASMR is the peak body for Australian medical researchers and in 2009 PHI researcher Dr Sarah Meachem was ASMR President. Sarah led dozens of further related events and activities which raised community awareness of Victorian medical research and innovation.

MONASH HEALTH TRANSLATION PRECINCT

The Institute is proud to be associated with Southern Health, Monash University and Monash Institute of Medical Research in the Monash Health Translation Precinct (MHTP). The Precinct has been awarded $71M by the Commonwealth Government towards the development of a new translation research facility.

MHTP
Monash Health
Translation Precinct

MHTP vision

Monash Health Translation Precinct (MHTP) will be a world leader in delivering the best healthcare by translating innovative scientific discoveries into best clinical practice in a dynamic and collaborative environment.

MHTP purpose

Monash Health Translation Precinct is dedicated to translating medical research to improve healthcare; uses clinical insights to focus the agenda of basic research; is committed to innovative research development and enhances research collaboration.

MHTP aims

- To develop the Precinct's capacity for world-leading innovative translational research
- To identify new opportunities for the translation of research into advances in healthcare
- To improve the health and wellbeing of the population
- To encourage collaboration and partnerships between clinicians and researchers
- To optimise productive interactions between MHTP partners and external stakeholders
- To increase efficiency in the utilisation of shared resources and cutting edge platform technologies

MHTP key facts

We are:

- Prince Henry's Institute – world leaders in the field of endocrinology, the study of hormones
- Southern Health – Victoria's largest public health service providing uniquely integrated care across the entire lifespan
- Monash Institute of Medical Research – leaders in stem cell, infection, immunity and cancer research
- Monash University – Australia's largest university with an international reputation for innovative health research

The Precinct is located in Melbourne's South Eastern corridor within the grounds of Southern Health's 640 bed tertiary teaching and research hospital, Monash Medical Centre, and in close proximity to some of Australia's leading research organisations and companies, including the Australian Synchrotron, Monash on-campus Centres, CSIRO and emerging biotechnology entities.

MHTP research themes are specifically aligned to national health priorities:

- Cancer
- Cardiovascular
- Endocrinology and metabolism
- Inflammatory and infectious diseases
- Men's health
- Mental health and neurosciences
- Paediatrics
- Women's health

For further information about Monash Health Translation Precinct visit www.mhtp.org.au

CHAIRMAN'S REPORT

The Institute's report this year is the first under its new structure. In 2009 PHI became a corporate entity limited by guarantee, having previously operated under the Prince Henry's Institute of Medical Research Act.

This change, recommended by the Victorian Government and endorsed by Parliament in 2008, allows the Institute to operate under a structure that better supports the Institute's operations and governance as a modern medical research institute.

Changes to the Board have also occurred and I would like to acknowledge the contribution of former Board members Mr Richard Amos, Mrs Margaret Lothian, Ms Carmel Mortell, Mr Trevor Montgomery, Professor Nicos Nicola, Mr John Robinson and Mr Bob Stensholt.

I would particularly like to thank Trevor Montgomery for his more than 15 years of service during which he made significant and long lasting contributions. Mr John Robinson, should also be recognised for his leadership as the past Chairman of the Board taking the Institute safely through its transition to a corporate entity.

The Institute has been fortunate to secure new Board members - Ms Jennifer Joiner, Professor Steve Wesselingh and Mr John Weste, who all bring with them a range of skills and expertise that will guide PHI through the coming years.

The job of a Board is always easier when it has confidence in the organisation's operational leadership. Institute Director Professor Matthew Gillespie has now been with the Institute for two years and on behalf of the Board I would like to acknowledge his leadership and direction.

The coming year marks the 50th anniversary of Prince Henry's Institute and it is with great pride we look back over achievements of the past five decades and see the contributions PHI has made to the world of medicine.

Highlighted throughout this report are some recent scientific discoveries made by our researchers such as discovering a molecular link that contributes to the increased incidence of breast cancer in obese older women; demonstration of the importance of immune cells in hypertension; identifying a protein which inhibits the spread of cancer and finding that an experimental drug with potential as a diabetes treatment results in rapid bone loss.

It is discoveries such as these and their wide-reaching impact that are at the heart of PHI and why the work conducted here is so important. The new members of the Board are greatly impressed by the calibre of the PHI research team and the importance of the work conducted at the Institute. I hope readers of this report will gain insight into these discoveries as well the ones we are hoping to make in the future.

Bob Edgar
Chairman

DIRECTOR'S REPORT

I am delighted to present the Institute's Scientific Report for the period 1 July 2008 to 31 December 2009. This 18 month reporting period is a consequence of the organisation's transition to become a company limited by guarantee effective 1 January 2009. In order to align our business practices to a calendar year, we provide an 18 month Scientific Report.

A requirement of the new legal entity was a differently constituted Board, and I thank the former Chair, John Robinson and Deputy Richard Amos, as well as Dean Ireland from Egon Zehnder for their assistance and guidance in the recruitment of the new Board. PHI's CFO, Peter Murray, also provided invaluable support in negotiating the transition of the Institute to a Company.

In 2009 the Institute successfully negotiated a variation and extension to its Certified Agreement, and I thank the consultative committee consisting of Maria Alexiadis, Jock Findlay, Caroline Foo, Christina Matisons, Andrew McCallum, Peter Murray, Mai Sarraj and Diane Yallop, for its work in developing the new agreement.

In May 2009 the Commonwealth Government announced a $71M commitment to develop a translational research precinct at Monash Medical Centre Clayton. The facility will unite the efforts of Prince Henry's Institute with its three partners - Southern Health, Monash University and Monash Institute for Medical Research - to form the Monash Health Translation Precinct which will provide high-level knowledge-based clinical delivery. This investment will provide a substantial component of the capital required to develop the Precinct and allow for the seamless transition of the hospital with the current research facilities.

Scientifically, the Institute continues to excel, and this report highlights the community engagement, individual recognition, grant success and training of future scientists. Notably, the work of Vincent Harley and his laboratory was recognised through support of a highly competitive NHMRC Program Grant.

I also wish to highlight two significant individual awards. Firstly, Evan Simpson will be awarded the 2011 Dale Medal from the British Society for Endocrinology. This award is made to a member of the scientific community in recognition of outstanding studies which have changed our understanding of endocrinology in a fundamental way. Secondly, Peter Fuller is to be awarded the 2011 Hoffenberg International Medal from the Society for Endocrinology. This is made to Peter for his outstanding contributions to hormone research and his promotion of international collaboration between researchers. These two eminent international awards attest to the calibre of the research and staff of the Institute.

I would like to thank the Boards and its Committees, current and past, for their support and guidance as the Institute embarks upon 50 years of achievement which will be a focus of the Institute's activities in 2010. Also I extend my gratitude to Peter Fuller and to all members of the Institute for their support and passion for excellence.

I am delighted to extend to you this Scientific Report of Prince Henry's Institute, and am indebted to Ian Muchamore, Sue Panckridge and Katrina Wilkins for its development.

Matthew Gillespie
Director

INSTITUTE GOVERNANCE

Medical Research Institutes Repeal Act (2008)
As a consequence of the Medical Research Institutes Repeal Act (2008) the previous entity Prince Henry's Institute for Medical Research, established under a 1988 Victorian Act of Parliament, transferred all property, rights, liabilities and staff to a new entity, Prince Henry's Institute for Medical Research Inc, independent of Government.

This legislative change permitted the establishment of a new entity effective 1 January 2009. Two independent boards, representing these two entities, were in operation for part of the period covered by this report (1/7/08 to 31/12/09).

Board of Prince Henry's Institute of Medical Research Inc
ABN 48 132 025 024

As at 31/12/09

Chairman
Dr Robert (Bob) Edgar BEcon(Hons) PhD(Econ) FAICD
Bob retired from his position as the Deputy Chief Executive Officer of the ANZ Banking Group Limited in April 2009. He remains on the boards of three of ANZ's Asian banks: AMMB Holdings Berhad, Shanghai Rural Commercial Bank and Bank of Tianjin.
From: 1/4/09

Chief Executive Officer
Professor Matthew Gillespie BSc (Hons) PhD
Matthew is Director of Prince Henry's Institute where he also leads the Bone, Joint and Cancer laboratory. He serves on other scientific boards and Research Committee of the National Health and Medical Research Council.
From: 1/4/09

Treasurer
Ms Jay Bonnington BCom MBA FAICD FCPA
Jay has several non-executive positions on various government and non government boards, which include SE Water Ltd and St. John of God Healthcare Group. She serves on several investment boards.
From: 1/4/09

Mrs Jane Bell BEcon LLB LLM FAICD
Jane practised as a banking and finance lawyer for 22 years. She is also a non-executive director of Westernport Water Corporation, the Victorian Workcover Board and is a Fellow of the Australian Institute of Company Directors.
From: 1/4/09

Associate Professor Wayne Ramsey AM CSC MBBS MHA FRACMA
Wayne is Executive Director of Medical Services for Southern Health.
From: 1/4/09

Mr John Weste MBA BSc
John is a business executive with over 25 years global experience within major organisations and leading management consulting firms. John is currently a Director of The Richelieu Group, an advisory firm focusing on business turnaround and performance improvement.
From: 1/4/09

Ms Jennifer Joiner BEcon CPA
Jennifer is the Acting President Asia Pacific for Applied Biosystems Group. Previous executive posts have included Vice President at Idexx Labs Inc, Vice President Commercial Operations at Bayer AG, and Managing Director of GE Medical Systems Australia Pty Ltd.
From: 1/4/09

Professor Steve Wesselingh BMBS PhD FRACP
Steve is Dean of the Faculty of Medicine, Nursing and Health Sciences at Monash University.
From: 5/11/09

Resignations

Mr John Robinson BSc MGSc FAusImm
From 1/1/09 until 30/3/09

Mr Richard Amos BA (Soc/Legal) BA (PR)
From 1/1/09 until 5/11/09

Board of Prince Henry's Institute of Medical Research

ABN 77 601 754 678

Entity established under the Prince Henry's Institute of Medical Research Act 1988

Until 31/12/08

Mr John Robinson BSc MGSc FAusImm
Chairman
Chairman, Global Mining Investment Ltd; Monash Health Research Precinct Ltd, Non Executive Director, Perserverance Corporation Ltd; Boom Logistics; PSI Ltd

Mr Richard Amos BA (Soc/Legal) BA (PR)
Deputy Chairman
Managing Director, Royce Communications

Professor Matthew Gillespie BSc (Hons) PhD

Ms Carmel Mortell BBus ICA EMBA
Partner, KPMG

Mrs Jane Bell BEc LLB LLM (Lon) FAICD
Non-executive director of Westernport Water Corporation, the Victorian Workcover Board,Fellow of the Australian Institute of Company Directors.

Ms Jay Bonnington BCom MBA FAICD FCPA
Non-executive positions of boards SE Water Ltd and St. John of God Healthcare Group

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
Nominee - NHMRC
Deputy Director, Walter and Eliza Hall Institute of Medical Research

Mr Bob Stensholt MP, BA BD (Hons) MIntLaw Dip Phil
Nominee - State Minister for Health
State Member for Burwood

A/Professor Wayne Ramsey AM CSC MBBS MHA FRACMA
Nominee - Southern Health

RESEARCH REPORTS

BONE, JOINT & CANCER

Bone diseases such as osteoporosis, arthritis and most cancers of bone result in a reduction in bone mass that can lead to fractures. We seek to identify the pathways that are required to build bone or limit bone destruction.

Last year we identified a protein, IL-33, made in the bone. We have found that the action of IL-33 may reduce bone loss and stimulate new bone formation. We are making significant advances in working out how it has these effects, which could be of clinical benefit.

However a complication in using IL-33 directly to treat bone conditions such as osteoporosis is that it can act as a type of hormone that provokes harmful inflammatory responses. To minimise these side effects our challenge is to find a way to increase IL-33 production within the bone without causing large amounts to be released into the bloodstream to cause inflammation.

In other research we are studying a type of anti-cancer drug 17-AAG that has previously been found to be very effective at shrinking tumours in mice. This drug is currently being evaluated in humans. Our studies have found that this anti-cancer drug can cause bone damage and, surprisingly, we have also found increased growth of breast cancer cells that have spread to bone.

This novel drug effect occurs by increasing the number of bone destroying cells in the bone. As the bone is broken down it releases chemicals that stimulate tumour growth.

Why these drugs should have this effect is puzzling, since drugs that block tumour cell growth usually stop bone destroying cells as well.

However, this drug is known to stimulate a type of stress response in cells. We have found that, indeed, cell stress may well encourage formation of bone destroying cells, as drugs that reduce stress responses in cells, blocks the action of this anti-cancer drug.

We have also found that other types of chemically induced cell stress also encourage bone destroying cells. These observations are significant well beyond cancer therapies, as many drugs and some types of bone diseases cause cell stress. This may help explain why in some cases they can damage bone.

Spread of cancers to bone
We have identified some genes that are differentially expressed between breast cancers in the breast and bone. These genes are also differentially expressed in various breast cancers that have different predilection for bone.

Role of osteoprotegerin in breast cancer growth
We identified that osteoprotegerin expression by breast cancers enhances their growth in the breast and bone. We aim to identify how osteoprotegerin enhances tumour growth and the role of stromal cells in this process.

Apo2L/TRAIL as a regulator of cell death
in transformed cells We have identified that Parathyroid hormone (PTH) related protein expression by breast cancers modulates tumour response to TRAIL.

We have identified TRAIL responsive genes and are identifying their contribution to regulation of cell death.

Factors affecting osteoblast differentiation
PTH is currently the best available drug to build new bone. We have identified some genes that respond to PTH and change cells from bone building cells to fat cells and *vice versa.*

Prevention of bone loss
We have defined several factors that inhibit osteoclast formation and wish to identify their mechanism of action and their function upon other cells in bone. This will advance knowledge about the biology of the osteoclast and mechanism to reduce bone loss.

Research Staff
Matthew Gillespie
Steve Bouralexis
Ally Chau
Vanessa Cheung
Vicky Kartsogiannis
Frances Milat
Julian Quinn
Nana Saleh
Melissa Solano

Collaborators
Geelong Hospital, Victoria
Monash University, Victoria
St. Vincent's Institute, Victoria

BRAIN AND GENDER

Our laboratory uses genetic, biochemical, anatomical, and behavioural approaches to determine the mechanisms underlying differences between the male and female brain.

In 2009 we published findings from the largest ever genetic study of male to female transsexuals. The genetic association study found a significant genetic link between gender identity and a gene involved in testosterone action.

From an early age people develop an inner sense of being male or female; their gender identity. Transsexuals however, identify with a physical sex opposite to their perceived biological sex. DNA samples were collected from 112 male to female transsexuals and researchers compared genetic differences with non transsexuals. We discovered that male to female transsexuals were more likely to have a longer version of a gene which is known to modify the action of the sex hormone testosterone.

We believe these genetic differences might reduce testosterone action and under-masculinise the brain during foetal development. As with all genetic association studies it will be important to replicate these findings in other populations. We are now planning even larger genetic studies and are investigating a wider range of genes that may be related to gender identity.

We are also studying the role of sex specific genes in several diseases and conditions where there is a difference between males and females in prevalence, onset and disease aetiology. Of particular interest in these gender differences is SRY, the sex-determining gene on the Y chromosome.

As well as being important in early embryonic gonadal development, SRY gene product is also found in the same areas of the brain that produce dopamine. This chemical plays an important role in behaviour and cognition, voluntary movement, motivation and reward, mood, attention and learning.

We are testing how abnormal SRY function, and abnormal regulation of dopamine, may increase susceptibility of men to neurological disorders such as Parkinson's disease, schizophrenia and drug addiction.

In the case of Parkinson's disease it is known that men are about 50% more likely than women to be diagnosed with the condition. Our research will help to understand the genetic reasons that underlie such gender differences.

Cognitive effects of SRY inhibition in the brain

We are currently testing the hypothesis that SRY, the male sex determining gene, regulates levels of enzymes and brain transmitters in a brain region known as the locus coeruleus. Outcomes from this work will shed light on why men and women differ in their susceptibility to stress and disorders such as anxiety and Attention Deficit Hyperactivity Disorder.

Role of the male-specific gene SRY in Parkinson's disease

We have established the rodent model of Parkinson's disease, including *in vivo* stereotaxic surgery, motor behavioural tests, and histology. We have demonstrated that inhibition of SRY in the substantia nigra, a brain region that controls movement, leads to motor deficits in male rats. Current studies are now determining the role of SRY in men with Parkinson's disease, which occurs when cells in the substantia nigra degenerate.

Sexual dimorphism in neurological disorders

We are interested in understanding the genetic factors that underlie gender differences in susceptibility to neurological disorders. We aim to test whether abnormal SRY function, and therefore abnormal regulation of dopamine, may increase the susceptibility of men to these neurological disorders such as schizophrenia, and addiction to illicit drugs.

Research Staff
Joohyung Lee
Vincent Harley
Daniel Czech
Lauren Hare
Charles Pritchard

Collaborators
Florey Neurosciences Institute, Victoria
Mental Health Research Institute of Victoria, Victoria
Monash Gender Dysphoria Clinic, Victoria
University of California Los Angeles, USA

CANCER DRUG DISCOVERY

This laboratory investigates the mechanisms regulating proliferation of breast cancer cells, with particular emphasis on the role of hormones and their effects on gene expression.

Many challenges still remain in the fight against breast cancer. Approximately two-thirds of patients have disease that can be treated by inhibiting the effects of oestrogen. However, the remaining one-third have fewer treatment options. New therapies are clearly urgently required.

We are working to identify molecules, known as nuclear receptors, that promote breast cancer progression and which may therefore be targeted by therapeutic agents.

Another issue is that inhibiting oestrogen throughout the body can cause distressing side-effects. If one could inhibit its action specifically in breast tissue, these effects could be alleviated. Our group is researching ways in which this might be achieved, and have made advances towards this goal, as described below.

We are also trying to understand how oestrogen production in breast is regulated. In the past we have focused on how hormones and other factors act to regulate oestrogen.

A new avenue that we are now working on is epigenetics. This refers to changes in the structure of genes that are not associated with alterations in the sequence of DNA, but can nonetheless be inherited. Importantly, these epigenetic changes can be reversed by therapeutics. We are working to understand how epigenetics affects oestrogen production and breast cancer risk, and have shown that epigenetics does indeed control oestrogen synthesis in breast.

Nuclear receptor pharmacology
Oestrogen receptor blockers are very successful breast cancer treatments; however, not all patients respond to these drugs and many that do eventually become resistant to their effects.

We are identifying alternative molecules related to the oestrogen receptor that could be exploited as novel breast cancer therapeutics. We have shown that one of these molecules stimulates breast cancer cell division, and as such is a potential exciting new target for drug development.

Breast-specific anti-oestrogens
This research aims to inhibit oestrogen production specifically in breast tissue, in order to reduce the side-effects associated with current anti-oestrogen treatments for breast cancer.

We have identified a protein that activates oestrogen production in breast, but not in other tissues. We have also designed drugs that inhibit this protein, and are currently testing them in experimental models.

Oestrogen regulation in breast cancer
Local oestrogen production within the breast is critically important for breast cancer progression. While the genetic factors that contribute to oestrogen production are fairly well understood, epigenetic factors are much less well studied.

We have shown that oestrogen production in breast is under epigenetic regulation, and are currently unravelling how this occurs.

Aromatase and post-transcriptional regulation
This project is focussed on how these factors are regulated, and its significance for oestrogen production in breast. Our laboratory has identified the transcription factors LRH-1 and SF-1 as critical regulators of aromatase expression and these provide new avenues for the development of cancer therapies.

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CARDIOVASCULAR ENDOCRINOLOGY

One of our major research goals is to provide a better understanding of the underlying mechanisms of cardiac failure and hypertension by studying the function of the mineralocorticoid receptor in these disorders.

Our research is determining the specific cell types in the heart in which the mineralocorticoid receptor (MR) is critical for the development of heart failure. We have been identifying both the cellular and hormonal requirements for tissue-selective blockers of the MR.

Clinical studies have shown clear benefits for MR antagonists in the treatment of heart disease but the widespread use of these drugs is limited by their side-effects. Our studies aim to identify cell and hormone specific mechanisms that will allow for the development of tissue-specific drugs that are free of these side-effects.

We have previously shown an important role for the MR in the onset and development of heart disease. An important step in this disease is the recruitment of inflammatory cells to the heart as part of a tissue inflammatory response. We now have novel data showing that not only are MR signals in the heart tissue required for the onset of disease, but that MR activation, specifically in the inflammatory cells, is central to both heart failure and high blood pressure.

An important observation, from clinical studies, is that the MR antagonists were equally effective in patients that did not have high levels of aldosterone, the hormone normally required for MR activation. We have now shown that cortisol, another closely related hormone, can also activate the MR and cause disease. We have very recently shown that there can be subtle differences in the profile of genes that are regulated by both aldosterone and cortisol binding to the MR. This suggests that the regulation of the MR can be both complex and potentially "fine tuned".

Tissue specific MR activation in heart disease

This research project uses transgenic models to determine the role of specific cell types in the heart that are important for the development of heart disease and hypertension. These studies will facilitate the development of tissue-selective antagonists for the MR in the treatment of heart disease.

Identification of hormone-selective MR antagonists

We are working to identify differences in the activity and conformation of the MR in response to different hormones. This knowledge will form the basis for screening and the development of novel agents for the treatment of hypertension and cardiovascular disease.

Novel mechanisms of MR activation

We have found that some cells cortisol can bind but does not activate the MR under normal circumstances. We now have data to show that these receptor-hormone complexes can be activated by oxidative stress in the heart.

Salt as a novel enhancer of MR function

Elevated levels of aldosterone, in the context of high salt, are a potent mechanism for the development of cardiovascular disease. We have investigated the mechanisms whereby salt acts together with these hormones to promote disease and found that the combination of both treatments results in the expression of a unique set of genes.

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CLINICAL ANDROLOGY

We conduct clinical and basic studies in male reproductive health. Our research is discovering the factors regulating sperm production, why this process can fail in infertility and how it can be reversibly suppressed in contraception. We are also focussed on the important roles across life of the male sex hormone, testosterone.

A safe, effective and reversible contraceptive choice for men is needed as neither condoms nor vasectomy meet these criteria. Injections of testosterone, along with a synthetic type of progesterone, markedly lower the pituitary hormonal drive essential for sperm production resulting in suppression of spermatogenesis, yet maintaining normal blood level of testosterone and thus sexual function and general health.

After years of 'proof of concept' research, PHI continues its involvement in this field through participation in an international multicentre trial of testosterone plus norethisterone enanthate as a reversible male hormonal contraceptive regimen. Commencing in 2008, the study is sponsored by the World Health Organisation and CONRAD, USA. Internationally, several hundred potentially fertile healthy couples in stable relationships will participate in this two year study. Eligible couples use this method as their only contraceptive for a one year period. The primary endpoint is the prevention of pregnancy but a range of secondary and safety endpoints are monitored.

One in eight couples experience difficulty in achieving a pregnancy. In one third, a male factor seems responsible, particularly the production of inadequate numbers of motile and functional sperm. In a minority, clear causes can be found but in most a complex genetic problem involving the 3,000 genes important in spermatogenesis are likely at fault.

Animal studies have not contributed greatly to understanding human spermatogenic disorders, the role of clinical research and genetic must be emphasised. The regulation of the cell division and structural changes involved must be described so that new diagnostic tests and treatments to improve sperm output can be developed.

Testosterone deficiency can have profound effects on males at all stages of life, for example during male foetal and pubertal development, and in adult life when it affects not only sexual function but also bone, muscle and cardiovascular health, and mood and cognition. Testosterone's potential role in preventing or ameliorating declining physical and psychosexual function in ageing and in prevalent disease states such as obesity and diabetes is the subject of intense research interest.

Genetics of male infertility

We are researching the importance of DNA, chromosomal defects and oxidative sperm DNA damage in male infertility. We are utilising a database of clinical information and DNA from over 2000 men. These studies have implications for diagnosis and management infertility, and for the health of children conceived using Assisted Reproduction Technologies.

Developing new reversible male contraceptives

During 2009 about a dozen couples were recruited into the WHO-sponsored trial. Sperm output has been seen to drop within a few months and several have already begun using the method as their only contraception. In addition we are using human and animal models to explore exactly how the withdrawal of pituitary hormones blocks sperm production such as through disruption of cell junctions in the wall of the seminiferous epithelium.

Testosterone replacement therapy in obese men

We have completed a placebo controlled study of testosterone replacement with 40 men. These middle-aged and older obese men were also offered dietary advice. Many endpoints were assessed including body composition (muscle and fat content), insulin sensitivity, lipids, markers of cardiovascular health, sexual and quality of life questionnaires and various safety parameters. Preliminary outcomes from this study are expected to be presented later in 2010.

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EMBRYO IMPLANTATION

Our laboratory is understanding how the endometrium prepares itself for implantation and how a healthy placenta develops. Further, it is exploring female contraceptives that can also be combined with agents that prevent sexually transmitted diseases.

Our research aims to determine the molecular changes in the placenta that are critical for establishing pregnancy. Manipulating these molecules may then be used to either enhance pregnancy outcomes or useful as new non-hormonal contraceptive strategies.

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 embryo trophoblasts cells with the mother's blood supply, from which the developing foetus will obtain nourishment and oxygen. Trophoblasts cells eventually form part of the placenta.

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.

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Endometrial-placental interactions and healthy pregnancy

Successful implantation of a human embryo into the endometrium is an important early step towards the formation of a healthy placenta (placentation) and a healthy baby. Impaired implantation can result in inadequate placentation and lead to miscarriage, preeclampsia and even maternal death.

Research is focussed upon understanding how fetal-trophoblast cells interact and invade through the endometrium to form a healthy placenta. We have determined how endometrial proteins interact with placental trophoblast cells to restrict trophoblast invasion. These interactions are critical for the establishment of a healthy pregnancy.

Implantation factors, fertility and IVF

The failure of a human embryo to implant in an adequately prepared maternal endometrium (receptive endometrium) results in infertility. There is significant evidence that such endometrial infertility is important in many failed IVF attempts. Presently, there is no available clinical method of diagnosing endometrial infertility, however our research is addressing this gap.

We have recently identified two cytokine factors that prepare the endometrium for implantation. These molecules regulate the adhesive properties of both endometrial and trophoblast cells. We therefore believe that these factors may have a role in the attachment of the human blastocyst to the endometrium.

Development of non-hormonal contraceptives

We have demonstrated that blocking the action of two cytokines with unique inhibitors results in total pregnancy failure in mice. We are currently investigating the effect of delivering these cytokine inhibitors with agents that also block sexually transmitted diseases including HIV on pregnancy outcome. We have determined that vaginally applied compounds reach the endometrium and block implantation in mice suggesting that these compounds could be coupled either with or without vaginal microbicides.

New treatments for endometrial cancer

Endometrial cancer is the most common gynaecological malignancy. It typically affects postmenopausal women however there is also a significant increased risk in women over 40 years old. Current treatment options for advanced disease remain inadequate.

We have now identified two proteins that may be important in the progression of this disease. Research is determining the effect of targeting these proteins with specific inhibitors and this approach may ultimately lead to novel cancer treatments.

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ENDOMETRIAL REMODELLING

We study how the endometrium is restored after menstruation and how it becomes receptive for embryo implantation. Failure of these events can result in abnormal uterine bleeding and infertility.

The lining of the womb, known as the endometrium, is completely shed at menstruation and rebuilt during the next menstrual cycle. At about 20 days, following the onset of menstruation, the endometrium reaches a state known as 'receptive'. Only at this time is it possible for an embryo to implant, for a placenta to develop and a pregnancy to be successfully established.

We have recently discovered critical factors that drive endometrial repair following menstruation and others that are important for development of uterine receptivity. We are now determining just how these factors work and how they may be applied to improve women's health.

Repair of the endometrium is unique in that it occurs without scarring, the only adult tissue to heal in this fashion. We have developed two important models that are helping us understand endometrial repair. This will lead to new treatments for uterine bleeding problems in women, and will also identify factors that may help in treating wound healing so that it occurs without scarring.

Before embryo implantation can occur, the endometrium must become 'receptive' and the early embryo must appropriately prepare so that it can attach to and invade the endometrium. At this time it is bathed in uterine fluid, secreted by the receptive endometrium.

Using new proteomic techniques, developed at PHI, we have been able to identify regulatory molecules in the fluid. These may enable us to develop new tests for endometrial receptivity that can be used to establish causes of infertility and guide clinicians to improve the success rates in IVF treatment.

New approaches are being taken to study endometriosis, an enigmatic disease in which endometrial tissue grows outside the uterus often causing debilitating pain. The condition affects the quality of life of one in eight Australian women, yet we know very little of how it occurs and why it often causes infertility.

Understanding scar-free endometrial repair

Using a mouse model and a human cell culture model of endometrial breakdown and repair, along with laser captured tissue, we have identified a number of critical molecules for endometrial repair. These are components of the extracellular matrix, cell adhesion molecules and proteases.

The proteome of uterine fluid

We have identified many previously unknown proteins in uterine fluid. Most are produced by the cells of the endometrium that interface with the uterine cavity and change with the menstrual cycle. Some are disturbed in infertile women. We are looking at how these factors affect both the endometrium and the embryo to promote implantation.

How the embryo talks to the endometrium

We have shown how a hormone produced by the early embryo is essential for implantation and pregnancy. The hormone acts on the outermost cells of the endometrium, changing the products they secrete into the endometrium and hence improving the chance of successful attachment and implantation.

Endometriosis related proteins

We have analysed in detail the proteins present in the endometrium of women without and with endometriosis and shown that there are many proteins that are dysregulated in women with endometriosis, both in terms of their abundance, but also in their biochemistry.

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GROWTH FACTOR SIGNALLING

The TGF-beta family of proteins plays crucial roles throughout development and in the maintenance of tissue homeostasis in adult life. Our group is exploring the mechanisms that govern the availability of active TGF-beta ligands and the consequences of dysregulated TGF-beta signalling.

We are developing methods to control TGF-beta superfamily signalling in disease.

It is recognised that inhibiting the activity of TGF-beta ligands is an effective strategy for restoring homeostasis in disease-affected tissues.

Based on this approach, pharmaceutical companies have administered TGF-beta antagonists (e.g., binding proteins or soluble receptors) to restore tissue homeostasis in a range of conditions, including neuromuscular diseases, metabolic disorders and cancer-related bone and muscle loss.

Significantly, several of these antagonists have already proven effective in Phase I clinical trials. However, within the TGF-beta superfamily, extracellular binding proteins and signalling receptors have multiple specificities and result in significant off-target effects.

Thus, there is a need to develop specific antagonists of individual TGF-beta ligands. To accomplish this important goal, we are leveraging our understanding of the structure-function of TGF-beta superfamily proteins.

Recently, we have determined how TGF-beta ligands are synthesised, processed and secreted from the cell, and the regions within these proteins that determine their extracellular activation. These findings are novel and provide us with a unique opportunity to develop specific antagonists of TGF-beta ligands that control tissue homeostasis or are implicated in the pathogenesis of disease.

Synthesis, secretion and activation of TGF-beta proteins

We have discovered that a common biosynthetic pathway governs the synthesis and secretion of TGF-beta proteins. This has enabled us to understand why some TGF-beta ligands are secreted in an “active” form, while others are secreted in a “latent” form.

Inhibin A and B in the reproductive system

Inhibins, members of the TGF-beta family, regulate fertility by inhibiting follicle stimulating hormone (FSH) secretion by the pituitary. We have shown that inhibin B is the primary regulator of FSH *in vivo* and that its activity is dependent upon the co-receptor, betaglycan.

Nodal signalling in cancer

Nodal is a critical factor during early embryo development. Until recently, Nodal expression was thought to be embryonically restricted; however, we and others have shown that Nodal pathway activity is up-regulated in many human cancers. We are characterising the components of the Nodal receptor complex, in order to develop reagents to inhibit Nodal signalling in cancer.

Myostatin and muscular dystrophy

The use of broad-spectrum TGF-beta antagonists may be an effective strategy for promoting muscle growth in a variety of myopathies, including Duchenne muscular dystrophy. We are utilising gene transfer to deliver TGF-beta antagonists directly to muscle.

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IMPLANTATION AND PLACENTAL DEVELOPMENT

The uterus provides a "fertile soil" for the embryo to implant and grow. Implantation failure is a significant cause of female infertility. We seek to understand how the uterus becomes receptive for embryo implantation and how a healthy placenta develops.

Our previous research has identified that proprotein convertase 6 (PC6) is tightly controlled in the uterus during its preparation for receptivity and is critical for embryo implantation. The challenge was to understand how PC6 works to facilitate uterine conversion from a non-receptive to a receptive state. We have made significant advances in this area of research.

We have hypothesised that PC6 activates a cohort of other proteins to change the uterine microenvironment to make it favourable for implantation. We utilised a contemporary technique called proteomics and set out to search for these PC6-target proteins. This led to the discovery that PC6 regulates key cytoskeletal proteins as well as essential growth and differentiation factors in the uterus. These novel and exciting findings have proved our hypothesis and significantly advanced our understanding of how PC6 works. Importantly these discoveries suggest that PC6 acts as a critical "master-switch" molecule for the establishment of uterine receptivity.

We had already discovered a new gene called HtrA3 and identified that it was a previously unrecognised factor important for placental formation and function. We have now shown that HtrA3 is regulated by oxygen tension during placental formation, and that abnormal maternal blood HtrA3 levels during early pregnancy may be associated with development of pre-eclampsia.

Role of PC6 in regulating embryo implantation and fertility
We are determining the molecular mechanisms of PC6 action in the uterus for embryo implantation. We are also investigating the clinical implications of uterine PC6 regulation in evaluating uterine receptivity, uterine fertility and infertility. We have successfully applied proteomics technology and identified a number of novel proteins that are regulated by PC6.

PC6 is a potential target for simultaneous prevention of pregnancy and HIV infection
Our studies suggest that PC6 is a novel target for the development of new female contraception which could also protect women from HIV infection. We are currently conducting experiments to prove this concept in animal and cell models.

HtrA3 in placental development and pregnancy disorders
We are investigating the molecular mechanisms of HtrA3 action during placental development, and the contribution of HtrA3 dysregulation in pregnancy disorders such as pre-eclampsia and intra-uterine growth restrictions. We are also establishing a sensitive and high through-put assay to measure HtrA3 in the blood.

HtrA3 in cancer and ageing
In addition to placental development, HtrA3 is also known to be a tumour suppressor. Our research indicates that the involvement of HtrA3 in cancer is intertwined with ageing. We are characterising the biochemical properties of HtrA3, and investigating its role in cancer in general and in the context of ageing.

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MALE FERTILITY REGULATION

Our overall aim is to identify how hormones control sperm production, or spermatogenesis. This research is central to finding new mechanisms of contraception in men and also in understanding causes of male infertility.

We approach this problem by first identifying the key hormone-regulated cell types in the testis, and then finding the key proteins and molecules within these cells.

During sperm production, the Sertoli cells of the testis nurture the immature germ cells as they develop into mature sperm. We have identified processes that are regulated by hormones and are critical for sperm production. In particular we focus on the junctions between the Sertoli cells that are critical for normal germ cell development and also the process by which sperm are released from Sertoli cells at the end of their maturation phase. We study all aspects of these processes, including what genes and proteins are involved, how they are regulated and how we can modulate them.

We also have initiated a series of studies aimed at discovering new hormone-regulated genes and proteins in the testis using genomic and proteomic technologies. These technologies allow us to discover new genes and proteins that are important in sperm production, but have never been studied in this process. This gives us the opportunity to find new targets for male fertility regulation, as well as providing us with a much more comprehensive understanding of sperm production.

We also aim to identify serum protein markers that reflect cellular processes, such as germ cell differentiation or response to hormones, for use in basic and clinical research in andrology. We do this by applying state-of-the-art proteomic technologies to blood samples from normal men and from men in which sperm production is compromised. By studying which proteins differ, we have the potential to discover ways in which different types of infertility can be diagnosed by a simple blood test, rather than by a testis biopsy as is currently required.

How hormones regulate gene expression during sperm production

In 2009 we completed a study which revealed new complexities in how hormones co-ordinate the expression of genes during sperm production. By utilising genomic technologies and databases, we were able to simultaneously study thousands of genes as they were increased or decreased by hormones in the different cell types of the testis. This study provided a “3-dimensional” view of sperm production, and has become a fundamental resource providing new information as to how this process is regulated.

Regulation of Sertoli cell junctions

We have identified that growth differentiation factor 9 (GDF9), which is essential for ovarian function, is also produced by germ cells in the testis. GDF9 acts locally to regulate Sertoli cell functions, including cell junctions. Our ongoing studies will identify the molecular pathways that are activated by GDF9 and related growth factors, to provide potential new ways to control the function of Sertoli cell junctions.

Proteomic discovery programme in male reproduction

We have identified a number of serum-based proteins which differed in a comparison between normal and infertile men. We are now determining whether these proteins will act as markers of testicular function.

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METABOLISM AND CANCER

Our goals are to understand the role of sex hormones in energy homeostasis, and how disregulation of metabolism leads to increased risk of breast cancer. We believe that the role of obesity and ageing in increased breast cancer risk is mediated in part through the regulation of oestrogen formation within the human breast.

Last year we reported that the LKB1/AMPK pathway inhibits oestrogen formation in the breast and we showed that the association of obesity with increased breast cancer risk is a consequence of inhibition of this pathway. This effect is mediated by the opposing actions of the adipokines leptin and adiponectin.

We have also been pursuing studies to understand the molecular basis of insulin resistance in the aromatase knockout (ArKO) mouse, which cannot synthesise oestrogens.

ArKO mice have an elevated androgen to oestrogen ratio and we are investigating the role of androgens to induce insulin resistance in female adipose tissue. This is being conducted since androgen excess in women may be a modifiable risk factor for type 2 diabetes and the Metabolic Syndrome.

Obesity and breast cancer risk

The anti-diabetic drug Metformin has been implicated as protective in terms of breast cancer risk. We have now shown that this protective action is mediated in part by stimulation of the LKB1/AMPK pathway resulting in inhibition of oestrogen formation in the breast.

Insulin resistance in the ArKO mouse

We are pursuing this work by conducting glucose, insulin and pyruvate tolerance tests, and by studying the insulin signalling pathways in muscle and liver. Our conclusion is that insulin resistance in this model occurs primarily in the liver and not in the muscle.

Adipose tissue metabolism in women

We have shown that androgens, when added directly to adipocytes derived from subcutaneous adipose of women in culture, inhibit insulin uptake by the cells, and this action is inhibited by blockers of the androgen receptor. Moreover, spironolactone, commonly used in women with androgen excess, improves uptake of insulin in these cells, independently of insulin action.

Regulation of somatic and germ cells in the testis

We are studying the regulation of somatic and germ cells in the testis, using well-characterised models and clinical samples of infertility to identify mechanisms of control in the healthy and diseased testis.

We have shown that infertility in men due to impaired spermatogenesis is due to malfunctioning of their Sertoli cells. This is a consequence of immaturity of the Sertoli cell population.

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OVARIAN BIOLOGY

Our laboratory is broadly interested in the roles that local and systemic hormones and TGF-beta superfamily members play in regulating ovarian development, function, and disease, as well as identifying the factors that regulate the supply of eggs in females.

The pool of oocytes (eggs) in a female is set at or around birth, and thereafter there is a steady decline in this pool until the ovarian supply of eggs is exhausted – in women this is called menopause. We do not know what factors control the activation and growth of a small number of these primordial follicles each day, nor do we know with any certainty what local and systemic factors control the subsequent growth or death. Our research findings in this area underpin novel approaches to regulate the supply of eggs with a view to extending the fertile period and thus delaying the onset of menopause.

A major unwanted side effect of many cancer therapies is infertility. The chemo- or radiation therapies used to treat cancers can destroy the ovarian primordial pool of eggs leaving the individual infertile. This is a particular problem for young women being treated for cancer who may desire to have children later in life. Current practices to reduce these side effects are limited and inefficient.

In collaboration with colleagues we are determining the regulatory factors that control the development of immature oocytes and the establishment and maintenance of the primordial follicular pool, both of which impact upon adult reproductive capacity. We are now exploring how this work might be applied to a therapy to prevent infertility in girls and young women undergoing cancer treatments.

Hormonal regulation of folliculogenesis

We have been investigating the role of members of the transforming growth factor beta (TGF-beta) family in follicle growth and found that both activin and TGF-beta itself, can influence these processes.

We have used an in vitro culture system to examine the effects of members of the transforming growth factor-beta family on growth and death of rat egg follicles. The data shows that both activin and TGF-beta can influence these processes, confirming that local growth factors are important in the development of follicles in the ovary. Disruption of the action of these factors could lead to abnormal or inappropriate development including cancer. In collaborations we are now examining the role of follistatin, an endogenous inhibitor of activin, in the development of follicles.

Developmental origins of infertility disorders and ovarian disease

The size of the primordial pool of eggs is set at or around birth after an extensive wave of oocyte proliferation and death in the foetus. The factors responsible for these processes are not understood. We have made the novel observation that BH3-only genes in the cell death pathway are involved. We are now exploring how and when these genes are involved and if the extra eggs that can be generated at birth by preventing oocyte death result in prolonged fertility.

These same genes are involved in oocyte death after radiotherapy. When these genes are 'knocked out', radiation damage of the eggs is significantly reduced, and the mice remain fertile. This opens the possibility of targeting these genes as a way of protecting the ovary from chemo- or radiation damage.

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OVARIAN CANCER BIOMARKERS

Ovarian cancer is one of the most lethal gynaecological cancers, owing to a lack of recognisable symptoms and the often late diagnosis. We are applying proteomics technologies to identify new biomarkers for the development of an early stage screening test.

In order to develop a suitable screening test for ovarian cancer, markers must be identified that can accurately detect tumours at a very early stage, while the cancer is still confined to the ovary and of low volume.

Over the past year we have made good progress and are now exploring in detail multiple proteins that we believe may be useful candidates for the development of an early stage screening test. We have identified several key molecules involved in the growth and development of tumours and observed that these are significantly elevated in patients diagnosed with early stage tumours. We are examining these new markers for their sensitivity and specificity in multiple patients, to evaluate whether they might be useful clinical markers of cancer.

We are also continuing to recruit patients for the ovarian cancer research program. This recruitment has been highly successful, with over 450 women generously providing tissue and blood samples for our research. The clinical collection program is now being expanded beyond Victoria to include recruitment through hospitals in Sydney and Brisbane. This larger pool of clinical samples will provide enough statistical power to test new candidate proteins and evaluate their potential as clinical markers of ovarian cancer.

Circulating markers of ovarian cancer

We have identified nine proteins that may be suitable as clinical markers of ovarian cancer. These proteins are present at higher levels in patients with early stage tumours than women with other benign or malignant gynaecological conditions. We are now examining these proteins to determine whether these changes are found in all patients.

Auto-immune response in cancer patients

Cancer patients exhibit an immune response to their tumours at the earliest stages of progression This response is often before other clinical symptoms are apparent. We have now developed a platform to isolate and identify auto-antigenic proteins directly from patient plasma. Studies are ongoing to identify and characterise such proteins as specific markers of the early stages of tumour formation.

Nanoparticle technology for the identification of novel cancer markers

Our team has developed and refined a novel nanoparticle technology which allows us to capture and compare proteins from patient samples. Using this technology we have been able to identify large numbers of proteins that are usually not present at sufficient levels to be detected by proteomics technologies. One protein identified thus far appears to be unique to cancer patients, and is being evaluated further.

Fallopian tube as the origin of epithelial ovarian cancers

Recent evidence suggests that many epithelial-type ovarian tumours may arise on the fimbriae of the fallopian tubes. We have cultured cells from the fallopian tubes of cancer patients, and further work will examine whether these cells can be developed as a model for cancer development.

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REPRODUCTIVE DEVELOPMENT & CANCER

Our laboratory uses combined molecular and cellular approaches to determine the mechanisms underlying cell growth and migration in the ovary and testis, both during normal foetal development and during cancer progression.

Our current work focuses on identifying key factors governing the formation and maintenance of healthy ovaries and testes. The aims of our work are to discover new knowledge about these processes and apply these discoveries to the treatment of diseases of the reproductive organs.

The processes by which the ovary and testis are formed during foetal life are poorly understood. We have previously shown that a protein called betaglycan, which facilitates the actions of several cellular growth factors, influences the development of the gonads.

In particular, we have recently shown that mice which are depleted of this protein have birth defects in the ovary, testis, and kidney.

We recently showed that betaglycan is essential for the successful establishment of foetal testis structure and function. Without betaglycan, the foetal testis produces significantly less of the reproductive hormones that regulate the development and functioning of the male reproductive tract.

As compromised testis development is associated with low sperm counts, infertility, and testicular carcinoma *in situ* in adult men, our results have relevance to human clinical disease.

We have also found that betaglycan has important roles in controlling the growth and motility of human granulosa cells, the key support cells for the developing eggs in the ovary.

We showed that granulosa ovarian cancers exhibit a significant reduction in betaglycan expression, resulting in increased motility and invasiveness of the tumour cells, two cell behaviours which underly the ability of cancer cells to metastasise.

Furthermore, re-introducing betaglycan into human ovarian cancer cells resulted in nearly complete blockage of cell motility and invasion.

Ovarian cancers are the most lethal gynaecological cancers in women, with most women dying from the spread of cancer to distant organs. Thus, our current work on betaglycan may help to develop new therapeutic strategies to block the spread of cancerous ovarian granulosa cells.

Controlling the spread of ovarian cancer

We established in human ovarian granulosa cancer cells that betaglycan blocks cell motility and invasiveness, and thus has the potential to block metastasis in clinical disease. We aim to determine how betaglycan regulates cell motility and to establish the therapeutic potential of this protein.

Factors that regulate the death of cancer cells

We have recently established that TGF-beta, betaglycan, and their downstream signalling molecules regulate ovarian granulosa cell survival. We are determining the contribution of this dysregulated granulosa cell growth to the development of ovarian pathologies and cancer.

Mechanisms of foetal urogenital system development

We have demonstrated that betaglycan and the factors that interact with this protein are required for the successful development of the foetal gonads and kidneys. We are establishing the mechanisms underlying the actions of these factors during the development of these organ systems, with the aim of advancing the knowledge about human birth defects and their impact on human health.

Research Staff
Kaye Stenvers
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Ruth Escalona
Mai Sarraj
Kenneth Walker
Yao Wang

Collaborators
Institute for Molecular Bioscience, Queensland
Monash University, Victoria
Murdoch Childrens Research Institute, Victioria
The Royal Women's Hospital, Victoria
Washington State University, USA

REPRODUCTIVE HORMONES

We study how pituitary hormones regulate the ovary and testis and conversely how the hormones produced by these organs regulate the pituitary gland. This research has clinical relevance in understanding how hormones regulate fertility.

We have a long standing interest in studying how hormones in the circulation are important in regulating fertility. The pituitary gland produces two hormones, follicle stimulating hormone (FSH) and luteinising hormone (LH). These two hormones stimulate ovaries to produce follicles containing eggs. The ovary in turn produces hormones such as inhibin and estradiol to suppress these pituitary hormones so that the formation of multiple eggs is controlled.

Endocrinology of menopausal transition

As women get older the number of eggs available diminishes. This leads to an alteration in the balance between pituitary and ovary hormones. In collaboration with researchers from Sydney we have been exploring how this balance changes in women approaching to menopause.

The hormone patterns in ovulatory menstrual cycles in late reproductive years are similar to those seen in younger women although it is recognised that fertility is diminished since older eggs are more likely to be defective.

We showed that levels of the ovarian hormone inhibin decreases with age, presumably because the number of developing egg follicles has diminished. As a further consequence we have observed increased levels of the pituitary hormone, FSH. Thereafter the menstrual cycles become increasingly more disorganised, in part because we believe there are less eggs developing and because the pituitary hormones levels are now too high resulting in an overstimulated ovary.

We are now collaborating with Canadian researchers to explore changes in the pattern of egg follicles during this process. We are combining detailed ultrasound imaging with an examination of the age related changes in fertility hormones.

Anti- Mullerian Hormone and fertility

One of the conclusions of our menopause transition studies has been the apparent importance of another ovarian hormone, anti-mullerian hormone (AMH). This hormone also appears to be a good marker of egg reserve in women, however little detail is known.

In collaboration with a research group in the Netherlands we are investigating what forms of this hormone are secreted into the circulation. These studies will help establish AMH's bioactivity in regulating the pituitary hormones, FSH and LH.

Understanding Ovarian Hyperstimulation Syndrome

In a collaborative project we are using proteomic methods to identify a panel of blood proteins that are predictive of ovarian hyperstimulation syndrome. This clinical condition is a rare but important consequence of hormonal stimulation of ovaries in women undergoing an in vitro fertilisation stimulation program.

Ovarian Health Study

There are currently no programs to assess ovarian health in postmenopausal women. This Ovarian Health Study has described the ovaries in 500 healthy women at least five years after menopause. The survey collected data using by questionnaires, transvaginal ultrasound (TVU) and blood ovarian cancer markers.

We have concluded that the use of TVU in women at least 5 years after menopause is problematic because the ovaries cannot be visualised in all women and also that it may pick up many benign lesions. These are important considerations in weighing up the risks and benefits of using TVU as a community screening tool.

Research Staff
David Robertson
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Enid Pruysers
Debora Romero

Collaborators
Erasmus University, The Netherlands
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University of Saskatchewan, Canada

SEX DETERMINATION AND GONADAL DEVELOPMENT

Between one in 100 and one in 300 babies are born each year with some form of Disorder of Sexual Development (DSD). These conditions encompass a wide range of abnormalities including hypospadias, gonadal dysgenesis, ambiguous genitalia, or sex reversal.

Using human genetics, molecular, cell and developmental biology approaches, our research is identifying the genes causing DSDs and the molecular mechanisms underlying testis and ovary formation in the embryo.

The molecular battle between the sexes

Testis and ovary development have long been considered independent pathways, with the Y chromosome 'master' gene, SRY, acting as the dominant inducer of testis development and ovarian development being considered the 'default' pathway. Our recent studies, and those of others, indicate that sex determination in males and females is complex and regulated by both positive and opposing signals.

In XX females, the Wnt/beta-catenin pathway, activated by R-spondin 1, is involved in both ovarian differentiation and the blocking of male testicular differentiation. R-spondin-1 is a key ovarian gene in this process since certain DSD patients (XX males) carry R-spondin 1 gene mutations.

In XY individuals, SRY expression triggers the upregulation of SOX9 that directs the differentiation of the Sertoli cells within the testis. In recent studies we have shown that SRY expression also triggers a cascade of events leading to the inhibition of the ovarian development, specifically by inhibiting Wnt/beta-catenin signalling.

Conversely, during ovarian development, we have demonstrated that beta-catenin inhibits SOX9 gene expression. Ongoing studies are now mapping the precise molecular mechanisms by which Wnt/beta-catenin and SRY/SOX9 pathways antagonize one another during the formation of either a testis or an ovary.

Identification of novel genes causing DSDs

We are identifying the underlying molecular and cellular events that cause human disorders of sexual development (DSD). In one approach, we are undertaking a mutagenesis screen using N-ethyl-N-nitrosourea (ENU) to identify novel genes involved in gonad development. We have now identified several strains of mice which have affected testis development and these models are under investigation.

In a second approach, we are using Array Comparative Genomic Hybridisation (CGH). This procedure compares the genomes of individuals with DSDs of unknown etiology, to identify genomic regions that are absent or extra, that might be causative.

Nuclear hormone receptor function and DSD

Our aim is to uncover the function of two nuclear hormone receptor proteins, SF-1 and DAX-1, which are critical during human sexual development. Disruptions to the gene encoding SF-1 are a common cause of DSD affecting both males and females. Our laboratory has measured the sex-determining function of SF1 protein from affected DSD individuals. In recent studies, we have made key correlations between the biochemical functioning of the gene SF-1 and the severity of DSDs.

Conversely, males with a genetic duplication of DAX-1 are born with a DSD. Using transgenic mice and cell-based assays we have also identified a molecular mechanism for DAX-1 action in cases of DSD in humans.

ATRX, an important regulator of spermatogenesis

Infertility issues affect about one in 20 Australian men. Studies of the molecular action of the gene ATRX are providing a better understanding of some the underlying causes of male infertility.

We have found that ATRX protein is an important modulator of androgen receptor activity. Our studies have shown that loss of function of ATRX in testes of mice leads to defects in spermatogenesis and reduced fertility.

Research Staff

Vincent Harley
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Paisu Tang

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Institute for Molecular Bioscience, Queensland
Institute of Molecular Medicine, United Kingdom
Hospital General de Mexico, Mexico
Monash University, Victoria
Murdoch Childrens Research Institute, Victoria
University of California Los Angeles, USA

STEROID RECEPTOR BIOLOGY

We are currently focussed on two principle themes; that of the mechanism of action of the adrenal steroid hormone aldosterone and the molecular pathogenesis of granulosa cell tumours of the ovary.

Steroid hormones are fundamental to many aspects of endocrine function. These hormones interact with their target cells through an intracellular receptor to regulate gene expression. They play a role in diseases as diverse as cardiovascular disease and gynaecological malignancy.

The laboratory is exploring not only how these steroid hormone receptors act at the molecular level but the role that they play in these diverse diseases and their potential as therapeutic targets.

Understanding the mineralocorticoid receptor

The mineralocorticoid receptor (the receptor for the steroid hormone aldosterone) is an important therapeutic target in cardiovascular disease. We have identified structure-function relationships of the receptor that differ between the physiological ligands. Understanding these mechanisms is a fundamental step in the design of novel antagonsists for the mineralocorticoid receptor.

In 2009 we identified the molecular basis of the first case of aldosterone resistance, originally described 50 years ago. The team has now further characterised a series of interactions that discriminate between different steroids when they bind to the mineralocorticoid receptor. We have also identified genes that are regulated by the mineralocorticoid receptor and are seeking to understand the mechanisms of that regulation *in vitro* and *in vivo.*

Granulosa cell tumours of the ovary

We are studying the molecular pathogenesis of granulosa cell tumours of the ovary. These endocrine tumours of the ovary both make hormones and respond to hormones. Our research seeks to understand the molecular events that lead to development of these tumours.

Dr Stacey Jamieson has recently confirmed the presence of a defining genetic mutation in our panel of tumours. This finding radically alters the way we both think about and investigate granulosa cell tumours. The role of nuclear receptors in granulosa cell tumours has also been explored using a novel platform in collaboration with colleagues in Brisbane.

Role of ERβ in folliculogenesis

It is our hypothesis that the hormone oestrogen, acting via ERβ, limits granulosa cell proliferation by opposing anti-proliferation, anti-apoptic signals such as the NFκβ pathway, and by promoting their differentiation into luteal cells. We are seeking to identify genes and proteins specifically activated by ERβ.

In 2009 Dr Simon Chu returned to the research group after several years working overseas. His return was enabled with the support of the Ovarian Cancer Research Foundation. Simon has now initiated several novel approaches to define the role of ERβ in granulosa cells.

Ovarian phenotype of the IKKβ

The role of the NFκβ signalling pathway in ovarian function is being investigated using transgenic mice. We have successfully bred mice in which a key component of the pathway, IKKβ, has been deleted (knocked-out) in granulosa cells. These conditional knockout mice are yielding novel insights into ovarian function.

Dr Ann Drummond has found that these modified mice are delayed in the onset of ovulation and also have several other defects in granulosa cell function. These mice will also prove a powerful model for defining the role of NFκβ signalling in granulosa cell tumours.

Nuclear Receptors in breast cancer

The role of the receptors for oestrogen and progesterone is well characterised in breast cancer however the role of the other 46 members of this receptor family has not been systematically examined. Together with the breast cancer laboratories at PHI, we are part of a multicentre collaboration, funded by the National Breast Cancer Foundation, which is engaged in a large scale examination of the contribution of each of these receptors to breast cancer and their potential as novel therapeutic targets.

Research Staff

Peter Fuller
Maria Alexiadis
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Simon Chu
Ann Drummond
John Funder
Sonay Hussein-Fikret
Stacey Jamieson
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Yizhou Yao
Morag Young

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Monash Medical Centre, Victoria
Monash University, Victoria
Royal Children's Hospital, Victoria
Sydney University, New South Wales
University of Adelaide, South Australia
University of Helsinki, Finland
Walter and Eliza Hall Institute, Victoria
Western Australian Institute for Medical Research
Westmead Institute, New South Wales

COMMERCIALISATION, SCIENTIFIC SERVICES AND CLINICAL FACILITIES

Commercialisation

One of the Institute's objectives is to commercialise its intellectual property and our Intellectual Property and Commercialisation Committee advises on protection and eventual licensing of intellectual property generated through the research of PHI's scientists and clinicians.

Achievements during the eighteen month review period:

• PHI's Immuno-interactive Fragments of the Alpha-C sub-unit of Inhibin was granted in Canada, USA and Europe.

• Patent application was granted in Europe *Methods for Diagnosing Infertility.*

This Committee has convened four times and overseen a number of new commercial agreements, negotiated between PHI, other research institutes, universities and biotechnology companies. The existing agreement with our U.S. licensee continues to yield pleasing royalties to the extent we have now exceeded $800,000 since they commenced flowing in 2002.

Sequencing Facility

During 2009 the Gandel Charitable Trust Sequencing Centre proudly celebrated ten years of service to researchers and clinicians.

DNA sequencing is an essential "platform technology" underpinning a majority of research programs currently undertaken at the Monash Health Translation Precinct (MHTP).

DNA Sequencing is also a critical diagnostic method for a number of inherited diseases and the centre provides support to the Southern Health Clinical Genetics Laboratory, the Thalassaemia and Haemophilia reference centre for Victoria.

The Sequencing Centre maintains the highest quality of service delivery while initiating innovative applications of the technology.

During 2009 the Centre undertook a pilot study with the pathology service at Monash Medical Centre and Southern Cross Pathology. The study evaluated a Genetic Microbial Identification System with the aim of possible introduction and use within the clinical pathology unit of the hospital and research institutes of the MHTP. Microbial identification can be achieved by sequencing specific genes within bacteria and fungal species. Microbial Identification using DNA Sequencing represents the "gold standard" for identification of bacteria and fungi and produces extremely accurate results within a fraction of the time it can take for identification using conventional biochemical techniques.

The DNA sequence from an unknown strain (isolated from a patient) is compared against a fully validated microbial library (database) containing DNA sequences from thousands of known species. The results from the pilot study were very promising and a full evaluation of the system is currently being undertaken.

PHI / Southern Health Androgen Replacement Service

In the last two years the number of patients using the Androgen Replacement Service has increased by almost 50 percent.

The clinic, at Monash Medical Centre in Clayton, was developed in 2004 as a joint venture between PHI and the Southern Health Department of Endocrinology. The clinic is one of very few such tailored services available through the Australian public hospital system.

The service provides clinical care to men with androgen deficiency who require testosterone therapy, either as a result of testicular disorders or as a consequence of pituitary disease. Testosterone deficiency is the commonest hormonal disorder in men, affecting about 1 in 200 adult males.

This outpatient clinic now runs twice weekly and is staffed by endocrinologists, andrologists and clinical nurse specialists. The number of men attending has continued to rise with the clinic now providing care for almost 150 Victorian men. A typical patient will visit the clinic about four times per year.

Individualised, evidence based management plans are established and, where appropriate, shared care protocols with General Practitioners are developed. In conjunction with Andrology Australia, the service provides educational material for both patients and medical professionals.

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.

AWARDS & PRIZES
SERVICE TO THE SCIENTIFIC COMMUNITY

Awards and Prizes
1/7/08-31/12/09

Jock Findlay
– Life Membership - Society for Reproductive Biology

Peter Fuller
– Hoffenberg International Medal 2011 - Society for Endocrinology (UK)
– Life Membership - Endocrine Society of Australia

John Funder
– 2008 Novartis Award for Hypertension Research - American Heart Association
– Inducted by invitation - Royal College of Physicians, London

Amanda Rickard
– Endocrine Scholars Award 2008,The Endocrine Society, USA.
– Student Poster First Prize. High Blood Pressure Research Council of Australia Meeting, 2008

Lois Salamonsen
– Founders Award - Society for Reproductive Biology

Evan Simpson
– Dale Medal 2011 - Society for Endocrinology (UK)

Mai Sarraj
– Best overall presentation - 9th Royan International Research Congress, Royan Institute, Iran, August 2008

Kaye Stenvers
– Best oral presentation - 13th World Congress on Advances in Oncology and 11th International Symposium on Molecular Medicine, Greece, October 2008

Photo:
Research Officer Dr Ashwini Chand, Metabolism and Cancer Laboratory

Service to the Scientific Community
1/7/08-31/12/09

Anthony Argentaro
– Partner, CSIRO Scientists in Schools program

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

Ashwini Chand
– Chair, Careers Sub-Committee Victoria, Australian Society for Medical Research
– Member, Editorial Advisory Board, Virtual Endocrine Centre

Colin Clyne
– Member, Editorial Board, Endocrinology

Evdokia Dimitriadis
– Member, Reviewing Board, Journal of Reproductive Immunology
– Member, Endometriosis Special Interest Group, European Society of Human Reproduction and Embryology

Ann Drummond
– Member, New Investigator Award Committee, Society for Reproductive Biology
– Member, Editorial Board, Reproduction
– Member, Editorial Board, Journal of Endocrinology

Jock Findlay
– Member, Board; Chair, Scientific Advisory Committee, Bio21
– Member, Hospital Research Directors Committee, Bio21
– Chair, Infertility Treatment Authority, Victoria
– Member, Biobank Management Committee, Melbourne Health
– Member, Council; Chair, Embryo Research Licensing Committee, National Health and Medical Research Council
– Member, Board; Chair, Scientific Committee, Victorian Breast Cancer Research Consortium

Peter Fuller
– Member, Council; Member, Executive Committee;
– Member, Venture Grants Committee, Cancer Council Victoria
– Deputy Chair, Consultative Council, Victorian Cancer Agency, Department of Human Services (Victoria)
– Member, Council, Cabrini Clinical Education and Research Institute, Cabrini Hospital, Melbourne
– Member, Council of Governors, Florey Neurosciences Institutes, Melbourne
– Chair, Career Advancement Award Committee, Murdoch and Children's Research Institute, Melbourne
– Member, Hormone Research and Diabetes Research Review Panel, Murdoch Children's Research Institute, and Royal Children's Hospital, Melbourne
– Co-Editor, Hormone and Metabolic Research
– Editor, Endocrine and Metabolic Section, Expert Opinion on Investigational Drugs
– Editorial Board, Steroids
– Editorial Board, Endocrinology
– Member, Faculty of 1000, Medicine
– Associate Editor, Endocrinology
– Member, Editorial Board, Journal of Molecular Endocrinology

John Funder
– Chair, Medicine Research Infrastructure Panel, OSMR, NSW
– Director, Grattan Institute
– Director, Alan and Elizabeth Finkel Foundation
– Director, Harold Mitchell Foundation
– Member, Judging Panel, Victorian Premier's Award for Medical Research
– Secretary-Treasurer, International Aldosterone Conference
– Chair, International Taskforce, Endocrine Society, USA
– Member, Board; Chair, Scientific Advisory Committee, Liggins Institute, New Zealand
– Member, Editorial Board, Endocrinology
– Member, Editorial Board, Current Trends in Endocrinology
– Member, Editorial Board, Hypertension
– Member, Editorial Board, Trends in Endocrinology and Metabolism
– Member, Editorial Board, Encyclopaedia of Endocrine Diseases
– Member, Editorial Board, NeuroImmunoModulation
– Member, Editorial Board, Stress
– Member, Editorial Board, Current Opinion in Endocrinology
– Member, Editorial Board, Steroids
– Member, Editorial Board, Journal of Endocrinological Investigation
– Member, Editorial Board, Journal of Steroid Biochemistry and Molecular Biology

Matthew Gillespie
- President-Elect, Australian and New Zealand Bone and Mineral Society
- Member, Council; Member, Science Advisory Committee, Cancer Council Victoria
- Member, Victorian Breast Cancer Research Consortium
- Member, Research Committee, National Health and Medical Research Council, Australia
- Member, Audit Committee, National Health and Medical Research Council, Australia
- Member, Board, Ovarian Cancer Research Foundation
- Member, Board of Directors, Australian and New Zealand Bone and Mineral Society
- Member, Board of Directors, International Bone and Mineral Society
- Member, Board of Directors, Cancer and Bone Society
- Member, Board of Directors, Monash Health Research, Precinct Pty Ltd
- Member, Editorial Board, Arthritis and Rheumatism
- Member, Editorial Board, Bone
- Member, Editorial Board, BoneKey
- Member, Editorial Board, Endocrinology
- Member, Editorial Board, Journal of Bone and Mineral Research
- Advisor, Journal of Oral Biosciences

Vincent Harley
- Member, Editorial Board, Molecular Endocrinology
- Member, Editorial Board, International Journal of Biochemistry and Cell Biology
- Member, Editorial Board, Sexual Development
- Vice President, Lorne Genome Conference

Karla Hutt
- Partner, CSIRO Scientists in Schools program

Kevin Knower
- Partner, CSIRO Scientists in Schools program

Rob McLachlan
- Associate Editor, International Journal of Andrology
- Associate Editor, Journal of Andrology
- Associate Editor, Journal of Clinical Endocrinology and Metabolism

Sarah Meachem
- President, Australian Society for Medical Research
- Member, Editorial Board, Journal of Endocrinology

Ian Muchamore
- Member, Victoria Branch Committee, Australian Science Communicators

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

Julian Quinn
- Member, Editorial Board, Bone

David Robertson
- Editor, Women's Health

Lois Salamonsen
- Member, Editorial Board, Endocrinology
- International Advisory Panel, Reproduction, Fertility and Development
- Member, Board of Reviewing Editors, Biology of Reproduction
- Associate Editor, Biology of Reproduction

Mai Sarraj
- Partner, CSIRO Scientists in Schools program

Evan Simpson
- Member, Editorial Board, Journal of Steroid Biochemistry and Molecular Biology
- Member, Executive Committee, International Society for Endocrinology
- Chair, Nominations Committee, Endocrine Society (USA)
- Committee for Governance Affairs, Endocrine Society (USA)
- Member, Council, Endocrine Society of Australia
- Member, Council, Society for Endocrinology (UK)
- Member, Board, Ovarian Cancer Research Fund

Peter Stanton
- Member, Editorial Board, Journal of Endocrinology

Kaye Stenvers
- Member, Institutional Biosafety Committee, Ludwig Institute, Melbourne

Andrew Stephens
- Scientific Representative, Ovarian Cancer Research Foundation

Sarah To
- Partner, CSIRO Scientists in Schools program

Morag Young
- Convener, Medical Research Week 2008, Australian Society for Medical Research
- Member, Editorial Board, Endocrinology
- Member, Faculty of 1000, Physiology

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1/7/08 – 31/12/09

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Evdokia Dimitriadis PhD - Embryo Implantation

Jock Findlay AO PhD DSc - Ovarian Biology

Peter Fuller BMedSci MBBS PhD FRACP - Steroid Receptor Biology

Matthew Gillespie PhD - Bone, Joint & Cancer

Vincent Harley PhD - Sex Determination and Gonadal Development / Brain & Gender

Craig Harrison PhD - Growth Factor Signalling

Joohyung Lee PhD - Brain & Gender

Rob McLachlan MBBS FRACP PhD - Clinical Andrology

Guiying Nie PhD - Implantation & Placental Development

David Robertson PhD - Reproductive Hormones

Lois Salamonsen PhD - Endometrial Remodelling

Evan Simpson PhD FAA - Metabolism & Cancer

Peter Stanton PhD - Male Fertility Regulation

Kaye Stenvers PhD - Reproductive Development & Cancer

Andrew Stephens PhD - Ovarian Cancer Biomarkers

Morag Young PhD - Cardiovascular Endocrinology

NHMRC Career Development Awardees
Evdokia Dimitriadis PhD

Craig Harrison PhD

Terry Fox Foundation Fellow
Kristy Brown PhD

L'Oréal Paris Research Fellow
Simon Chu BSc (Hons) PhD (from Apr 09)

Visiting Endocrinology Fellow
Siang Chin Lim MD MRCP (until Jan 09)

Endocrine Society Fellow
Izabella Czajka-Oraniec MD PhD (until May 09)

US Department of Defense Fellow
Kevin Knower PhD

Witchery & Madison Research Fellow
Katie Meehan PhD

The Lalor Foundation Fellow
Ellen Menkhorst PhD

The Michael, John and Phoebe Jones Fellow
Frances Milat MBBS (Hons) FRACP MD (from Feb 09)

NAB OCRF Research Fellow
Andrew Stephens PhD

Witchery Research Fellow
Adam Rainczuk PhD

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Laura Pellatt BSc (Hons) (from Nov 08 - Dec 08)

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Kati Matthiesson MBBS FRACP PhD

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Karla Hutt PhD (from Dec 08)

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Nicole Fairweather RN

Elise Forbes RN

Judi Hocking RN

June Lee RN (from Dec 08 - Mar 09)

Anna Zamojska RN

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Liza O'Donnell PhD

Kyriakos Pratis PhD (until Sept 08)

Julian Quinn DPhil

Helena Sim PhD

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Maree Bilandzic PhD

Neil Borg PhD (until Jan 09)

Jemma Evans PhD (from Oct 08)

Nicholas Fleming PhD

Natalie Hannan PhD

Belinda Hardman PhD (until Dec 08)

Louisa Ludbrook PhD

Chantal Magne Nde PhD (from Sep 08)

Yogeshwar Makanji BAppSci (Hons) PhD

Premila Paiva PhD

Sarah Paule PhD (from Dec 08)

Jyotsna Pippal BSc MSc MBA PhD (until Jul 09)

Amanda Rickard PhD

Mai Sarraj MSc PhD

Harmeet Singh MSc PhD (from Nov 08)

Kelly Walton PhD

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Ruth Escalona BSc (Hons) MSc

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Anne Reilly BSc (Hons) (until Mar 09)

Melissa Solano BSc (Hons)

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Yizhou Yao MD

Research Assistants

Georgia Balourdos BSc (Hons)

Lyndsay Brogan BSc (Hons) (from Mar 09 - Aug 09)

Karen Chan BAppSc

Greg Cranston BSc (Hons) (from Jul 08)

Rebecca Crook BSc (Hons) MSc

Kemperly Dynon BSc (Hons) (from Aug 09)

Lauren Hare BA/BSc (Hons)

Sophy Heng BSc

Kerrie Herridge BSc

Cassandra Hincks BSc (Hons) (from Nov 08)

Ileana Kuyznierewicz BAppSc (Hons)

Ming Yee Lee BBiomedSci, BSc (Hons)

Priscilla Li BSc (Hons) (from Sep 09)

Melinda Marwood BSc (Hons) (until Sep 08)

Hamish Morgan (until Apr 09)

James Morgan

Charles Pritchard BSc (Hons) (from Mar 09)

Enid Pruysers

Michelle Puryer BSc (Hons) (until Nov 08)

Saw Eng Tan BVet MedTech (until Dec 08)

Alex Umbers BSc (Hons)

Elizabeth Verghese BSc (Hons) (from Sep 09)

Peter Wilson BSc (Hons) (until Sept 09)

Joanne Yap BSc (Hons)

Jin Zhang MD

Laboratory Technicians

Robin Leuba BA Dip Ed

Florence Pierre BSc

Susan Taleh BA

Occupational Trainees

Irem Avcilar (from Jul 08 - Sep 08)

Anja Dietrich (from Aug 09)

Nicole Hunger BSc (until Nov 08)

Rianne Wind (from Sep 08 - Feb 09)

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Development & Commercialisation Services Manager

Andrew McCallum BE (Met) MEngSc GAICD

Laboratory & Technical Services Manager

Sach Jayasinghe BSc (Hons)

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Michele Prusa (until Jul 08)

Accounts Officer

Jennifer Watson

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Bruce Watson DipEng

Clinical Administration Officer

Abigail Lewis (until Dec 08)

Grants and Education Officer

Neil Owens PhD

Graphic Communications

Sue Panckridge DipArt

Human Resources Officer

Christina Matisons MAHRI, Prof DipHR

HR/Payroll Officer

Lesley Bowyer

Laboratory Support Officer

Shilo Desira (from May 09)

OHS Officer

Brett Sargeant BSc GradDip OHS (until Jun 09)

Purchasing and Facilities Officer

Henry Wos

Receptionist

Janelle Fisher (until May 09)

Science Communications Officer

Ian Muchamore BSc (Hons)

Sequencing Manager, The Gandel Charitable Trust Sequencing Centre

Vivien Vasic BSc

Executive Assistant

Diane Yallop

Personal Assistants / Administrative Officers

Dianne Arnold BSc

Jeanette Birtles BSc (Hons)

Sue Elger

Claudette Thiedeman

Jeana Thomas

STUDENTS

PHI currently has over 40 students studying towards Honours, Masters and PhD degrees. We pride ourselves on the flourishing and supportive research environment offered to students.

Novo Nordisk Awards

Each November the PHI Student Symposium provides a showcase which allows students to develop their communication skills. This two day meeting is an opportunity for them to present their research in a formal environment to peers and colleagues at the Monash Medical Centre Clayton campus.

Awards at the Student Symposium are sponsored by our long standing partner Novo Nordisk. Student presentations are judged by an independent panel of academic assessors comprised from PHI and affiliated institutions.

2008 Novo Nordisk Awards

Overall PhD Presentation: **Jason Liew** "Hormonal manipulation of the phenotype of the female ArKO mouse"

Special Commendation: **Amanda Rickard** "Mineralocorticoid receptor signalling in endothelial cells is critical for monocyte recruitment in the mineralocorticoid/salt model"

1st Year PhD Presentation: **Peter Nicholls** "Hormonal regulation of miRNAs in the testis"

Honours / Masters Presentation: **Courtney Simpson** "The role of GDF9 as a modulator of Sertoli cell function"

Novo Nordisk Award 2008 - Student Symposium - Best Overall PhD - Jason Liew L - R: Senior Regional Sales Director of Novo Nordisk Guy Murray, Jason Liew, with adjudicators Assoc. Prof. Tim Cole (Monash University) and Dr Joohyung Lee (PHI)

Quantum Scientific Award 2008 L - R: Mr Gavin Williamson (Quantum Scientific), Ken Walker and Associate Director Prof. Peter Fuller

2009 Novo Nordisk Awards

Best Overall PhD Presentation: **Ken Walker** "Characterisation of cardiovascular and renal function in a high nephron number phenotype"

Special Commendation: **Jun Yang** "The Mineralocorticoid Receptor: exploring its ligand specificity"

Best 1st Year PhD Presentation: **Sarah To** "The role of TNFα in post-menopausal breast cancer"

Best Honours Presentation: **Justin Chen** "The molecular mechanisms that govern BMP-7 biosynthesis and extracellular matrix localisation"

Quantum Scientific Awards for Scientific Excellence

During their studies many PHI students travel to national and international scientific meetings to present their research findings.

Excellence in these presentations is recognised by awards sponsored by Quantum Scientific Ltd.

2008 Quantum Scientific Award

Winner - **Ken Walker** for his presentation "Augmented nephron number and metanephric development in betaglycan heterozygous mice" at the Queenstown Kidney Biology Meeting in New Zealand.

STUDENT LIST 2008/09

Highly Commended - **Peter Nicholls** for his presentation "GDF9 and BMP15 are germ-cell regulators of Sertoli cell function" at the Endocrine Society of Australia / Society for Reproductive Biology Joint Conference in Melbourne.

2009 Quantum Scientific Award

Winner - **Jun Yang** for his presentation "The Mineralocorticoid Receptor: exploring its ligand specificity using peptide phage display" presented at the Royal Australasian College of Physicians Annual Conference in Sydney.

Highly Commended - **Janelle Ryan** for her presentation "Gene delivery into cultured mouse embryonic gonads" presented at the 5th International Symposium on Vertebrate Sex Determination in Hawaii.

Quantum Scientific Award 2009 L - R: Mr Oliver Bonaccorso (Quantum Scientific), Jun Yang Associate Director Prof. Peter Fuller

PhD Graduates
1/7/08 – 31/12/09

Marissa Bowden PhD BA BSc
(Hons)
Thesis: A novel serine protease, Htra3, in rat and rhesus monkey ovary, and in human gynecological cancers

Jenny Chow PhD
BBiomedSci (Hons)
Thesis: The role of oestrogen in triglyceride homeostasis

Emily Lam PhD
BBiomedSci (Hons)
Thesis: Differential Regulation of the Mineralocorticoid Receptor by corticosteroids and
high salt in cardiovascular disease

Louisa Ludbrook PhD
BBiomedSci (Hons)
Thesis: Roles of DAX1 and SF1 in sex determination and Disorders of Sex Development

Mark McCabe PhD
BAppBiol/Biotech (Hons)
Thesis: Hormonal regulation of the testicular Sertoli cell tight junction

Yogeshwar Makanji PhD
BAppSc (Hons)
Thesis: Biological characterisation of inhibin A and inhibin B

Premila Paiva PhD BSc (Hons)
Thesis: Roles for Interleukin-11 human trophoblast function

Niroshani Pathirage PhD
BSc (Hons)
Thesis: Aromatase expression and transcriptional regulation in post-menopausal gynaecological cancers

Amanda Rickard PhD
BBiomedSci (Hons)
Thesis: Mineralocorticoid receptor signalling in vascular inflammation and cardiac fibrosis

Chelsea Stoikos PhD BSc (Hons)
Thesis: Endometrial proteins critical for embryo implantation: implications for infertility and endometriosis

Gerard Tarulli PhD BSc (Hons)
Thesis: Regulation of adult sertoli cell differentiation

Sean Yang PhD BSc
Thesis: Ion channels in the regulation of growth hormone secretion by regulatory hormones

Honours Completed
1/7/08 – 31/12/09

Marina Bashir BSc (Hons)
Justin Chen BSc (Hons) BA
Brett Fisher BSc (Hons)
Jenna Haverfield BSc (Hons)

PhD Students

Dimuthu Alankage
BBiomedSci
- Sex Determination & Gonadal Development

Ally Chau BSc (Hons)
Bone, Joint & Cancer

Vanessa Cheung BSc (Hons)
- Bone, Joint & Cancer

Davina Cossigny BSc, GradDip Reprod Sci - Ovarian Biology

Daniel Czech BSc (Hons) - Brain & Gender

Amy Herlihy BSc GradDip Genetic Counselling - Clinical Andrology

Hui Ting Ho BSc (Hons)
- Implantation & Placental Development (from May 2009)

Sonay Hussein-Fikret
BBiomedSci (Hons) - Steroid Receptor Biology

Stacey Jamieson BA/BSc (Hons) - Steroid Receptor Biology

Irumini Jayakody PhD
BBiomedSci (Hons) - Sex Determination & Gonadal Development

Jason Liew BBiomedSci (Hons) - Ovarian Biology

Peter Nicholls BBiomedSci (Hons) - Growth Factor Signalling

Irene Papageorgiou BSc (Hons) - Growth Factor Signalling

Jyothsna Rama Rao BSc MSc (until Oct 08)

Nana Saleh BSc (Hons) - Bone Joint & Cancer

Nirukshi Samarageewa
BBiomedSci
- Metabolism & Cancer

Courtney Simpson BSc
- Growth Factor Signalling

Paisu Tang BSc (Hons)
- Sex Determination & Gonadal Development

Sarah To BSc
- Cancer Drug Discovery

Michelle Van Sinderen BSc (Hons) - Metabolism & Cancer

Kenneth Walker BSc (Hons) - Reproductive Development & Cancer

Jun Yang MBBS (Hons)
- Cardiovascular Endocrinology

Masters Students

Lorraine Lin BSc - Embryo Implantation (from Apr 09)

Debora Romero BSc GradDipRSc - Reproductive Hormones

Janelle Ryan BSc - Sex Determination & Gonadal Development

Honours Students

Justin Chen BSc (Hons) BA
- Growth Factor Signalling (from Jan 09)

Karen (Ying Jie) Chua
- Brain & Gender (from Nov 09)

Paige Everingham BSc (forensics) BA
- Sex Determination & Gonadal Development (from Jun 09)

Jenna Haverfield BSc (Hons)
- Metabolism & Cancer (from Feb 09)

Tamara Howard
- Cancer Drug Discovery (from Jul 09)

Deborah John BSc
- Steroid Receptor Biology (from Nov 09)

Emily Kelly
- Growth Factor Signalling

Nirushi Sam BSc
- Metabolism & Cancer

Sarah To BSc
- Cancer Drug discovery

Jaslyn Lee BSc (until Dec 08)

Monash/Kings Scholar

Abigail Rickard
(from Oct 08 - Dec 08

Vacation Students

Dimuthu Alankage BSc (Hons)
Frances Barber
Xylia Chan
Calvin Chee MBBS 2nd Year
Justin Chen BSc (Hons) BA
Karen Chua
Cameron Ewert
Brett Fisher BSc
Kerrie Herridge BSc (Hons)
Deborah John BSc
Amali Kumarage Dip Lab Tech (Biotech)
Alice Greenhill
Rim Nour BSc
Justine Olcorn
Han Tan
Daniel Payne
Kong Toh
Jessica Truong
Dhilushi Wijayakumara
Joyee Yeung
Mei Yun Yong BSc Biomed
Maria Zaldivia

Practical Placement Students

Pei Leng Chong BSc (Hons)
Lauren Cramer
Amelia Hanos BPharm
Agustinus Prijanto
Chantal Samardzija
Max Yan

UROP Students

Namita Bhojani
Cameron Ewert
Jun Gu BSc
Christopher Ip
Lynsey Marshall

Novo Nordisk Award 2009 - Student Symposium - Best Honours - Justin Chen L - R: Student Symposium adjudicator Dr Steve McPherson (MIMR), Justin Chen and Novo Nordisk Representative Saras Singam

Novo Nordisk Award 2009 - Student Symposium - Best Overall PhD - Ken Walker L - R: Adjudicator Dr Jemma Evans (PHI), Ken Walker, Novo Nordisk Representative Saras Singam and adjudicator Dr Elizabeth Williams (MIMR)

Novo Nordisk Award 2009 - Student Symposium - Best First Year PhD - Sarah To L - R: Adjudicator Dr Jemma Evans, Sarah To, Novo Nordisk Representative Saras Singam and adjudicator Dr Elizabeth Williams (MIMR)

HONORARY APPOINTMENTS

PHI Fellows

PHI has a longstanding history of research delivery, academic mentoring and community engagement.

In recognition of their substantial contribution to the Institute the following individuals have been appointed as PHI Fellows:

Dr Nuzhat Ahmed
Women's Cancer Research Centre, Royal Women's Hospital, Melbourne, Victoria

Professor John Aitken
ARC Centre of Excellence in Biotechnology & Development, University of Newcastle, New South Wales

Professor John Bertram
Department of Anatomy & Developmental Biology, Faculty of Medicine, Nursing & Health Sciences, Monash University, Victoria

Associate Professor Timothy Cole
Dept of Biochemistry & Molecular Biology, Faculty of Medicine, Nursing & Health Sciences, Monash University, Victoria

Professor David Healy
Chair, Department of Obstetrics and Gynaecology, Monash University, Victoria

Associate Professor Jeff Kerr
Department of Anatomy & Developmental Biology, Faculty of Medicine, Nursing & Health Sciences, Monash University, Victoria

Professor Gab Kovacs AM
Monash IVF, Victoria

Professor David de Kretser AC
The Governor of Victoria

Associate Professor Mark Frydenberg
Australian Urology Associates, Cabrini Medical Centre, Victoria

Associate Professor Tom Jobling
Chairman, Ovarian Cancer Research Foundation

Associate Professor Kate Loveland
Faculty of Medicine, Nursing & Health Sciences, Monash University, Victoria

Associate Professor Moira O'Bryan
Department of Anatomy & Developmental Biology, Faculty of Medicine, Nursing & Health Science, Monash University, Victoria

Dr David Nikolic-Paterson
Department of Nephrology, Monash Medical Centre, Monash University, Victoria

Dr Luk Rombauts
Monash IVF, Victoria

Professor Ian Smith
Deputy Dean, Research, Monash University, Victoria

Associate Professor Peter Temple-Smith
Monash Institute of Medical Research, Victoria

Dr Greg Tesch
Department of Medicine, Faculty of Medicine, Nursing & Health Sciences, Monash Medical Centre, Victoria

Honorary Research Associates

Dr Wah Chin Boon
Dr Tu'uhevaha Lino (from Sep 08)

COMMITTEES

PHI Board Committees As at 31/12/09

PHI Foundation

The role of this Committee is to provide the Institute with strategic advice and direction for fundraising, and building public and corporate awareness of PHI and its research.

Members:
Mr John Weste (Chair)
Professor Matthew Gillespie
Mr Ronnie Atlas
Mr Dylan Simmons

Finance and Audit Committee

The role of this 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.

Members:
Mr Stuart Alford (Chair)
Ms Jay Bonnington
Dr Bob Edgar
Ms Carmel Mortell
Mr Peter Murray (Secretary)

Investment Committee

The Investment Committee provides advice to the Board for investment policies, and within the Delegation of Executive Authorities to approve investments and engage investment managers, and to determine the effectiveness of investments.

Members:
Dr Bob Edgar (Chair)
Ms Jay Bonnington
Mr Martin O'Meara
Mr Richard Condon
Professor Jock Findlay
Mr Peter Murray (Secretary)

Intellectual Property and Commercialisation Committee

The role of this Committee is to advise the Board and Director on statutory requirements for corporate governance and commercialisation of the Institute's intellectual property and related issues

Members:
Mrs Jane Bell (Chair)
Ms Jennifer Joiner
Mr Grant Fisher
Dr Michael Pannaccio
Professor Matthew Gillespie
Assoc Professor David Robertson
Professor Lois Salamonsen
Mr Andrew McCallum (Secretary)

Internal PHI Committees As at 31/12/09

Authorship & Publications Committee

The PHI Authorship & Publications Committee exists to set down guidelines to ensure sound scientific practice, to maintain a system of peer review of all publications prior to submission to scientific journals and to maintain a complete and readily accessible bibliography of publications by Institute members.

Members:
Dr Peter Stanton (Chair)
Dr Neil Owens

Education Committee

The Education Committee oversees the implementation of seminars and educational programs for the Institute to permit knowledge transfer and skill acquisition.

Members:
Dr Andrew Stephens (Chair),
Ms Stacey Jamieson
Dr Kevin Knower
Dr Neil Owens
Dr Mai Sarraj
Professor Evan Simpson
Ms Vivien Vasic

Equipment Committee

The Equipment Committee assesses applications from Institute staff for equipment purchases which are considered on the basis of their suitability for proposed use, strategic intent of PHI, and applicability across the Institute.

Members:
Dr Julian Quinn (Chair)
Dr Colin Clyne
Dr Peter Fuller
Mr Sach Jayasinghe
Dr Joohyung Lee
Dr Neil Owens
Dr Adam Rainczuk
Dr Kaye Stenvers

Information Communication Technology Committee

The Information Communication Technology Committee supports PHI in developing and maintaining ICT infrastructure and resources.

Members:
Dr Steve Bouralexis (Chair)
Dr Stefan Bagheri-Fam
Dr Colin Clyne
Ms Stacey Jamieson
Mr Sach Jaysinghe
Dr Yogheshwar Makanji
Dr Guiying Nie
Ms Sue Panckridge

Institute Scientific Group

The Scientific Group provides a forum to foster collaboration and information sharing within the Institute, permitting the opportunity for advice and implementation of the vision of the Institute.

Members:
Dr Kaye Stenvers (Chair)
Dr Anthony Argentaro
Dr Stephan-Bagheri-Fam
Dr Pascal Bernard
Dr Steve Bouralexis
Dr Kristy Brown
Professor Henry Burger
Dr Ashwini Chand
Dr Simon Chu
Dr Colin Clyne
Dr Eva Dimitriadis
Dr Ann Drummond
Professor Jock Findlay
Professor Peter Fuller
Professor Matthew Gillespie
Assoc. Professor Vincent Harley
Dr Craig Harrison
Mr Sach Jayasinghe
Dr Vicky Kartsogiannis
Dr Joohyung Lee
Professor Rob McLachlan
Dr Sarah Meachem
Dr Katie Meehan (Secretary)
Dr Guiying Nie
Dr Liza O'Donnell
Dr Neil Owens
Dr Julian Quinn
Dr Adam Rainczuk
Assoc. Professor David Robertson
Professor Lois Salamonsen
Professor Evan Simpson
Dr Peter Stanton
Dr Andrew Stephens
Dr Morag Young

Occupational Health and Safety Committee
The OH&S Committee provides a forum for consultation and forms a pivotal role in implementing the Institute's OH&S management system.

Members:
Professor Matthew Gillespie (Chair)
Ms Francine Brennan
Mr Sach Jayasinghe
Ms Ileana Kuyznierewicz
Dr Yogeshwar Makanji
Mr Charles Pritchard
Dr Mai Sarraj

OGTR Committee
This Committee ensures that the research conducted by the Institute, and the Institute's facilities, are within the framework of the Gene Technology Act 2000 that relates to regulations for genetically modified organisms.

Members:
Associate Professor Vincent Harley (Chair)
Dr Anthony Argentaro
Ms Jeanette Birtles (Secretary)
Dr Kristy Brown
Dr Craig Harrison
David Nikolic-Paterson
Dr Kaye Stenvers
Ms Yizhou Yao
Ms Joanne Yap

Promotions & Classifications Committee
The Promotions & Classifications Committee assess the requirement for the classification of new and re-classified positions, the suitability of employees for promotion and in some cases, for progression.

Members:
Professor Lois Salamonsen (Chair)
John Gibson (Monash University)
Dr Peter Stanton

Research Advisory Group
This group advises and assists the Director on matters of policy to be recommended to the Board of the Institute.

Members:
Professor Matthew Gillespie (Chair)
Professor Peter Fuller
Professor Jock Findlay
Associate Professor Vincent Harley
Professor Rob McLachlan
Dr Guiying Nie
Assoc. Professor David Robertson
Professor Lois Salamonsen
Professor Evan Simpson

Student Welfare Committee
The role of the Student Welfare Committee is to support students in both research and non-research related matters.

Members:
Dr Colin Clyne (Chair)
Dr Kristy Brown
Ms Davina Cossigny
Mr Daniel Czech
Dr Neil Owens
Assoc. Professor David Robertson
Dr Kelly Walton

Consultative Committee
The Consultative Committee was established to develop a variation and extension to the PHI Certified Agreement.

Members:
Professor Jock Findlay (Chair)
Ms Maria Alexiadis
Ms Caroline Foo
Ms Christina Matisons
Mr Andrew McCallum
Dr Mai Sarraj
Mrs Diane Yallop

Photo:
Sue Elger (left) and Claudette Thiedeman, Administrative Support

PUBLICATIONS

PUBLICATIONS 2008/09

2008

1. Allan CA, Forbes EA, Strauss BJG & McLachlan RI. (2008). Testosterone therapy increases sexual desire in ageing men with low-normal testosterone levels and symptoms of androgen deficiency. International Journal of Impotence Research 20, 396-401.

2. Allan CA, Strauss BJ, Burger HG, Forbes EA & McLachlan RI. (2008). Testosterone therapy prevents gain in visceral adipose tissue and loss of skeletal muscle in nonobese aging men. Journal of Clinical and Endocrinology and Metabolism 93, 139-146.

3. Bagheri-Fam S, Sim H, Bernard P, Jayakody I, Taketo MM, Scherer G & Harley VR. (2008). Loss of Fgfr2 leads to partial XY sex reversal. Developmental Biology 314, 71-83.

4. Bayne S, Jones MEE, Li H, Pinto AR, Simpson ER & Liu JP. (2008). Estrogen deficiency leads to telomerase inhibition, telomere shortening and reduced cell proliferation in the adrenal gland of mice. Cell Research 18, 1141-1150.

5. Bazer FW & Salamonsen LA. (2008). Let's validate those cell lines. Biology of Reproduction 79, 585.

6. Bernard P, Fleming A, Lacombe A, Harley VR & Vilain E. (2008). Wnt4 inhibits beta-catenin/TCF signalling by redirecting beta-catenin to the cell membrane. Biology of the Cell 100, 167-177.

7. Bernard P, Sim H, Knower K, Vilain E & Harley V. (2008). Human SRY inhibits beta-catenin-mediated transcription. International Journal of Biochemistry & Cell Biology 40, 2889-2900.

8. Bowden MA, Li Y, Liu YX, Findlay JK, Salamonsen LA & Nie GY. (2008). HTRA3 expression in non-pregnant rhesus monkey ovary and endometrium, and at the maternal-fetal interface during early pregnancy. Reproductive Biology and Endocrinology 6, 22.

9. Bulun SE & Simpson ER. (2008). Aromatase expression in women's cancers. Advances in Experimental Medicine & Biology 630, 112-132.

10. Burger H. (2008). The menopausal transition - Endocrinology. Journal of Sexual Medicine 5, 2266-2273.

11. Burger HG, Hale GE, Dennerstein L & Robertson DM. (2008). Cycle and hormone changes during perimenopause: the key role of ovarian function. Menopause (New York, NY) 15, 603-612.

12. Chu S, Alexiadis M & Fuller PJ. (2008). Expression, mutational analysis and in vitro response of imatinib mesylate and nilotinib target genes in ovarian granulosa cell tumors. Gynecologic Oncology 108, 182-190.

13. Corbould A. (2008). Effects of androgens on insulin action in women: is androgen excess a component of female metabolic syndrome? Diabetes-Metabolism Research and Reviews 24, 520-532.

14. Corbould A. (2008). Insulin resistance in skeletal muscle and adipose tissue in polycystic ovary syndrome: Are the molecular mechanisms distinct from type 2 diabetes? Panminerva medica 50, 279-294.

15. Czajka-Oraniec I, Zgliczynski W, Kurylowicz A, Mikula M & Ostrowski J. (2008). Association between gynecomastia and aromatase (CYP19) polymorphisms. European Journal of Endocrinology 158, 721-727.

16. Daggag H, Svingen T, Western PS, van den Bergen JA, McClive PJ, Harley VR, Koopman P & Sinclair AH. (2008). The Rhox homeobox gene family shows sexually dimorphic and dynamic expression during mouse embryonic gonad development. Reproductive Biology 79, 468-474.

17. Davis SR, McCloud P, Strauss BJ & Burger H. (2008). Testosterone enhances estradiol's effects on postmenopausal bone density and sexuality. Maturitas 61, 17-26.

18. Dias V, Meachem S, Rajpert-De Meyts E, McLachlan R, Manuelpillai U & Loveland KL. (2008). Activin receptor subunits in normal and dysfunctional adult human testis. Human Reproduction 23, 412-420.

19. Dietz JD, Du S, Bolten CW, Payne MA, Xia C, Blinn JR, Funder JW & Hu X. (2008). A number of marketed dihydropyridine calcium channel blockers have mineralocorticoid receptor antagonist activity. Hypertension 51, 742-748.

20. Feng DD, Zhao YF, Luo ZQ, Keating DJ & Chen C. (2008). Linoleic acid induces Ca+-induced inactivation of voltage-dependent Ca2+ currents in rat pancreatic beta-cells. Journal of Endocrinology 196, 377-384.

21. Fuller PJ. (2008). Minireview: Stem cells in endocrine research: More than just Dolly. Endocrinology 149, 4301-4302.

22. Fuller PJ & Young MJ. (2008). Molecular genomics of mineralocorticoid actions. In Hormones, Brain and Behaviour, 2nd edn, ed. Pfaff D, Arnold A, Etgen A, Fahrbach S & Rubin R. Elsevier, San Diego.

23. Funder J. (2008). Chipping away at "essential" hypertension. American Journal of Hypertension 21, 600.

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25. Funder JW, Carey RM, Fardella C, Gomez-Sanchez CE, Mantero F, Stowasser M, Young WF & Montori VM. (2008). Case detection, diagnosis, and treatment of patients with primary aldosteronism: An endocrine society clinical practice guideline. Journal of Clinical Endocrinology & Metabolism 93, 3266-3281.

26. Gustin SE, Western PS, McClive PJ, Harley VR, Koopman PA & Sinclair AH. (2008). Testis development, fertility and survival in Ethanolamine kinase 2-deficient mice. Endocrinology 149, 6176-6186.

27. Hannan NJ & Salamonsen LA. (2008). CX3CL1 and CCL14 regulate extracellular matrix and adhesion molecules in the trophoblast: Potential roles in human embryo implantation. Reproductive Biology 79, 58-65.

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33. Hill RA, Simpson ER & Boon WC. (2008). Evidence for the existence of an estrogen-responsive sexually dimorphic group of cells in the medial preoptic area of the 129SvEv mouse strain. International Journal of Impotence Research 20, 315-323.

34. Jamieson S & Fuller PJ. (2008). Management of granulosa cell tumour of the ovary. Current Opinion in Oncology 20, 560-564.

35. Jamsai D, Reilly A, Smith SJ, Gibbs GM, Baker HWG, McLachlan RI, De Kretser DM & O'Bryan MK. (2008). Polymorphisms in the human cysteine-rich secretory protein 2 (CRISP2) gene in Australian men. Human Reproduction 23, 2151-2159.

36. Jones GM, Cram DS, Song B, Magli MC, Gianaroli L, Lacham-Kaplan O, Findlay JK, Jenkin G & Trounson AO. (2008). Gene expression profiling of human oocytes following in vivo or in vitro maturation. Human Reproduction 23, 1138-1144.

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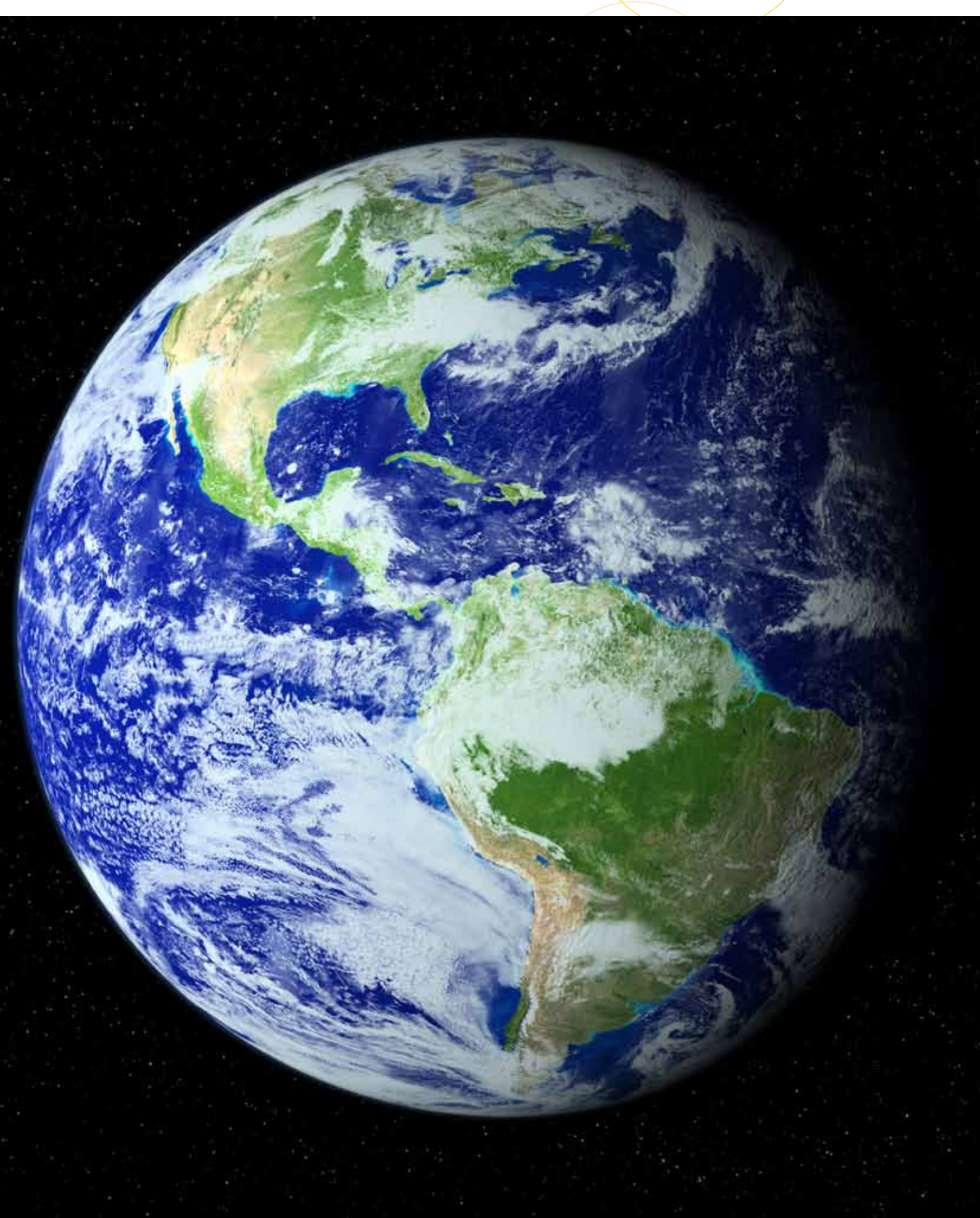
INVITED PRESENTATIONS



INVITED PRESENTATIONS

1/7/08 – 31/12/09

Maree Bilandzic
- Invited Speaker, 39th Annual Meeting of the Society for Reproductive Biology, Melbourne, Aug 2008
- Invited Speaker, 52nd Annual Scientific Meeting of the Endocrine Society of Australia, Adelaide, Aug 2009

Steve Bouralexis
- Invited Speaker, VIII International Meeting on Cancer induced Bone Disease, Cancer and Bone Society, Sydney, March 2009

Kristy Brown
- Servier Award Lecture, 52nd Annual Scientific Meeting of the Endocrine Society of Australia, Adelaide, Aug 2009

Henry Burger
- Plenary Speaker, Thai Menopause Society, Pattaya, Thailand, March 2009
- Symposium Chair, 8th European Congress on Menopause, London, United Kingdom, May 2009

Ally Chau
- Invited Speaker, VIII International Meeting on Cancer Induced Bone Disease, Cancer and Bone Society, Sydney, March 2009

Colin Clyne
- Invited Speaker, 48th Annual Meeting Society of Toxicology, Baltimore, USA, March 2009

Evdokia Dimitriadis
- Invited Speaker, Society for Gynaecological Investigation Annual Meeting, Glasgow, Scotland, March 2009
- Plenary Speaker, International Federation of Placental, Association Annual Congress, Adelaide , Oct 2009

Jock Findlay
- Invited Speaker, Clinical Research Excellence Conference, Brisbane, Aug 2008
- Invited Speaker, Queenstown Molecular Biology Conference, Queenstown, New Zealand, Sep 2008
- Invited Speaker, Second International Symposium on Animal Biology of Reproduction, Sao Paulo, Brazil, Nov 2008
- Invited Speaker, The Sixth Greek Conference, Corfu, Greece, Sep 2009

Peter Fuller
- Invited Seminar, The Mineralocorticoid Receptor - Update on Biology, Structure and Ligands, Berlin, Germany, Sep 2008
- Invited Seminar, Western Australian Medical Research Institute, Perth, Oct 2008
- Invited Speaker, 16th Annual Scientific Meeting of the Japanese Society of Steroid Hormones, Fukui, Japan, Nov 2008
- Invited Seminar, University of Tokyo Graduate School of Medicine, Tokyo, Japan, Nov 2008
- Invited Speaker, 2nd Australia-China Biomedical Research Conference, Tianjin, China, April 2009
- Invited Speaker, Congenital Adrenal Hyperplasia Support Group Australia Inc, Melbourne, July 2009
- Invited Speaker, 52nd Annual Scientific Meeting of the Endocrine Society of Australia, Adelaide, Aug 2009
- Invited Speaker, Combined Scientific Research Meeting, Kolling Institute for Medical Research, Sydney, Nov 2009

John Funder
- Invited Speaker, Workshop on Prereceptor Steroid Metabolism, Eibsee, Germany, July 2008
- Invited Speaker, Bayer Colloquium on Mineralocorticoid Receptor Antagonists, Berlin, Germany, Sep 2008
- Plenary Lecturer, International Congress of Hormonal Steroids and Hormones in Cancer, Quebec City, Canada, September 2008
- Invited Speaker, 13th International Congress on Endocrinology, Rio de Janeiro, Brazil, Nov 2008
- Invited Speaker, German Society for Cardiology, Workshop on Novel Therapies in Cardiovascular Medicine, Wurzburg, Germany, Dec 2008
- Invited Speaker, Clinical Endocrinology and Diabetes, Aspen, USA, Jan 2009
- Japan Endocrine Society Clinical Endocrinology meeting, Tokyo, Japan, March 2009
- Invited Speaker, China-Australia Congress of Medical Research, Tianjin, China, April 2009
- Invited Speaker, International Aldosterone Forum, Tokyo, Japan, May 2009
- Presidential Lecture, ENDO 2009 - The Endocrine Society Annual Meeting, Washington DC, USA, June 2009
- Invited Speaker, Primary Aldosteronism Conference, Turin, June 2009

Matthew Gillespie
- Invited Speaker, Australian and New Zealand Bone and Mineral Society Postgraduate Meeting, Melbourne, April 2008
- Invited Speaker, Cancer-induced Bone Disease VII, Edinburgh, Scotland, July 2008
- Invited Speaker & Chair, 2nd Joint Meeting International Bone & Mineral Society and Australian & New Zealand Bone & Mineral Society, Sydney, March 2009

Guiying Nie
- Invited Speaker, International Conference on Reproductive Immunology, Shanghai, China, Aug 2008
- Invited Speaker, 14th International Federation of Placenta Associations, Seggau Castle, Austria, Sep 2008
- Invited Speaker, 40th Annual Meeting of the Society for Reproductive Biology, Adelaide, Aug 2009
- Invited Speaker, 3rd SGI International Summit, Sendai, Japan, Nov 2009

Vicky Kartsogiannis
- Invited Speaker, Australian & New Zealand Bone & Mineral Society Annual Scientific Meeting, Melbourne, Aug 2008

Rob McLachlan
- Invited Speaker, Australian Diabetic Educators Association, Melbourne, Aug 2008
- Invited Speaker, Australian Men's Health Congress, Melbourne, Oct 2008
- Invited Speaker, Serono Symposium, Brisbane, Oct 2008
- Invited Speaker, Fertility Society of Australia, ASM, Brisbane, Oct 2008
- Invited Speaker, 13th International Congress on Endocrinology, Rio de Janeiro, Brazil, Nov 2008
- Invited Speaker, Australasian Association of Clinical Biochemists, Melbourne, Feb 2009
- Invited Speaker, International Congress of Andrology; Postgraduate Course, Barcelona, Spain, March 2009
- Invited Speaker, 5th Asia Pacific Fertility Expert Meeting, Ho Chi Min City, Vietnam, May 2009
- Invited Speaker, ENDO 2009 – The Endocrine Society Annual Meeting, Washington DC, USA, June 2009

- Invited Speaker, Andrology Australia Annual Forum, Gold Coast, June 2009
- Invited Speaker, Australasian Society of Cytogenetics Annual Scientific meeting, Melbourne, Aug 2009
- Invited Speaker, 43rd World Congress of Surgery of International Society of Surgery, Adelaide, Sep 2009
- Invited Speaker, Australasian Fire & Emergency Service Authorities Council and Bushfire CRC Conference, Gold Coast, Sep 2009
- Invited Speaker, Asia Pacific Society of Andrology, Nanjing, China, Oct 2009
- Invited Speaker, North Sichuan Medical College, Nanchong, China, Oct 2009
- Invited Speaker, Fertility Society of Australia Meeting, Perth, Oct 2009

Guiying Nie

- Invited Speaker, International Conference on Reproductive Immunology, Shanghai, China, Aug 2008
- Invited Speaker, 14th International Federation of Placenta Associations, Seggau Castle, Austria, Sep 2008
- Invited Speaker, 40th Annual Meeting of the Society for Reproductive Biology, Adelaide, Aug 2009
- Invited Speaker, 3rd SGI International Summit, Sendai, Japan, Nov 2009

Amanda Rickard

- Invited Speaker, The RAS Club, Monash University, Melbourne, Victoria, Oct 2009

Nana Saleh

- Invited Speaker, 2nd Joint Meeting International Bone & Mineral Society and Australian & New Zealand Bone & Mineral Society, Sydney, March 2009

Lois Salamonsen

- Invited Speaker, 9th Royan International Twin Congress, Tehran, Iran, Aug 2008
- Invited Speaker, 5th International Conference on the Female Reproductive Tract, Frauenchiemsee, Germany, May 2009
- Invited Speaker, IUPS Congress, Kyoto, Japan, July 2009
- Invited Speaker, 40th Annual Meeting of the Society for Reproductive Biology, Adelaide, Aug 2009
- Invited Speaker, Queenstown Molecular Biology meeting cluster (Reproductive Biology), Queenstown, New Zealand, Sep 2009
- Invited Speaker, Fertility Society of Australia Meeting, Perth, Oct 2009

Mai Sarraj

- Invited Speaker 9th Royan International Research Congress, Tehran, Iran, Aug 2008
- Invited Seminar Speaker, Tehran University of Medical Sciences, Medical Genetics Department , Tehran, Iran, Aug 2008
- Invited Seminar Speaker, Kuwait University, Department of Microbiology, Faculty of Medicine, Kuwait, Sep 2008
- Invited Speaker, 5th International Symposium on the Biology of Vertebrate Sex Determination, Kona, Hawaii, USA, May 2009

Evan Simpson

- Invited Speaker, 9th International Aromatase Congress, Beijing, China, Oct 2008
- Invited Speaker, 13th International Congress on Endocrinology, Rio De Janeiro, Brazil, Nov 2008
- Invited Speaker, 56th Annual Meeting of the Society for Gynecological Investigation, Glasgow, Scotland, March 2009
- Invited Speaker, Laboratory of Reproductive and Developmental Toxicology – NIEHS, Research Triangle Park, North Carolina, USA, June 2009
- Invited Speaker, 16th International Conference on Cytochrome P450, Okinawa, Japan, June 2009
- Invited Speaker, Annual Scientific Conference, The Egyptian Association of Endocrinology, Diabetes and Atherosclerosis, Alexandria, Egypt, Oct 2009

Kaye Stenvers

- Invited Speaker, 39th Annual Meeting of the Society for Reproductive Biology, Melbourne, Aug 2008
- Invited Speaker, 13th World Congress on Advances in Oncology and 11th International Symposium on Molecular Medicine, Crete, Greece, Oct 2008
- Invited Speaker, TGF-beta Workshop, Adelaide, Aug 2009
- Andrew Stephens, Invited Speaker, Pharmacy Women's Congressm, Melbourne, Aug 2008

Yao Wang

- Invited Speaker, 51st Annual Scientific Meeting of the Endocrine Society of Australia, Melbourne, Aug 2008
- Invited Speaker, 52nd Annual Scientific Meeting of the Endocrine Society of Australia, Adelaide, Aug 2009

Ken Walker

- Invited Speaker, 16th International Society of Developmental Biologists Meeting, Edinburgh, United Kingdom, Sep 2009
- Invited Speaker, 1st Annual Melbourne Cell and Developmental Biology Meeting, Melbourne, Nov 2008

Morag Young

- Invited Speaker, ENDO 2008 - Endocrine Society Annual Meeting, San Francisco, USA, June 2008
- Invited Speaker, 17th Asian Pacific Congress of Cardiology, Kyoto, Japan, May 2009
- Invited Seminar, IRCCS San Raffaele Pisana, Rome, Italy, July 2009

VISITING SPEAKERS

1/7/08 – 31/12/09

PHI/MIMR Joint Seminars

Dr Lynette Airey
CSIRO, Victoria
"Scientists in schools"

Professor John Aitken
ARC Centre of Excellence in Biotechnology and Development, New South Wales
"Function and failure in the male germ line: a spermatozoon's perspective"

Professor David Berman
The Johns Hopkins University, USA
"Deja vu all over again: how prostate and bladder cancers reuse developmental programs"

Associate Professor Christine Clarke
Westmead Institute for Cancer Research, New South Wales
"Progesterone signalling in normal and malignant breast"

Professor Suzanne Cory
The Walter and Eliza Hall Institute, Victoria
"The Bcl-2 family: an Achilles' Heel for cancer?"

Dr Nathan Cowieson
Monash Synchrotron Center, Victoria
"101 things to do at the synchrotron with your favourite protein"

Dr Ben Croker
The Walter and Eliza Hall Institute, Victoria
"Inflammation and autoimmunity caused by a SHP1 mutation depend on MyD88 and a microbial trigger"

Professor Peter Currie
Australian Regenerative Medicine Institute, Victoria
"Modelling muscle development,disease and regeneration in zebrafish"

Professor Lex Doyle
The Royal Women's Hospital, Victoria
"The effect of changes in perinatal care over the past 50 years"

Professor Paul Gleeson
Bio21, The University of Melbourne
"Manipulation of the membrane trafficking pathways in vivo using interference RNA"

Professor Robert Graham
Victor Chang Cardiac Research, New South Wales
"The cryptic regeneration of the adult mammal"

Dr Daniel Häusermann
Australian Synchrotron, Victoria
"The Australian Synchrotron Imaging and Medical Facility: building for clinical Research"

Professor Henry Jabbour
Medical Research Council Human Reproductive Sciences Unit, United Kingdom
"Prokineticins: novel reproductive function"

Ms Rebecca James
Chief Executive Officer, Research Australia
"Capturing hearts and minds"

Dr Benjamin Kile
Walter and Eliza Hall Institute of Medical Research, Victoria
"The molecular regulation of platelet production and function"

Professor Peter Koopman
Institute for Molecular Bioscience, Queensland
"Sex determination: Biology's great balancing act"

Dr Kenneth Korach
Laboratory of Reproductive and Developmental Toxicology, NIEHS/NIH
"Consequences from the loss of oestrogen receptor function"

Professor Peter Leedman
Western Australian Institute for Medical Research, Western Australia
"MicroRNAs, nuclear receptors and cancer"

Dr Camden Lo / Mr Stephen Firth
Monash Micro Imaging, Victoria
"Imaging at MMI: capabilities, applications and future developments"

Dr Ijad Madisch
ResearchGate
"ResearchGATE – a platform for scientific networking"

Professor John Mattick
Institute for Molecular Bioscience, Queensland
"The central role of RNA regulation in human development, physiology and cognition"

Dr Gavin Meredith
Invitrogen
"Analysing epigenetic changes in cancer"

Dr Mike Payne
Applied Biosystems
"The SOLiD Sequencer"

Professor Marilyn Renfree
Department of Zoology, The University of Melbourne, Victoria
"A tale of two sexes"

Associate Professor Sarah Robertson
School of Reproductive Health and Paediatrics, South Australia
"Seminal fluid signalling in the female reproductive tract and its role in immune adaptation for pregnancy"

Professor Stefan Rose-John
Christian-Albrechts-Universität zu Kiel Medical School, Germany
"Analysis of the role of IL-6 trans-signaling and the Metalloproteinase ADAM17 in Inflammation and Cancer"

Dr Jon Sherlock
Applied Biosystems
"Gene expression & regulation: new technologies enabling break-through research"

Professor Ian Smith
Monash University, Victoria
"Proteomic advances for the identification, characterisation and accurate quantitation of proteins"

Dr Paul Trainor
Stowers Institute for Medical Research, USA
"Making faces: the role of neural crest cells in craniofacial development and congenital birth defects"

Professor David Vaux
Department of Biochemistry, La Trobe University
"Ten rules for the presentation and interpretation of data in publications"

Professor Brandon Wainwright
Institute for Molecular Bioscience,Queensland.
"The hedgehog pathway in stem cell regulation and tumorigenesis"

Dr Trevor Wilson
Monash Institute of Medical Research, Victoria
"High content screening"

PHI Seminars

Dr Anthony Albiston
Howard Florey Institute, Victoria
"The ins and outs of IRAP, a novel aminopeptidase"

Dr Sofianos Andrikopoulos
Monash Institute for Medical Research, Victoria
"Type 2 diabetes and insulin secretion – when too much is not good for the islet beta cell"

Professor John Cidlowski
National Institute of Environmental Health Sciences, USA
"Tissue specific actions of glucocorticoids: how little we really know!"

Professor Mark Cooper
Baker IDI Heart and Diabetes Institute, Victoria
"Why do diabetic vascular complications continue to progress?"

Dr Dennis Dowhan
Diamantina Institute, Queensland
"The role of splicing factors and alternative RNA splicing in cancer"

Professor Sally Dunwoodie
Victor Chang Cardiac Research Institute, New South Wales
"Placental insufficiency and its impact on embryonic development"

Dr Mathias Francois
University of Queensland, Queensland
"SOX18 induces development of the lymphatic vasculature in mice"

Dr Caroline Gargett
Monash Institute for Medical Research, Victoria
"Uterine stem/progenitor cells and their role in endometrial proliferative disorders"

Dr Paul Gregorevic
Baker IDI Heart and Diabetes Institute, Victoria
"Using gene therapy tools to study muscle biology and disease"

Dr Lynda Harris /
Ms Samantha Smith
University of Manchester, United Kingdom
“Human tissue models of the materno-fetal interface in early pregnancy”

Dr Anna Lauber-Biason
University Children’s Hospital, Switzerland
“X and Y: pathways to sex development”

Professor Andrew McMahon
Harvard University, USA
“From progenitor to product: development and repair of the mammalian kidney”

Associate Professor Moira O’Bryan
Monash Institute for Medical Research, Victoria
“Mouse models of male infertility”

Professor Tsutomu Ogata
National Research Institute for Child Health and Development, Japan
“Genetic studies on endocrine disorders”

Dr Belinda Parker
Peter MacCallum Cancer Centre, Victoria
“Suppression of Type 1 IFN defence pathways as a mechanism for breast cancer metastasis to bone”

Professor Rob Pike
Monash University, Victoria
“The role of protease-activated receptor-2 in periodontal (gum) disease”

Professor Rob Ramsay
Peter MacCallum Cancer Institute, Victoria
“GI stem/progenitor cells in homeostasis and disease”

Professor Ray Rogers
Robinson Institute, South Australia
“Roles of extra-cellular matrix in the ovary”

Dr Natalie Sims
St Vincent’s Institute
“LIFR and gp130 signals in bone formation and destruction”

Dr Craig Smith
Murdoch Childrens Research Institute, Victoria
“Sex determination and gonadal development in an avian model, the chicken embryo”

Dr Gregory Steinberg
St Vincent’s Institute, Victoria
“Inflammation in obesity is a common link between defects in lipid metabolism and insulin resistance”

Professor Neil Watkins
Monash Institute for Medical Research, Victoria
“Overcoming barriers to differentiation in cancer”

GRANT FUNDING

Program Support

Cancer Council Victoria
Victorian Breast Cancer Research Consortium (VBCRC) Program Grant
– Evan Simpson; $1,605,470 (2009-2011)

NHMRC Program Grant in partnership
Disorders of Human Sexual Development
– Vincent Harley (PHI Chief Investigator); $5,000,000 (2008-2012)

Project Support

Cancer Council Victoria - Project Grants:
– Molecular endocrinology of Granulosa Cell Tumours of the Ovary. Peter Fuller, $300,000 (2009-2011)
– Role of LHR-1 in breast cancer proliferation (Role of LRH-1 in breast cancer proliferation). Colin Clyne, $196,500 (2009-2010)
– Characterisation of the molecular pathogenesis of ovarian granulosa cell tumours. Peter Fuller, $70,000 (2008)
– Role of Parathyroid Hormone related Protein in DNA repair and breast cancer susceptibility to TRAIL-mediated apoptosis. Matthew Gillespie, $100,000 (2008)

CASS Foundation - Proof of Concept:
– Male susceptibility to Parkinson's Disease: A role for SRY? Jooyung Lee, $60,000 (2008-2009)

Contraceptive Research and Development (CONRAD)
– Inhibition of embryo implantation in the rabbit by Poly-R. Guiying Nie, US$78,000 (2008)

Helen Macpherson Trust:
– Male susceptibility to Parkinson's Disease: A role for SRY? Jooyung Lee, $39,310 (2008)

National Breast Cancer Foundation (VBCRC):
– Role of Parathyroid Hormone related Protein in DNA repair and breast cancer susceptibility to TRAIL-mediated apoptosis. Matthew Gillespie $256,500 (2008-2009)

NHMRC - Project Grants:
– Role of PC6 in uterine-epithelium for embryo implantation and clinical implications. Guiying Nie, $620,925 (2009-2011)
– The role of Interleukin-33 and T cells in the maintenance of bone mass. Julian Quinn, $571,500 (2010-2012)
– Crosstalk between Wnt/β-catenin and SOX signalling in mammalian sex determination. Pascal Bernard, $547,500 (2010-2012)
– Macrophage mineralocorticoid receptors and heart disease. Morag Young, $488,276 (2008-2010)
– Cytokines critical for optimal pregnancy outcomes. Evdokia Dimitriadis, $590, 250 (2008-2010)
– TGFβR3 receptor in testis development. Mai Sarraj, $319,500 (2008-2010)

Perpetual Trustees, Ramaciotti Foundation - Establishment Gift:
– When good eggs go bad: Identification of genes associated with the loss of oocyte quality with age. Karla Hutt, $50,000 (2009)

Victorian Cancer Agency - Early Career Seed Grant:
– Identifying a sensitive molecular switch important for the development of breast cancer. Ashwini Chand, $50,000 (2008)
– Identification of novel auto-antigens as early markers for the detection of ovarian cancer. Andrew Stephens, $48,520 (2008)

People Support

Evdokia Dimitriadis
NHMRC Career Development Award (Level 2). $409,000 (2009-2012)

Kristy Brown
National Cancer Institute of Canada, Terry Fox Postdoctoral Fellowship CA$127,188 (2008-2011)

Simon Chu
L'Oréal Paris Research Fellowship $120,000 (2009-2010)

Anne Corbould
Training Fellowship – Clinical $229,500 (2009-2012)

Nicole Fairweather
Nurses Board of Victoria, Div 2 Practice Enhancement Grant
$2,504 (2009)

Karla Hutt
Australian Menopause Society, Young Investigator Grant. $5,000 (2009)
NHMRC Training Fellowship (Australia). $274,000 (2009-2012)

Kevin Knower
US Department of Defense Fellowship. US$188,487 (2010-2011)

Katie Meehan
Witchery & Madison, Research Fellowship. $120,000 (2009-2010)

Ellen Menkhorst
The Lalor Foundation, Postdoctoral Basic Research Fellowship.
US$35,000 (2009)

Frances Milat
The Michael, John and Phoebe Jones Fellowship. $15,000 (2009-2010)

Evan Simpson
NHMRC Senior Principle Research Fellowship. $766,250 (2009-2013)

Jun Yang
NHMRC Postgraduate Scholarship. $94,266 (2009-2011)

Equipment and educational support

Support for purchase of essential equipment and travel to present at learned society meetings:

- Australian & New Zealand Bone & Mineral Society (ANZBMR)
- Australian & New Zealand Placental Research Association
- Australian Menopause Society (AMS)
- Australian Research Council (ARC)
- CASS Foundation
- Cancer Council Australia
- Cancer Council Victoria
- Collier Charitable Fund
- Flack Trust
- Endocrine Society of Australia (ESA)
- Harold and Cora Brennen Benevolent Trust
- Harold Mitchell Foundation
- Helen Macpherson Smith Trust
- Howard Family Trust
- International Federation of Placental Associations (IFPA)
- Lord Mayor's Charitable Trust
- Montgomery Foundation Pty Ltd
- National Breast Cancer Foundation (NBCF)
- Ovarian Cancer Research Foundation (OCRF)
- Rebecca L. Cooper Medical Research Foundation
- Society for Reproductive Biology
- The Ian Potter Foundation
- The Lalor Foundation Inc.
- The Marian and E.H. Flack Trust
- The Medical Advances Without Animals (MAWA)
- Trust Co Ltd
- Victorian Cancer Agency (VCA)

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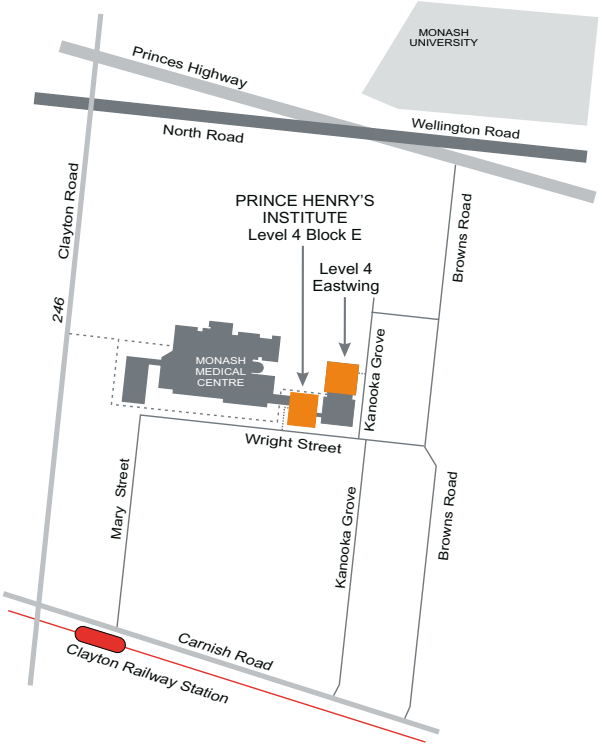


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