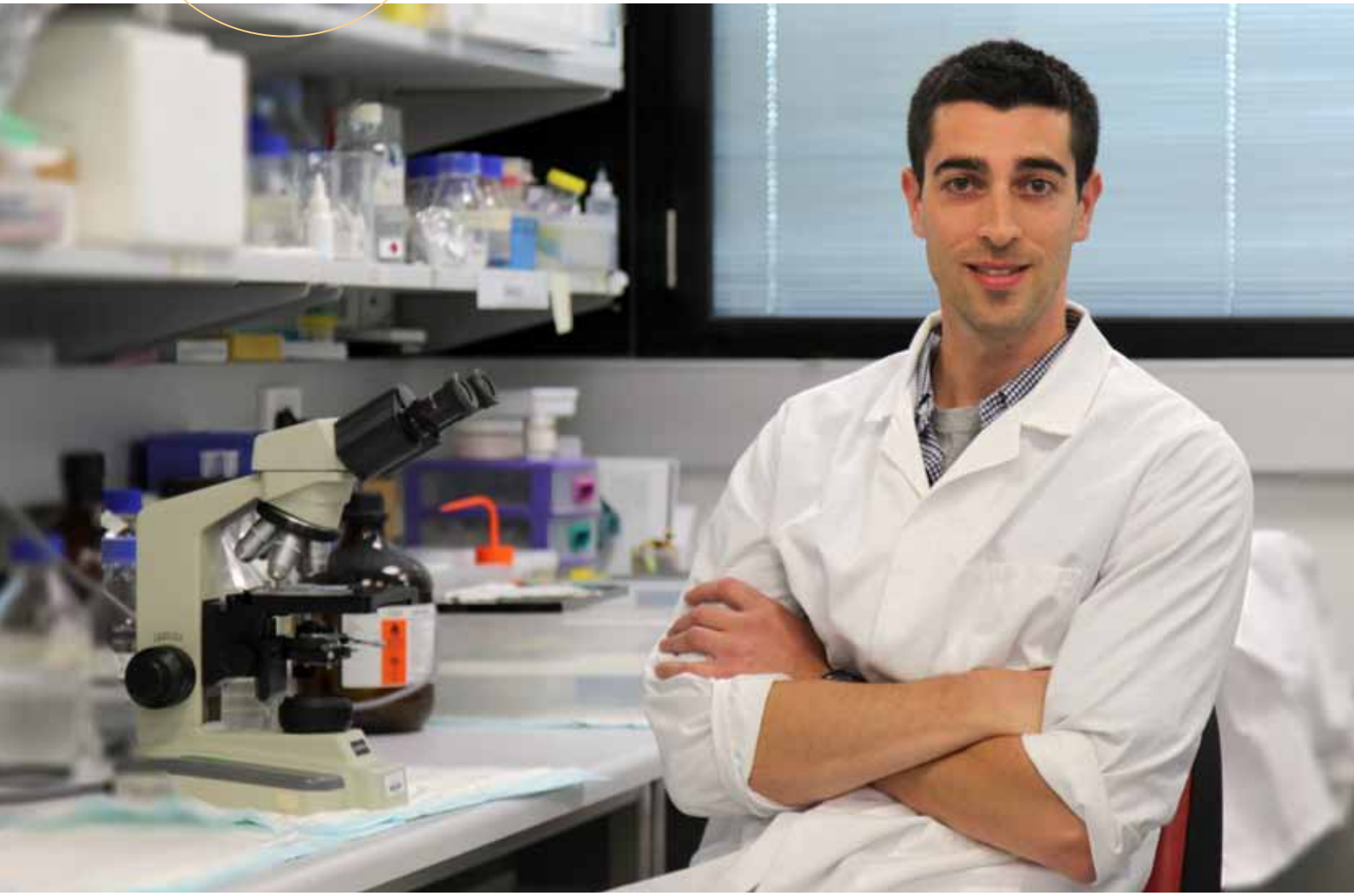

prince henry's institute
2010 scientific report

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Cover image

Peter Nicholls, PhD student, Prince Henry's Institute, Growth Factor Signalling Laboratory

Peter is an early career researcher, completing the third year of his PhD. He is investigating the molecular mechanisms of hormonal action in the testis which will contribute to our understanding of male fertility problems. In 2010, Peter won a New Investigator Award from the Society for Reproductive Biology. He is the holder of a Graduate Excellence Award from Prince Henry's Institute, and this year won the award for best PhD student presentation at the Prince Henry's Institute annual Student Symposium.

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OUR VISION
To improve health through hormone research

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

Research Themes:
- Cardiovascular disease
- Cancer
- Genes and healthy development
- Men's health
- Women's health

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We acknowledge the contribution of the clinicians and scientists of Prince Henry's Institute, who over the last five decades, have influenced the course of medical research into health and hormones and established our international reputation for innovative research.

celebrating 50 years

As innovators, their role in the discovery of the vital reproductive hormone, inhibin, revealed its critical function in fertility and led to our development of the first test for ovarian cancer. Equally, their discovery of a brand new class of drugs to treat breast cancer, aromatase inhibitors, continues to influence our understanding of its role in breast cancer development, sperm formation and the metabolism of body fat.

As pioneers in an emerging field, they successfully developed a progressive and supportive research environment that continues today. In our 50th year, our researchers have demonstrated great progress, building on these influential discoveries.

CHAIRMAN AND DIRECTOR'S REPORT

Medical research is a sound investment by the Australian community in improving our health and quality of life. This investment produces positive returns during our lifetime and beyond.

Prince Henry's Institute is an independent medical research institute, and our singular focus is medical research from the laboratory to the clinic. In this highly productive environment, our researchers undertake detailed laboratory studies and clinical trials which are translated into new, more effective treatments and preventative measures that benefit our health and wellbeing at all stages of our lives.

During 2010, our scientists energetically pursued discoveries such as unravelling the complexities of human development and infertility, identifying markers of pre-cancerous ovarian disease and searching for better targetted therapies for breast cancer and heart disease.

Rising concerns about risk factors, such as the steady increase in obesity rates have opened up new avenues for research into heart disease and breast cancer. We recently instigated a clinical trial of a well-known diabetes drug for the treatment and prevention of estrogen-dependent breast cancer to advance our knowledge of several metabolic pathways linking obesity and breast cancer.

New technology platforms have been installed during 2010 and are being used effectively to increase the pace and productivity of our research. This investment has especially accelerated our discoveries of markers of early-stage ovarian cancer in our search for an early detection test.

The social trend to delay parenthood has an effect on fertility which declines with age. This year, our researchers published the first in a series of papers exploring the critical 'window of receptivity' for the establishment of a successful pregnancy. Our discoveries could guide clinical practice for diagnosing infertility and for improving success rates of reproductive technologies. They could also lead to wider contraceptive options for women. We also have promising hopes for new options to prevent serious infertility problems for girls and young women which have resulted from chemo- and radiation therapies during their treatment for cancer.

New studies are underway to address the health needs and clinical care for women in mid life.

We are collaborating with a Canadian research team to investigate how blood hormones change as women approach menopause. Thirty women have participated in this two-year study which combines our expertise in blood hormone analyses and Canadian ultra-sound technology. Women are at greater risk of osteoporosis once they have reached menopause. Patients are receiving a drug used to treat osteoporosis, and its effects beyond the skeleton are being measured to determine whether it provides more far-reaching, general well-being effects for women in mid life.

We continue to maintain our focus on translating research to benefit health care for men. Our new insights into the evolution of sex determination have uncovered strong evidence of the genetic link between sex determination and the neurological decline evident in Parkinson's disease. This discovery could hold the clue as to why more men develop Parkinson's than women, and lead to new methods for slowing the disease's progression in men, or reduce their susceptibility. In 2010, we introduced a clinical research service to assist men with medically-induced testosterone deficiency which has resulted from their treatment for

prostate cancer. Utilising proteomic techniques, our researchers progressed toward producing a blood test for certain types of male fertility as an alternative to the current intrusive test.

In 2010, applications by our researchers for highly competitive research grants proved to be very fruitful.

Over $6.6 million was awarded by the National Health and Medical Research Council for research and development over the next three to five years. This is a three-fold increase over the previous year, and our 57% success rate for project grant applications well-exceeded the national average of 23%. Many of the awardees are early career researchers and emerging scientific leaders in their field, and this is a promising factor for increased research output.

Increased philanthropic support has enabled our researchers to explore bold ideas in the laboratory, and to travel and present their research in international settings. Significantly, we have utilised philanthropic support and donations to attract talented medical researchers to take up new employment opportunities with us on their return to Australia.

Our valued partnership with Southern Health is vital to facilitate the translation and integration of our research discoveries into clinical care. Medical research also translates into important economic benefits that reduce the burden and cost of disease on our health system. Equally significant, is our partnership with Monash University to ensure the sustainability of our scientific workforce through educating and training future research leaders. Our innovative collaboration - the Monash Health Translation Precinct (MHTP) - was consolidated in 2010 with active seminar programs and equipment allocations. We continue to work together to realise the potential of this partnership, with co-location of MHTP in a new capital development.

As a member of the newly formed multi-site Monash Comprehensive Cancer Consortium with Monash University, Southern Health, Alfred Health, Peninsular Health and Cabrini Health, our collaborative goal is to interconnect research and clinical strengths in ways that benefit Victoria's cancer patients.

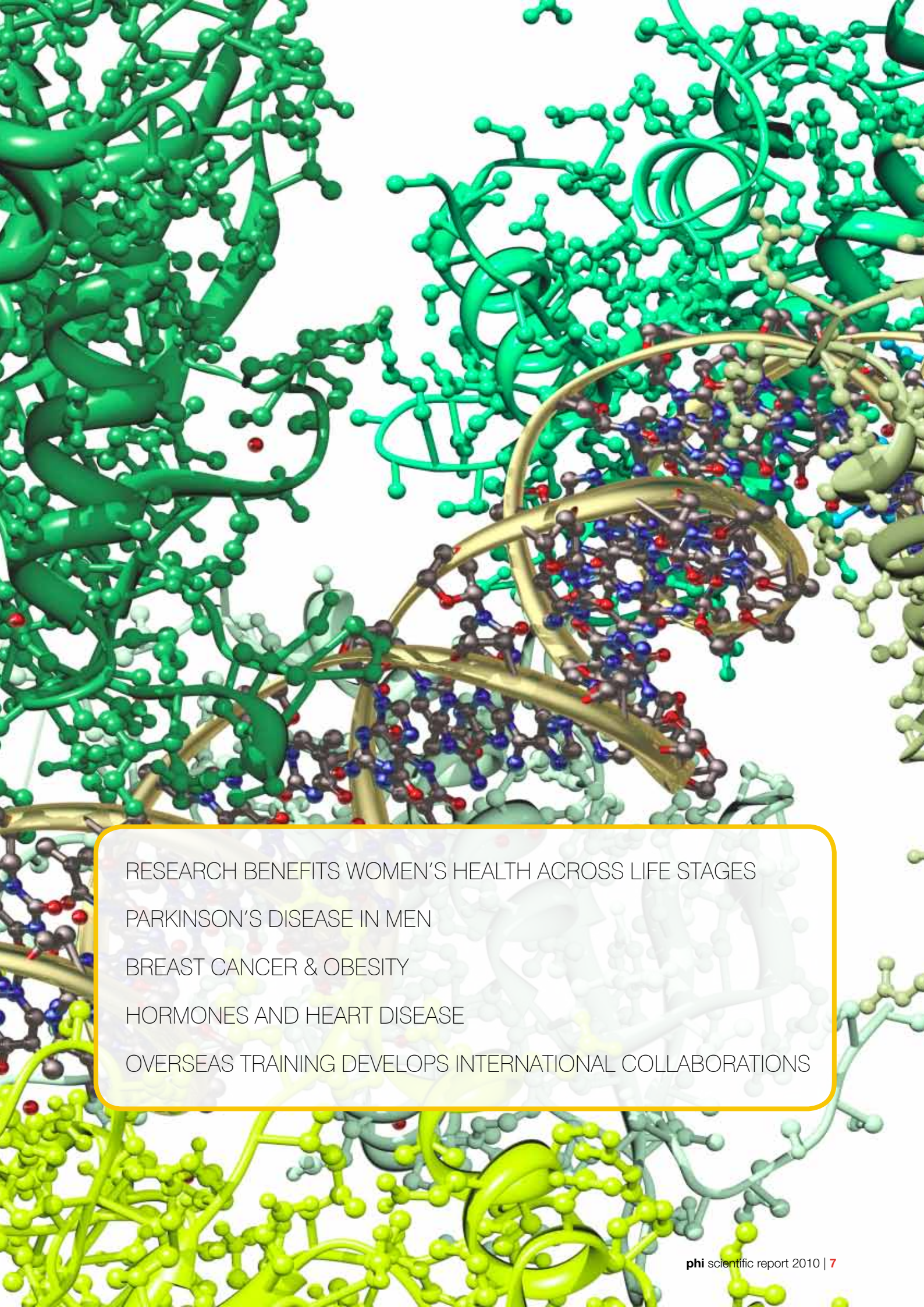
Celebrating our 50th year during 2010 saw us renew and extend valued relationships with our partners, research collaborators and our respected alumni. A stimulating one-day scientific summit was followed by a reception at Government House, generously hosted by a member of our alumni and Governor of Victoria, Professor David de Kretser and Mrs de Kretser. We recognised our research leaders, past and present and reached out to our broader community of supporters.

The ongoing financial support of the Australian and Victorian Governments, major gifts from philanthropic organisations and many individuals are greatly valued and appreciated.

To the leadership team, staff and students, we acknowledge your many talents and dedication in striving for our vision of improved health through hormone research.

Dr Bob Edgar,
Chairman

Professor Matthew Gillespie,
Director/CEO



RESEARCH BENEFITS WOMEN'S HEALTH ACROSS LIFE STAGES

PARKINSON'S DISEASE IN MEN

BREAST CANCER & OBESITY

HORMONES AND HEART DISEASE

OVERSEAS TRAINING DEVELOPS INTERNATIONAL COLLABORATIONS

RESEARCH BENEFITS WOMEN'S HEALTH ACROSS LIFE STAGES

In conjunction with the release of the National Women's Health Policy in December 2010, we showcase the major research initiatives that researchers at Prince Henry's Institute are pursuing to benefit women's health and their quality of life.

Medical advances in recent decades have led to increased longevity and we are living longer and healthier lives. However, many women continue to experience disadvantages in accessing health services. Increasingly, obesity, physical activity and mental health are bringing health challenges for women. The ageing of the population, the projected increase in dementia and the costs of health care are challenges we face as individuals, and as a society.

It is recognised there is a complex interplay between health, and factors such as sex and gender, access to resources and changing social and economic expectations. For women, their ability to access income, education, employment, social connection and security impacts on their lives and health throughout the course of their lives.

Our vision – medical research improving the quality of life - is informed by the health and life experiences of girls and young women, women in their reproductive years, women in mid-life, and women seeking to age well.

Cardiovascular Disease

Despite remarkable health gains in the prevention and treatment of cardiovascular disease, it is still the leading cause of death in Australian women. There is also evidence of a lack of awareness of how significant a threat cardiovascular disease is to women's health, and that it affects many younger women, as well as older women.

We have an enviable track record in cardiovascular hormones research and clinical application of research findings, with major contributions from eminent researchers and physician scientists, including Professor John Funder. With new funding, we are expanding our studies of the role played by steroid hormones in the development of cardiovascular disease. Our aim is to develop heart-specific alternatives to existing drugs for cardiovascular disease, whose wide-spread use has been limited by their side effects.

Cancer

Survival rates for women from cancer continue to improve, but the falling death rate from cancer is being offset by increased population in the 65 years and over age group.

In 2006, the lifetime risk of a woman developing breast cancer before the age of 85 was 1 in 9.

Obesity is a major risk factor for breast cancer, due in part to the synthesis of the steroid, estradiol by fat tissue and its known role in promoting breast cancer. We are studying metabolic pathways that link obesity and breast cancer, conducting clinical trials of potential new drugs for breast cancer, and investigating proteins that may hold the key to developing drugs for a class of breast cancer that is particularly difficult to treat.

As a member of the Victorian Breast Cancer Research Consortium, we conduct longer-term research to improve knowledge of the basic biology and genetics of breast cancer and provide opportunities for developing better treatments and prevention strategies.

Ovarian cancer is a challenging cancer, as a lack of discernible symptoms and difficulty with diagnosis means there are a high proportion of women who are diagnosed with ovarian cancer at a late stage. We are working to develop a screening test that can accurately identify early or pre-cancerous ovarian disease. This will facilitate earlier and better treatment and lead to improved survival rates for women. We initiated a clinical collection program, with the goal of analysing over 1500 tissue samples, which will permit statistically-significant testing of candidate proteins as clinical markers for ovarian cancer. Over 600 women participated in this unique program in 2010.

We recently identified an important genetic marker for granulosa cell tumours, which account for five per cent of all malignant ovarian cancers. We are also investigating the clinical potential of betaglycan, a protein involved in gonad development, which we have shown can help to halt or prevent the spread of malignant cancer cells from the ovary.

Endometrial cancer is Australia's most common gynaecological malignancy, typically affecting postmenopausal women, but existing treatment options for advanced endometrial cancer are inadequate. We are testing a potential therapeutic agent produced by collaborators at Commonwealth Serum Laboratories.

Women's sexual and reproductive health

Sexual and reproductive health, including maternal health is a priority for Australian women.

In work, supported by a grand challenges explorations grant from the Bill and Melinda Gates Foundation, we have identified an enzyme that could serve as a target for a new female contraceptive. We are testing whether a peptide inhibitor could be used as a non-hormonal form of woman-controlled contraception, which also protects against HIV.

The rate of sexually transmitted infections in Australia, such as chlamydia, is increasing amongst young women and has the potential to impact on fertility later in life. Our work would simultaneously protect women against infection by organisms such as chlamydia and the AIDS virus. This has the potential to be developed and translated into health benefits on a global scale.

The broad social trend to delay parenthood can have an effect on fertility, which declines with age. A better understanding of the biological and hormonal processes behind fertility will help infertile couples and women who wish to conceive later in life. Approximately 15% of Australian couples of reproductive age have problems with fertility. We are working to understand the role hormones play in fertility; identifying the inter-relationships between the ovary, testis and pituitary in the hormonal regulation of fertility and the changes with age.

A major contributor to female infertility is when the uterus fails to become receptive to implantation by a healthy embryo, but there is no reliable biochemical test for this currently available. We have identified an enzyme that could potentially be used as the basis for a rapid uterine receptivity test requiring only minimal surgical intervention.

Impaired embryo implantation can affect placental development and may lead to miscarriage, pre-eclampsia or maternal death. We are identifying proteins associated with the failure of an embryo to implant even when the endometrium (uterus lining) is receptive.

We are working on a sensitive, high-throughput assay to predict pre-eclampsia, which causes almost one in five maternal and perinatal deaths in industrialised nations.

Our research into how the endometrium is restored after menstruation and becomes receptive to embryo implantation is improving our knowledge of the causes of infertility and assisting the development of new tests to improve IVF success rates. We have also identified new proteins that accelerate repair of the endometrium after menstruation that will have implications for treatment of abnormal uterine bleeding.

We are also studying protein differences associated with endometriosis, a poorly-understood condition that affects one in eight Australian women, often causing debilitating pain and potentially leading to infertility.

Women in mid-life

There are a number of health issues which are important for women of mid-age, and this is a time of transition physically, as well as in other ways. Menopause is a life stage often reached in a woman's late forties or early fifties. The transition to full menopause can seriously affect a woman's mental and physical health at a particularly challenging time in her life.

Our studies highlight the pattern of hormonal changes that occurs as menopause approaches. A key aim is to relate these changes to changes in ovarian egg follicle production, which may be a major cause of clinical difficulties associated with menopause. Our studies of age-related changes in fertility hormones are complemented by detailed ultrasound imaging.

Ageing well

Women moving into their late sixties and beyond often experience an increase in health concerns. The leading causes of death for women at this stage of life are heart disease, stroke, dementia, breast cancer and falls.

The consequences of a fall can be greatly exacerbated by fractures where bone mass has been reduced through diseases such as osteoporosis, arthritis and most bone cancers. Women are at much greater risk than men of osteoporosis, especially after menopause.

We recently showed that a bone protein called IL-33 can reduce bone loss and stimulate new bone formation. We are now looking for ways to use IL-33 to treat bone disease without provoking harmful inflammatory responses.

The role of Prince Henry's Institute

Our research strengths lie in our laboratory studies and the participation of women in our clinical trials.

Our detailed studies focus on individual genes and hormones and their roles within a highly complex network of metabolic pathways. Our collaborative clinical trials enable us to pursue opportunities to apply our findings to the development of new, more effective treatments and preventive measures that will benefit women's health at all stages of their life.

PARKINSON'S DISEASE IN MEN

Being male increases the risk of Parkinson's disease by at least 50 per cent. Our investigations of a genetic link between sex determination and the neurological decline evident in Parkinson's could lead to new methods for slowing the disease's progression or reducing male susceptibility.

Despite the prevalence of Parkinson's disease in ageing societies, our understanding of this neurodegenerative disorder remains scanty. The underlying causes are largely unknown, we have no simple test or marker to confirm a diagnosis and we cannot reliably predict how quickly the disease will progress following diagnosis.

To find out more about the mechanisms underlying male susceptibility to Parkinson's disease, our brain and gender research program is drawing on the combined expertise of neuroscientist, Dr Joohyung Lee and molecular geneticist, Associate Professor Vincent Harley.

Parkinson's disease becomes clinically apparent as a result of neuronal cell death in the substantia nigra, a brain region that controls motor function. Symptoms such as trembling, muscle rigidity and slowness of movement appear when over 70 per cent of the neurons that produce the chemical messenger, dopamine in this region have died.

Men are more likely to get the disease than women, and men living with the disease outnumber women about 3 to 2. This disparity may be partly due to the sex-determining region Y gene (SRY), which determines maleness and directs embryonic gonads to develop into testes.

Pioneering work by Associate Professor Vincent Harley at PHI with Professor Eric Vilain at the University of California showed that SRY is also found in the brain, where it controls movement and coordination in males, via production of dopamine. SRY is specifically expressed in the dopamine-producing cells of the substantia nigra where it regulates genes coding for enzymes that control both the production and destruction of dopamine. We think SRY might be a risk factor in men developing Parkinson's disease.

Dr Joohyung Lee, who joined PHI from the Howard Florey Institute in 2008, has over eight years of postdoctoral research experience with Parkinson's disease in Australia and Canada. Under his guidance, we have broadened our use of surgical and behavioural experiments to assess neurological damage (dopamine cell death) in animals.

Vince is a leading researcher in the biology of gender. He has been studying the molecular mechanisms of SRY action since its discovery in the Goodfellow laboratory in London where he was a postdoctoral fellow.

Our brain and gender team is investigating factors that influence the expression of SRY in Parkinson's disease, and behavioural effects that result from SRY inhibition in the brain. Daniel Czech, a PhD student at PHI, has already shown that dopamine-producing cells dramatically increase their SRY expression in response to stress or injury.

"We are looking for novel ways to target neurological disorders," says Joohyung. "This investigation of the role of a male-specific gene in Parkinson's disease is a world-first."

Vince is an NHMRC Senior Research Fellow who joined PHI in 2000. He says that PHI is well-equipped to undertake ground-breaking medical research. "We are a boutique institute in some respects—small but very good at what we do. We also have valuable links with other researchers in Australia and overseas in the fields of SRY biology and Parkinson's disease."

Our researchers are currently investigating a potential new therapy. By inhibiting SRY levels in the *substantia nigra,* it may be possible to slow the progression of Parkinson's in men or reduce their susceptibility.

The research may also assist our understanding of other neurological disorders that are more prevalent in men than in women, such as schizophrenia, attention deficit hyperactivity disorder (ADHD) and autism.

The research is funded by a US National Institutes of Health project grant and philanthropic organisations including the Helen McPherson Smith Trust, the CASS Foundation and the Rebecca Cooper Medical Research Foundation.

BREAST CANCER AND OBESITY

Breast cancer affects one in nine Australian women, a statistic that could rise as a result of increasing obesity. Our researchers are working to develop treatments that avoid the serious side-effects associated with existing hormone therapies.

In Australia, breast cancer screening programs are helping to detect the disease at a relatively early stage, which improves the likelihood of a favourable outcome. However, women with obesity are at greater risk of breast cancer, which means that the rising incidence of obesity in our society is likely to lead to more breast cancer cases.

In recent years, PHI has played an important part in developing new drugs for breast cancer that work by inhibiting aromatase, a key enzyme in estrogen biosynthesis.

Estrogen production in breast tissue is implicated in the development and progression of breast cancer in post-menopausal women. However, existing hormone therapies for breast cancer that inhibit estrogen production result in serious side-effects such as bone loss, joint pain and occasionally cognitive impairment.

Dr Kristy Brown and Professor Evan Simpson and colleagues are investigating several interrelated biological pathways that affect the development of breast cancer.

The group's aim is to identify cheaper and safer therapies for breast cancer, such as drugs that reduce tumour size and help patients avoid major surgery. Results so far are promising and may lead to a preventive medication for women at risk of contracting breast cancer.

Canadian-born Dr Kristy Brown joined PHI in 2006 after completing her PhD in the Centre de Recherche en Reproduction Animale at the Université de Montréal. Her PhD focussed on steroid regulation during ovulation, but when her aunt was diagnosed with estrogen-dependent breast cancer, Kristy decided that she wanted to apply her passion for steroid research to breast cancer.

Kristy says she is enjoying the challenges and rewards that come with her work. She was recently awarded an NHMRC Career Development Fellowship to help develop her research leadership.

"My research inspires me every day," Kristy says. "My team works so hard. Each new result is exciting and leads to new possibilities. Evan Simpson's research pertaining to estrogen production within the breast has been pivotal in the understanding and treatment of postmenopausal breast cancer, so I feel privileged to be able to draw knowledge from him and build on ideas to design new projects and expand existing ones."

Together with Professor Stephen Fox from The University of Melbourne, Kristy and Evan were recently awarded a $586,000 NHMRC project grant for further work aimed at understanding how estrogen production is regulated. Their goal is to develop breast-specific inhibitors of estrogen production to obviate side-effects associated with existing hormone therapies.

Some of the factors involved in estrogen production are linked to aromatase via the LKB1/AMPK pathway. When activated, this pathway strongly inhibits aromatase expression in breast adipose stromal cells.

The LKB1/AMPK pathway is also involved in the regulation of cell cycle (p53) and hypoxia-related (HIF-1α) signalling pathways. Preliminary results at PHI indicate that aromatase expression in primary breast adipose stromal cells is inhibited by p53 and stimulated by HIF-1α. Kristy and her colleagues will use the NHMRC funding to test the hypothesis that the inter-related p53 and HIF-1α pathways are key regulators of aromatase expression within the breast of women in the context of obesity and post-menopausal breast cancer.

Kristy says PHI is well recognised for its hormone research. "We have cutting-edge technology that allows us to perform the experiments needed to test our hypotheses. Without these resources, it would be impossible to generate results of high enough standard to enable translational research. To think that friends and family members may actually one day benefit from our research is the most satisfying feeling."

HORMONES AND HEART DISEASE

Our impressive track record in investigating the roles played by steroid hormones in heart disease and high blood pressure, and in developing clinical applications based on our research findings, is being further strengthened by a new generation of researchers.

Recent highlights include new NHMRC grants totalling $1.1 million for further work in this area, a major award from the journal, Hypertension and an INSERM biomedical training fellowship from the NHMRC for Dr Amanda Rickard, who recently completed her PhD at PHI.

Amanda is a member of the PHI cardiovascular endocrinology laboratory led by Dr Morag Young. This team is studying the roles played by the mineralocorticoid receptor (MR) in cardiac failure and hypertension (high blood pressure). MR is the chief target of aldosterone, an important adrenal steroid hormone.

Morag and Amanda have been working to identify the particular cell types in the heart in which MR is critical for development of heart failure. Their aim is to exploit the characteristics of these cells in the development of drugs that act specifically on the heart without the unpleasant side-effects associated with drugs currently available for blocking MR activity.

In 2010, a paper by Amanda and Morag and their colleagues was judged one of the top two papers of the previous year by Hypertension, the prestigious journal of the American Heart Association. The paper reported their study which discovered the importance of the MR in the macrophage (a key inflammatory cell) for the development of cardiac fibrosis. In the presence of elevated salt levels and deoxycorticosterone (a drug that activates the MR), mice without macrophage MR suffered less heart tissue damage and had lower blood pressure than mice.

The accompanying Hypertension editorial concluded that “the study by Rickard et al. has the potential to change the way we look at macrophage infiltration. It also presents another reason why MR antagonists remain important therapeutic agents. It is amazing to consider the meteoric rise in interest in this once-forgotten hormone and its receptor.”

Morag was awarded an NHMRC project grant worth $591,732 to further this work. This will enable her team to further explore the clinical finding that reducing MR levels can improve outcomes for patients with congestive heart failure or hypertension.

The NHMRC also awarded PHI’s Professor Peter Fuller $521,706 to investigate the mechanisms by which aldosterone receptors may be activated or blocked in specific tissues. Currently available aldosterone blockers are useful for treating heart disease, but limited by potassium retention in the kidney. Peter’s ultimate aim is to develop tissue-specific aldosterone blockers.

Amanda will travel to Paris in March 2011 to spend two years working with a major cardiovascular research centre involved in long-term collaborations with Professor Fuller and Dr Young. Her work in Paris will involve identifying the genes involved in primary aldosteronism, a common form of secondary hypertension (i.e. hypertension with an identifiable underlying cause). The INSERM/ NHMRC Fellowship, like other overseas biomedical fellowships, is offered to people of outstanding ability who wish to make biomedical research a significant component of their career. As part of the fellowship, Amanda will return to PHI at the end of her time in Paris.

Amanda is an outstanding example of a new generation of PHI researchers. She says her honours year at PHI in 2004 “was a fascinating and rewarding journey. I was fortunate to ‘stumble across’ an area of research which both fascinates me and has great potential for basic research”.

“Completing my PhD was one of the most valuable experiences of my life thus far,” Amanda says. “I have been fortunate to be able to publish my research, which gives you the feeling that you really are making a difference.”

OVERSEAS TRAINING DEVELOPS INTERNATIONAL COLLABORATIONS

Overseas biomedical training fellowships are playing a major role in determining the shape and strength of PHI's research into a family of 'growth factor' proteins that underpin many basic biological processes.

Our research into the transforming growth factor beta (TGF-β) superfamily of proteins is creating opportunities to develop improved drugs to restore internal balance (homeostasis) in tissues ravaged by diseases such as cancer.

The TGF-β superfamily proteins comprise the largest and potentially the most important structurally-related group of growth factors in the body. By interacting with specific cell surface receptors to generate intracellular signals, these growth factors regulate basic biological processes such as development, tissue repair and immune response. A deficiency or an excess of specific TGF-β proteins will typically lead to disease. PHI's work in this field has now resulted in the development of a protein with the potential to inhibit sepsis and reduce involuntary weight loss or cachexia in cancer patients.

Dr. Craig Harrison, who leads the growth factor signalling laboratory, joined PHI in 1999 as a postdoctoral fellow investigating the mechanism of action of inhibin A, a member of the TGF-β family that inhibits the synthesis and secretion of follicle stimulating hormone by the pituitary gland.

After receiving an NHMRC biomedical training fellowship in 2004, Craig worked at the preeminent Salk Institute for Biological Studies in California for three years, where he investigated the extracellular regulation of TGF-β signalling, the formation of the activin receptor complex and the mechanism of action of two activin antagonists.

"The Salk Institute consistently ranks among the leading research institutions in the world," Craig says. The Institute currently has four Nobel laureates on its faculty. "While I was there I was given an opportunity to develop my own research program and, importantly, I learnt the value of establishing strong collaborations with other scientists."

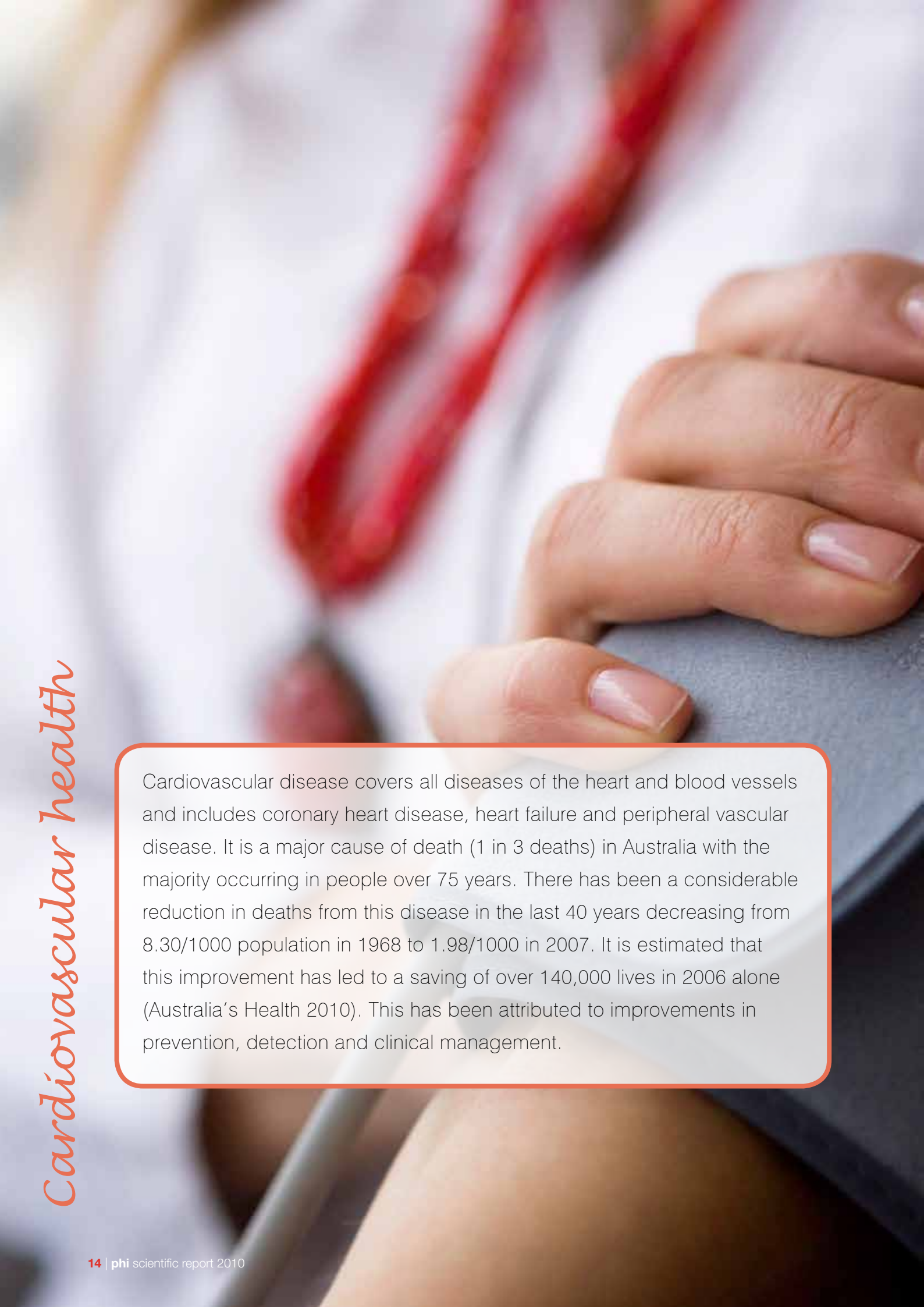
On his return to PHI in 2004, Craig established the growth factor signalling laboratory. Among its principal aims, the laboratory is seeking to develop new biomolecules able to target individual TGF-β proteins to restore tissue homeostasis during disease. Current antagonists of these ligands lack specificity and hence produce many unwanted side-effects. The laboratory's work has potential application in the treatment of neuromuscular disease, metabolic disorders, cancer and infertility.

"My most satisfying achievement so far is establishing a dynamic, motivated group of researchers who are making some important discoveries in the TGF-β field," Craig says.

In 2010, team member, Dr Yogeshwar Makanji was awarded an NHMRC biomedical training fellowship that will enable him to join the Woodruff Laboratory at Northwestern University in Chicago. Under the leadership of Professor Teresa Woodruff, this laboratory is pioneering the field of oncofertility, which aims to develop new fertility preservation methods for young patients experiencing fertility-threatening cancers or treatments, including chemotherapy and radiotherapy.

Yogesh says Woodruff's '3-D follicle culture' technique for preserving human eggs has untapped potential with other organs and diseases. "My time at Northwestern University will provide me with an opportunity to bring this new technology back to Australia and hopefully implement new clinical breakthroughs in other organ systems, including the ovary."

Cardiovascular health



Cardiovascular disease covers all diseases of the heart and blood vessels and includes coronary heart disease, heart failure and peripheral vascular disease. It is a major cause of death (1 in 3 deaths) in Australia with the majority occurring in people over 75 years. There has been a considerable reduction in deaths from this disease in the last 40 years decreasing from 8.30/1000 population in 1968 to 1.98/1000 in 2007. It is estimated that this improvement has led to a saving of over 140,000 lives in 2006 alone (Australia's Health 2010). This has been attributed to improvements in prevention, detection and clinical management.

CARDIOVASCULAR ENDOCRINOLOGY

New knowledge about how a hormone receptor contributes to heart failure and high blood pressure is assisting in the development of drugs that act specifically on the heart without the unpleasant side-effects associated with existing drugs.

Drugs that block the action of the mineralocorticoid receptor (MR) are used to treat cardiovascular disease, in particular heart failure. However, the significant benefits that these drugs provide for patients are often accompanied by negative side-effects in the kidney that limit their widespread use.

A primary goal of our work is to determine the particular cell types in the heart in which the MR is critical for the development of heart failure. We can then develop drugs that exploit the characteristics of these cells and act specifically on the heart without the side-effects associated with existing MR blockers. A related aim is to identify the hormonal requirements for tissue-selective MR blockers.

The MR plays an important role in the onset and development of heart disease, particularly in relation to the tissue inflammatory response. In 2010, we identified distinct and important roles for the MR in heart muscle cells, and showed that the MR in heart muscle cells is important for driving the inflammatory response.

From earlier clinical studies, we know that MR antagonists are equally effective in patients without high levels of aldosterone, the hormone normally required for MR activation. This is because cortisol, a closely related hormone, can also activate the MR and cause disease. Subtle differences in the MR when it is bound by either hormone suggest that regulation of the MR is complex and potentially 'fine-tuned'.

In 2010, we discovered a novel MR blockade mechanism that may lead to ligand- or tissue-selective MR blocking drugs to treat heart failure without side-effects such as hyperkalemia (high blood potassium levels). We also established that the MR plays a unique role in cardiac muscle cells.

Tissue-specific MR activation in heart disease

We have previously shown that inflammatory cells are key sites of MR action in the development of heart disease. In 2010, our paper was judged one of the top two papers of the previous year by Hypertension, the prestigious journal of the American Heart Association. The paper reported that in the presence of elevated salt levels and deoxycorticosterone (a hormone that activates the MR), mice without macrophage MRs suffered less heart tissue damage and had lower blood pressure than mice with active macrophage MRs.

Identification of hormone-selective MR antagonists

Following earlier work that found the MR is subtly different when it is bound by different hormones (i.e. aldosterone to cortisol) and that this causes differences in gene expression, we are now working to identify novel proteins that interact with the MR in the heart and in the kidney. Our overall aim here is to screen and develop novel agents for the treatment of hypertension and cardiovascular disease.

Novel mechanisms of MR activation

In some cells, cortisol can bind to the MR but does not activate it under normal circumstances. New data shows that novel genes are switched on when these receptor-hormone complexes are activated by oxidative stress in the heart.

Salt as a novel enhancer of MR function

We have previously investigated the mechanisms by which high salt levels and aldosterone combine to promote the development of cardiovascular disease. In 2010, a collaborative project with colleagues in Italy found that MR activation in the presence of increased salt also plays a role in adipose cell function.

• *Dr Morag Young and Professor Peter Fuller have been awarded an NHMRC Project Grant for 2011-13 to investigate the precise role of the mineralocorticoid receptor in heart muscle cells in normal physiology and in disease.*

STEROID RECEPTOR BIOLOGY

Research into the molecular interactions between steroidal hormones such as aldosterone and their cellular receptors offers new avenues for tackling a range of diseases, including heart failure and endocrine cancers.

Steroid hormones are the messengers of the body's complex endocrine system, which control many essential physiological functions. Through their interactions with intracellular nuclear receptors that regulate gene expression, these hormones play a role in the pathogenesis of cardiovascular disease and cancers of the prostate and breast.

Our research primarily focuses on investigating the mechanism of action of nuclear receptors, especially those associated with the adrenal hormones aldosterone and cortisol and the reproductive hormones secreted by the ovary. Studying these nuclear receptors is generating new therapeutic targets for the treatment of life-threatening diseases.

We recently identified a novel mechanism for inhibiting the action of the mineralocorticoid receptor and confirmed an important genetic marker for a particular ovarian cancer.

Understanding the mineralocorticoid receptor

The mineralocorticoid receptor (MR) is a nuclear receptor for the steroid hormone, aldosterone. Pathological activation of the MR promotes cardiac fibrosis and heart failure, but it can be effectively inhibited by diuretic drugs such as eplerenone and spironolactone, which are often administered to patients after a heart attack. However, these drugs also elevate potassium levels dangerously in some patients and can cause renal failure.

With Dr Morag Young and her team, we have been working to identify proteins that act as potent MR co-regulating proteins. Elucidation of this mechanism should assist the design of agents that can either antagonise the MR in heart tissue while leaving renal tissue unaffected, or compete more specifically with the ligands that activate the MR.

Granulosa cell tumours of the ovary

Granulosa cell tumours of the ovary, which make up about five per cent of all malignant ovarian cancers, are hormone-dependent tumours that produce, convert and respond to steroid hormones. Recent research indicates that the adult form of the granulosa cell tumour (GCT) arises from a unique mutation in *FOXL2*, a gene with a key role in the growth and maintenance of the ovary. In collaboration with the University of Helsinki, we have confirmed the presence of this mutation in at least 52 out of 56 GCT samples. The results suggest that the *FOXL2* mutation is a potential therapeutic target.

The role of nuclear receptors in the granulosa cell is not well understood. In collaboration with researchers at the University of Queensland, we are using human cell lines to systematically evaluate nuclear receptors expressed in GCTs. This extends our previous studies of the estrogen receptor, ER-β, in these tumours. The latest findings provide the basis for ongoing research to fully characterise the role of nuclear receptors in GCT and their potential as therapeutic targets.

Ovarian phenotype of the IKKβ null mouse

A family of transcription factors known as nuclear factor κ-B (NFκ-B) has been implicated in the initiation and progress of various cancers. Our studies in GCT cell lines indicate that the NFκ-B signalling pathway is involved in the inhibition of apoptosis (cell death) in granulosa cells. Its precise role in the development of the follicles in response to steroid hormones is yet to be elucidated.

To investigate the role of NFκ-B signalling in the ovary we have created a transgenic mouse model, the IKKβ conditional knockout mouse, in which NFκ-B signalling has been deactivated in the ovary. Our results so far appear to validate the hypothesis that ovulation is an inflammatory-like response.

Cancer

Cancer is a major cause of mortality in Australia (accounting for 1 in 3 deaths) with 1 in 8 males and 1 in 12 females dying from this disease before the age of 75. Although the detection of cancers is improving due to better detection methods, the survival rate is also improving as assessed from the number of patients surviving 5 years with the disease. For example, the 5 years survival rate has increased from 41% to 58% for males and 53% to 64% for females between 1982-6 and 1998-2004 (Australia's Health 2010). The Cancer Council of Australia has attributed this improvement to better diagnostic methods, earlier detection and improvements in treatment.

METABOLISM AND CANCER

Identification of the molecular pathways that link our bodies' normal metabolic processes with breast cancer is leading to potential new treatments and preventative measures.

We are studying several metabolic pathways associated with obesity and the production of the sex hormone estrogen and using this knowledge to develop and assess potential new treatments for breast cancer.

A highlight of 2010 was the combination of basic science – in the form of our ongoing investigations into two metabolic pathways that affect estrogen production in postmenopausal women and potentially also their likelihood of breast cancer – and clinical trials resulting from our earlier findings in this area.

As the most common cancer among Australian women, breast cancer affects one in 12 women under 85. Obesity is a major risk factor, due in part to molecular pathways that stimulate expression of the enzyme aromatase in body fat. This enzyme converts androgens such as testosterone into estrogen, which is known to promote cancer cell proliferation in most cases of breast cancer. Postmenopausal women, with an increased risk of obesity are twice as likely to develop breast cancer as premenopausal women.

We have have previously identified the LKB1/AMPK pathway is important in the inhibition of aromatase expression. LKB1 and AMPK are kinases associated with tumour suppression and carbohydrate and fat metabolism, respectively. AMPK is already a therapeutic target for treating diabetes and its biochemical linkage with LKB1 suggests that diabetes drugs may also be useful for treating some forms of cancer including breast cancer.

We are investigating several AMPK-activating drugs as candidates for the treatment and prevention of estrogen-dependent breast cancer. One such drug has proved successful in an *in vitro* study and we have commenced a clinical trial involving women with breast cancer.

LKB1/AMPK-related pathways and aromatase

We are also examining several LKB1/AMPK-related pathways, including the p53 pathway that regulates the cell cycle and inhibits cancer cells, and the hypoxia-inducible factor (HIF) signalling pathways, specifically HIF-1α. Most human cancers contain tumour cells with a genetic mutation or deletion that has caused loss of activity of the p53 protein or over-expression of HIF-1α.

Our current research aims to determine how estrogen production in the breast adipose stromal cells of postmenopausal women is regulated by the p53 and HIF-1α pathways and whether this is critical for the expression of aromatase.

New clinical trials

We have successfully demonstrated *in vitro* that the AMPK-activating drug, metformin, which is widely prescribed for type-2 diabetes, is a significant inhibitor of aromatase expression in adipose stromal cells.

In 2010, in collaboration with clinical colleagues at Southern Health, we commenced the design of a clinical trial of metformin involving 60 Victorian women scheduled to have surgery for breast cancer. The participants will take metformin orally prior to aromatase inhibitor treatment and subsequent surgery. It is hoped that the drug may help reduce tumour size and allow surgery to be less invasive.

Regulation of estrogen in obesity

Fat-derived factors such as adipokines and inflammatory factors, including prostaglandin E_2 (PGE_2), are altered in obesity and cancer. In previous research we demonstrated that the adipokine leptin, which is elevated in obese people, and PGE_2, both inhibit the LKB1/AMPK pathway, and can therefore increase the expression of aromatase and hence estrogen production. Conversely, we found that an adipokine, adiponectin, which is elevated in lean people, inhibits aromatase expression and lowers estrogen. We are further investigating the mechanisms by which these and other factors influence aromatase expression.

• *Dr Kristy Brown and Professor Evan Simpson and their Peter MacCallum Cancer Centre collaborator Professor Stephen Fox, have been awarded an NHMRC Project Grant for 2011-13. They will further investigate the regulation of estrogen production with the aim of developing breast-specific inhibitors of estrogen production.*

CANCER DRUG DISCOVERY

Proteins that promote the proliferation of breast cancer cells by a non-hormonal pathway are potential targets for new drugs for untreatable breast cancers.

Most patients diagnosed with breast cancer are treated with therapies which block production of the hormone estrogen that fuels the growth and spread of these cancers. However, about a third of patients exhibit cancer cells that lack the estrogen or other hormone receptors that make hormonal therapy effective. As a consequence, these cancers - classified as hormone-receptor negative - carry a much higher risk to the patient of the cancer returning following initial treatment.

Our research is focussed on a family of proteins known as orphan nuclear receptors. Nuclear receptors can regulate the expression of certain genes in a cell's DNA and typically they are responsive to the action of a specific ligand or binding molecule, often a hormone such as estrogen. Those receptors without a known ligand are considered to be orphans with a yet-to-be-determined biological function. Of interest to us is an orphan receptor known as liver receptor homologue-1 (LRH-1) and the proteins it interacts with during the proliferation of breast cancer. Our hope is that LRH-1 represents a target for new types of drugs to inhibit the spread of breast cancers that are hormone-receptor negative.

We are also investigating the various mechanisms that control estrogen production in the breast alone, including epigenetic factors that influence gene expression. Localised treatments that only block estrogen receptors in the breast could avoid or reduce the side-effects of estrogen-blocking drugs currently available.

Nuclear receptor pharmacology and LRH-1

In earlier research we identified the orphan nuclear receptor LRH-1, which can regulate estrogen production in breast cells but not in other tissues. Recently we established that LRH-1 promotes the proliferation of breast cancer cells in the absence of estrogen, suggesting a new pathway for the spread of invasive breast cancer.

The mechanism of action of LRH-1 in stimulating cell proliferation is unclear. However, we have identified the genes in the breast cancer cell that are controlled by LRH-1 and are working to identify the proteins that interact with it during the proliferative process.

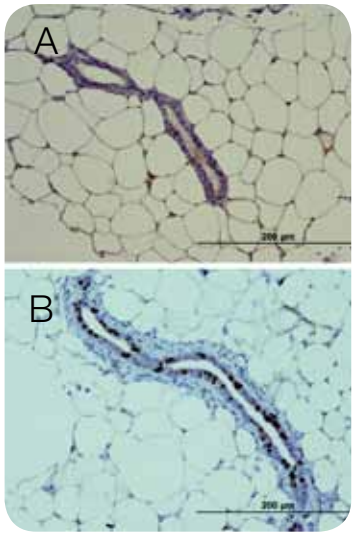
We are investigating several small molecules that inhibit the activity of LRH-1, as drug candidates for the treatment of cancers that are classed as estrogen-receptor negative. Our intention is to test these molecules in a model of breast cancer growth.

Epigenetic regulation of estrogen in breast cancer

The genetic factors that influence estrogen production in breast cancer are fairly well understood. However, the epigenetic factors that control gene expression without creating permanent mutations in the cell's underlying DNA sequence are not well understood. The value in exploring these epigenetic mechanisms is that they are typically reversible and offer potential new lines of attack in cancer therapy.

One such mechanism is DNA methylation - that is, the adding of methyl groups to the DNA. DNA methylation may have the effect of gene silencing, turning off of a particular gene that would be otherwise activated.

Our research has found that the activation of aromatase, an enzyme that synthesises estrogen, involves the removal of methyl groups from DNA. Drugs that inhibit aromatase are an established treatment for breast and ovarian cancer. We are identifying DNA sequences in the genome of the breast cancer cell that show altered methylation patterns compared with normal breast cells.



Dividing cells (black) in mammary glands: (A) low and (B) high levels of LRH-1. Images: Kyren Lazarus

BONE, JOINT AND CANCER

Loss of bone mass due to osteoporosis, arthritis and bone cancer increases the risk of fracture and the likelihood of serious consequences. A better understanding of the metabolic pathways that build or destroy bone cells is helping us identify new ways to combat these problems.

Bone consists of organic and inorganic (mineral) components. The organic component is mainly collagen, and the inorganic component of bone is formed from a protein mixture produced by osteoblast cells. Osteoblasts also produce hormones that act on bone. Some osteoblasts become trapped and are transformed into osteocytes, which are mature bone cells that fulfil various functions such as acting as mechano-sensory cells that detect bone distortion and micro-cracks.

Osteoclast bone cells secrete enzymes that break down bone releasing calcium and other minerals into the blood. The balance between bone formation and bone resorption changes with age, with bone growth predominating until early adulthood, and shifting to resorption in older adults.

With the aim of developing clinical applications, we are studying a range of factors that influence bone formation and destruction. In 2010, our studies revealed details of the mechanisms by which a protein called IL-33 acts to inhibit bone loss on the one hand – and to promote the building of new bone on the other.

Preventing bone loss and building new bone

In 2010, our investigations revealed that IL-33 assists bone formation by acting on osteocytes to suppress sclerostin, a factor that inhibits bone formation. IL-33 also assists bone formation by acting on osteoblasts to promote their maturation.

However, in some cases IL-33 is also known to stimulate inflammation, which means it cannot be directly used to treat bone conditions such as osteoporosis. Our challenge is to find a way to minimise this action of IL-33.

Osteoprotegerin and breast cancer

Osteoprotegerin is a protein that inhibits osteoclast production and therefore reduces bone destruction. However, we have previously found that osteoprotegerin expression by breast cancers enhances their growth in the breast and bone. Hormones normally act outside cells, but we have now found that osteoprotegerin is acting inside the cancer cell. With the aim of identifying the mechanism by which osteoprotegerin enhances tumour growth, we are investigating the finding that tumour cell interaction with normal stromal cells is important in this process.

Regulation of cell death in cancer cells

Also known as programmed cell death or sometimes even 'cell suicide', apoptosis is a normal biological process that enables cells to be 'killed' when they are old or unhealthy. Cancer cells do not undergo apoptosis, and as a result they continue to multiply unchecked.

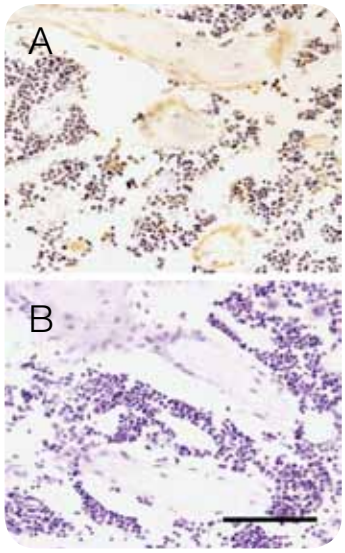
One of the proteins that regulates apoptosis is called TNF-related apoptosis-inducing ligand or TRAIL.

PHI research has previously discovered that some breast cancer-derived factors modulate the way that tumours respond to TRAIL.

We are currently studying genes that respond to TRAIL to identify how they help regulate cell death.

Anti-cancer drug 17-AAG

17-AAG is a new anti-cancer drug that is very effective at shrinking tumours in mice. However, in earlier studies we revealed that this drug can cause bone damage and, surprisingly, increase the growth of breast cancer cells that have spread to bone. In 2010, we found that 17-AAG acts on heat shock factor 1 in osteoclasts, and we are now working to translate these laboratory-based studies into preclinical models.



Anti-IL-33 immunostaining (A) and Antibody control (B). Images: Julian Quinn

GROWTH FACTOR SIGNALLING

Research into a family of growth factors that are fundamental to many basic biological processes, including cell differentiation and tissue repair, offers opportunities for improved drugs to restore homeostasis in tissues affected by neuromuscular disease, metabolic disorders and cancer.

The transforming growth factor beta (TGF-β) superfamily are structurally-related regulatory proteins that interact with specific cell surface receptors and generate intracellular signals. They play essential roles in the regulation of many basic biological processes such as growth, development, homeostasis, fertility and immune response.

A class of experimental drugs known as TGF-β antagonists is proving effective in restoring homeostasis (internal balance) in tissues ravaged by neuromuscular disease (eg. muscular dystrophy), metabolic disorders (eg. diabetes) and cancer-related bone loss and muscle-wasting. Several such antagonists, which have proved effective in phase I clinical trials, broadly reduce the action of TGF-β proteins in disease settings. Some superfamily members are involved in cell division, differentiation and apoptosis (cell death) – and are known to be protective, for example, against factors that promote heart disease and the proliferation of some cancers.

In 2010, our research revealed how TGF-β members are made and then secreted by a cell, and identified the regions within the protein structure of each ligand that determine its activation outside the cell. This work forms the basis of efforts to develop antagonists that, through more specific signalling, are able to target individual TGF-β members that influence tissue homeostasis and the pathogenesis of disease. One possible outcome would be drugs with fewer side-effects.

Synthesis, secretion and activation of TGF-β proteins

TGF-β proteins are synthesised first as a large inactive precursor, assembled from two structurally-independent and folded sub-units, a mature domain and a pro-domain, the latter requiring cleavage by proteases to become functional. The pro-domain aids the folding, formation of disulfide bonds between chains, secretion and activation of the TGF-β protein.

TGF-β1 is a member of the TGF-β superfamily that is secreted by most immune cells. We have identified two distinct regions within the TGF-β1 pro-domain that coordinate the formation and stability of a latent protein complex. Armed with this information, we were able to modify the pro-domain of another TGF-β protein, activin A, to develop the first specific activin inhibitor. Activin is a TGF-β ligand with many important roles in immune response, endocrine function and tissue homeostasis. Activin antagonists may also have therapeutic potential for treating inflammatory disorders such as sepsis.

Activation of GDF9 controls female fertility

Another TGF-β superfamily member is growth differentiation factor 9 (GDF9), which is essential for the development of primary follicles in the ovary. GDF9 controls early maturation of the follicle and the number of ovulating follicles in each oestrus cycle. When the factor is bioactive it has a major role in fertility.

By understanding the processes that activate human GDF9, we will increase our knowledge of the basic mechanisms that regulate human ovarian folliculogenesis and provide new avenues to manipulate this process.

TGF-β signalling and muscle-wasting

TGF-β proteins are implicated in a variety of muscle-wasting conditions, including cancer-related cachexia (wasting syndrome), muscular dystrophy and sarcopenia (age-related muscle wasting). We are using a gene transfer method to deliver TGF-β antagonists directly into muscle tissue and thereby block the TGF-β signalling that promotes muscle-wasting.

• *Dr Craig Harrison, and his collaborator Associate Professor Kate Loveland from Monash University, have been awarded an NHMRC Project Grant for 2011-13 to develop a specific activin antagonist for therapeutic applications that include promoting liver growth in severe hepatic disease and preventing fibrosis in numerous tissues.*

Women's Health

Women are living longer with considerable health gains in the treatment of cardiovascular disease and cancer. Increasingly, health issues around mental health and sexual and reproductive health, together with the rise in obesity heavily impact on women's lives. These include polycystic ovarian disease found in 10% of women or 30% of obese women, endometriosis, pregnancy conditions and menopause. The challenges of increased participation of women in the work force have resulted in increased demands on fertility regulation, and the treatments for infertility, particularly with the decline in fertility as women age. Advances in medical research have provided some limited progress in this area.

ENDOMETRIAL REMODELLING

Research into the critical factors that drive endometrial repair following menstruation or help the uterus prepare for embryo implantation is improving our knowledge of the causes of infertility and assisting the development of new tests to improve IVF success rates. Our findings may also lead to new treatments for uterine bleeding problems and ways to help wounds heal without scarring.

The lining of the uterus (womb), the endometrium, is completely shed at menstruation and rebuilt during the next menstrual cycle. About 20 days after the onset of menstruation, the endometrium becomes 'receptive' to an embryo for roughly four days; this is the only time at which the placenta can begin to develop and a pregnancy can successfully be established.

We are studying how the endometrium is restored after menstruation and how it becomes receptive to embryo implantation. If these processes fail, consequences can include abnormal uterine bleeding and infertility.

In 2010, we published the first of a series of papers identifying the different proteins present in uterine fluid from fertile and infertile women. This is a major advance on our previous work that showed how proteins in endometrial tissue (primarily structural proteins) vary during different phases of the menstrual cycle. Uterine fluid is relatively easy to sample and free of cellular protein. Some of the proteins found in very small quantities in uterine fluid have strong potential as markers for infertility or endometrial receptivity.

Endometrial and epithelial repair

The endometrium is the only adult tissue to repair without scarring. A better understanding of endometrial repair mechanisms will lead to new treatments for uterine bleeding problems in women, and may also identify factors that can assist wound healing so that it occurs without scarring.

We have developed two methods for investigating epithelial repair. These are a wound-healing assay in which we measure how quickly cultured endometrial epithelial cells can grow across a hole in the surface, and a method that measures the strength of the junctions between epithelial cells. Preliminary results in 2010 suggest that menstrual fluid aids endometrial repair after menstruation by enhancing the development of the first layer of cells to cover the wounded surface.

To improve our understanding of the scar-free aspects of endometrial repair, we are examining the mechanisms that underlie the actions of several molecules previously identified as enhancing or retarding endometrial repair.

Uterine receptivity

Prior to implantation, the embryo is bathed in uterine fluid secreted by the receptive endometrium. For embryo implantation to occur, both the endometrium and the embryo must be ready. In 2010, we examined the different roles played by factors previously identified as important for uterine receptivity. For example, several proteins influence the adhesive capacity of the endometrial surface; another protein cleaves inactive proteins to make them biologically active. Our aim is to understand how the different factors work so we can stimulate local production of appropriate proteins or possibly administer the required factors at the appropriate time. No good test for uterine receptivity is currently available.

We are continuing to use proteomic techniques to identify proteins in uterine fluid that are associated with endometrial receptivity. This work is complemented by immuno-histochemical studies of endometrial tissue that reveal differences in proteins between fertile and infertile women as well as showing that the proteins are produced locally by the endometrial epithelium.

How the embryo influences the endometrium

In earlier work, we showed that human chorionic gonadotrophin (hCG) secreted by the early embryo was essential for implantation and pregnancy. Our latest results suggest that this hormone acts on a specific selection of cytokines produced by the endometrium.

IMPLANTATION AND PLACENTAL DEVELOPMENT

Studies of how the uterus contributes to embryo implantation have revealed the mechanism of action of a key enzyme called PC6, pointing the way to a test for uterine receptivity important for embryo implantation and potentially also a novel contraceptive. Information about a new gene, *HtrA3,* involved in placental development offers hope of early detection of pre-eclampsia.

A major factor in female infertility is uterine incompetence, a condition in which the uterus fails to be receptive to implantation by a healthy embryo. No current biochemical test can reliably detect a non-receptive uterus.

Role of PC6 in uterine receptivity for embryo implantation and fertility

Our previous research identified that proprotein convertase 5/6 (PC6), an enzyme, was tightly controlled in the uterus as it prepares to become receptive and is critical for implantation success. We have been studying PC6's mechanisms of action in the uterus and investigating the clinical implications of these in evaluating uterine receptivity and fertility.

In 2010, we confirmed a strong link between PC6 levels and receptivity. By testing fertile women and women with unexplained infertility, we found that PC6 levels in uterine fluid (obtained by lavage) are closely associated with uterine receptivity. The finding suggests that detection of PC6 in uterine fluid may form the basis for a rapid test for receptivity for embryo implantation requiring only minimal surgical intervention.

Using proteomics, we have also found that PC6 regulates several key cytoskeletal proteins as well as essential growth and differentiation factors that alter the uterine environment prior to implantation, suggesting that PC6 is a 'master-switch' for the establishment of receptivity.

PC6 in prevention of pregnancy and HIV infection

We are also continuing our research into PC6 as a potential target for the development of a new female contraceptive that would protect simultaneously against pregnancy and HIV infection.

HtrA3 in placentation and pregnancy disorders

Our previous studies had identified a gene, *HtrA3*, as important for placentation. The HtrA3 protein, a serine protease closely linked to placentation and the menstrual cycle, is significantly elevated in the first-trimester of pregnancy. Our current research in this area aims to elucidate the mechanism of action of HtrA3 and its clinical implications.

In particular, we are investigating the role of HtrA3 in pregnancy-related disorders such as pre-eclampsia and intra-uterine growth restriction.

Pre-eclampsia accounts for almost one in 12 maternal and perinatal deaths in industrialised nations, and yet diagnosis is normally not possible until late in pregnancy.

In 2010, we established that HtrA3 levels in maternal blood during early pregnancy (at about 13-14 weeks of gestation) were abnormally high in women who subsequently developed pre-eclampsia.

We are developing a sensitive, high-throughput assay to measure HtrA3 in blood. We will determine whether HtrA3 levels in the blood during early pregnancy can predict pre-eclampsia.

HtrA3 in cancer and ageing

In addition to its role in placentation, the *HtrA3* gene is known to be down-regulated in some cancers, including endometrial cancer. The evidence suggests that HtrA3 is a tumour-suppressor gene that inhibits TGF-β signalling in the endometrium. Our research indicates that the involvement of HtrA3 in cancer is linked with the process of ageing.

We are continuing our study of the biochemical properties of the HtrA3 protein and investigating its role in cancer in the context of ageing.

• *Dr Guiying Nie has obtained funding in the form of two grants from the prestigious Bill and Melinda Gates Foundation for further investigations on the PC6 and HtrA3 proteins.*

EMBRYO IMPLANTATION

Studies of proteins that are critical for placenta formation and embryo implantation are assisting our efforts to develop ways to enhance pregnancy outcomes and devise non-hormonal contraceptives that can be combined with agents to prevent sexually transmitted diseases such as HIV/AIDS.

Embryo implantation is an extremely complex process and women experience a high percentage of failures in both natural and assisted conception.

After the embryo attaches to the lining of the uterus, it must grow through this endometrial tissue until the placenta is fully formed. Close contact is required between the embryo trophoblast cells and the mother's blood supply, which provides nourishment and oxygen for the developing foetus. The trophoblast invasion of the womb is very similar to the way in which white blood cells move from the blood into tissues where they are needed to counter infection.

We had previously found that two small regulatory molecules or cytokines were important during early implantation as well as during the trophoblast invasion. In 2010 we investigated how the levels of these proteins varied in the presence of placenta abnormalities that could lead to complications later in pregnancy.

Endometrial-placental interactions
When embryo implantation is impaired, this can affect placental development and may lead to miscarriage, pre-eclampsia or maternal death.
In earlier work we studied how endometrial proteins interact with placental trophoblast cells to restrict trophoblast invasion. In 2010, we used a proteomics approach to identify some of the protein molecules that are important in these interactions.

Implantation, fertility and IVF
Many unsuccessful IVF attempts are due to the embryo failing to implant even though the endometrium is adequately receptive. However, there is no available clinical method for diagnosing such endometrial infertility.

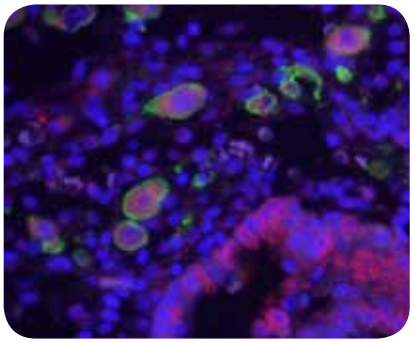
An embryo spends 24 hours in the uterus prior to implantation. We believe that during this period the embryo secretes factors that influence the endometrium. In 2010 we began studying culture media in which IVF embryos had been grown, to see if we could identify factors associated with particular pregnancy outcomes such as failure to implant. The culture media were provided by our collaborators at Monash IVF.

Non-hormonal contraceptives
We are working with US collaborators to conduct preclinical trials of a vaginally-applied, non-hormonal contraceptive based on two molecules we had previously identified as capable of preventing pregnancy in mice. Compared to delivery by injection, vaginal delivery reduces non-uterine side effects. We are also investigating the efficacy of combining these contraceptive molecules with other agents that block sexually transmitted diseases such as HIV/AIDS.

New treatments for endometrial cancer
The most common gynaecological malignancy, endometrial cancer typically affects postmenopausal women. However, women over the age of 40 also face a significantly increased risk. Current treatment options for advanced endometrial cancer are inadequate.

In 2010, we began testing a potential therapeutic produced by collaborators at Commonwealth Serum Laboratories to see if it can inhibit one particular protein that we had previously found to be important in the progress of endometrial cancer.

• *Dr Evdokia Dimitriadis received the 2010 Award for Excellence in Reproductive Biology from the Society for Reproductive Biology in recognition of her outstanding work in this area.*



Extravillous trophoblast (green; HLAG) invading through uterine decidua & expressing Galectin 7 (red). Image : Ellen Menkhorst

OVARIAN BIOLOGY

Greater knowledge of how and when the ovary produces hormones and eggs is assisting the development of clinical treatments for infertility associated with premature menopause, ovulation induction, polycystic ovarian disease and ovarian cancer.

A major highlight of 2010 is the identification of two genes that may hold the key to developing methods to protect oocytes from chemo- or radiotherapy damage during cancer treatment.

The number of eggs (oocytes) in a woman's ovary is set at or around birth - the primordial egg pool - and then gradually declines until menopause, the point at which the supply is exhausted. Despite their important contribution to female fertility, however, the regulatory factors that control the activation, growth and subsequent death of the fluid-filled follicles that support the eggs are not well understood. Together with our colleagues from Monash University and the Walter & Eliza Hall Institute (WEHI), we are investigating these factors. Our aim is to identify new ways to regulate the egg supply, extend the fertile period and delay the onset of menopause.

We are also conducting research that will assist the development of new options to help prevent infertility resulting from the use of chemo- and radiation therapies to treat cancers of any kind. These therapies can destroy the ovarian egg pool, potentially leading to serious infertility problems in girls and young women undergoing treatment for cancer. Our research in this area focuses on the development of immature oocytes and the establishment and maintenance of the primordial follicles, which are also formed before birth.

Hormonal regulation of follicle production

Our earlier research into the roles played by estrogen and the transforming growth factor beta (TGF-β) family indicated that both activin and TGF-β could influence follicular growth processes. In 2010, this was confirmed by data showing that local growth factors were important in the development of follicles in the ovary. Disrupting these factors could lead to abnormal or inappropriate development - including cancer. We are continuing to examine the role of follistatin, an endogenous inhibitor of activin, in follicle development.

Using a mouse model that lacks estrogen production, we have established that estrogen's impact on normal follicle production is by direct action on the ovary rather than via other indirect hormonal influences. In particular, we have identified the individual genes and molecular pathways influenced by estrogen. This new knowledge will help us to better understand how environmental estrogens such as plant preparations and synthetic chemicals in plastics may lead to infertility, and determine how to influence these important pathways.

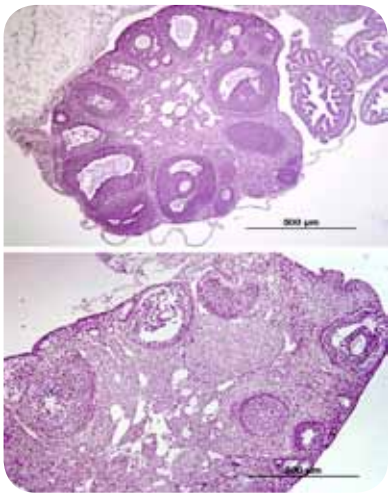
Developmental origins of infertility disorders and ovarian disease

The factors involved in the extensive wave of oocyte proliferation and death in the foetus that determine the size of the primordial egg pool are not well understood.

We have previously observed the involvement of BH3-only genes, which can initiate the process of apoptosis or cell death in response to particular types of stress. In 2010, we identified two genes that act to limit the size of the primordial pool before birth. We are now exploring how and when these genes are involved and whether generating extra eggs by preventing oocyte death at this stage can prolong fertility.

The same genes are implicated in oocyte death following radiotherapy. 'Knocking out' these genes in mice significantly reduces radiation damage to eggs and the mice remain fertile, highlighting the potential for protecting oocytes from chemo- or radiotherapy damage. Together with our collaborators at Monash University and WEHI, we have taken out a patent to protect the intellectual property in this area and will continue to pursue the development of therapies to protect oocytes against chemo- or radiotherapy treatment for any form of cancer.

• *Dr Karla Hutt has been awarded an NHMRC Project Grant 2011-13 to investigate cell death signalling pathways central to the establishment of a high quality primordial follicle reserve.*



Ovarian phenotype of the IKKβ conditional "knock out" mouse at 7 and 17 wks of age. Images: Ann Drummond

OVARIAN CANCER BIOMARKERS

Ovarian cancer is a challenging gynaecological cancer with few recognisable symptoms. There is no screening test currently available, and ovarian cancer is often diagnosed only after it has spread.

Our research aims to develop an accurate screening test to identify early or pre-cancerous ovarian disease. We are using proteomics and mass spectrometry technologies to identify early tumour-specific changes.

In 2010, we worked with a much larger patient group to verify our earlier finding that the blood and urine levels of 15 proteins can predict the early-stage presence of the most commonly diagnosed form of ovarian cancer, serous epithelial ovarian tumours. These protein levels can also accurately distinguish between benign and malignant ovarian disease. We have begun evaluating the 15 proteins for their accuracy in detecting ovarian tumours in a larger group of patients.

We are also identifying additional and highly specific markers of early-stage ovarian tumours. Our goal is 100 per cent accurate screening of early or pre-cancerous lesions, facilitating earlier and better patient treatment and leading to improved patient survival.

Mass spectrometry in ovarian cancer research

A highlight of 2010 was the installation of a state-of-the-art, two-dimensional nano-liquid chromatography and MALDI TOF mass spectrometry suite. This equipment enables very high resolution analysis and identification of proteins, and is of key importance in the identification and development of very low abundance markers of early-stage ovarian cancer. This new equipment has substantially increased both our throughput and the range of possible analyses and experiments that can be performed. The mass spectometer was supported through an equipment grant from the Ovarian Cancer Research Foundation.

Circulating markers of ovarian cancer

We are studying how the marker proteins we have identified can vary in concentration in a patient's blood or urine, particularly during tumour development. Our aim is to assemble a panel of such markers.

Auto-immune response in cancer patients

Cancer patients may exhibit an immune response to their tumours before other clinical symptoms become apparent. In 2010, we found that two proteins we previously identified, are recognised differently by the immune system in patients with early-stage ovarian cancer compared to healthy women or women with benign ovarian disease. We are working to characterise the nature of these changes, determine the extent to which they are found in individual patients and explore their potential to assist the early detection of tumours.

Fallopian tube as the origin of epithelial ovarian cancers

Recent evidence from other researchers suggests that many serous epithelial ovarian tumours might actually originate from damaged secretory epithelial cells in the fallopian tube. In 2010 we established cell culture techniques for growing cells taken from the fallopian tube. We are using these cultured cells for mutational, proteomic and gene array studies to investigate the molecular pathways behind tumour growth in the fallopian tube and subsequent metastasis. The fallopian tube may be a source of new cancer-specific markers.

Clinical collection program

By the end of 2010, almost 600 women had provided blood or tissue samples to our clinical collection program in Melbourne and our model has been applied to a collection program in Sydney, and will be rolled out in Brisbane this year. Our goal is to collect over 1500 samples, which will permit statistically-significant testing of candidate proteins as clinical markers for ovarian cancer.

Nanoparticle technology

In 2010, we completed developing our nanoparticle technology for capturing and comparing very small peptides and proteins from cancer patient samples. This has been published in the literature and now underpins several other projects in the laboratory.

REPRODUCTIVE HORMONES

The pituitary gland and the ovary influence each other's activity by means of a network of interacting hormones. Studies of the relationships between these hormones are improving our understanding of fertility, menstrual cycles and menopause.

Our work in this area focuses on detailed studies of changes in hormone levels during the menstrual cycle, particularly in women approaching or undergoing menopause.

Our studies highlight the pattern of hormonal changes that occurs as menopause approaches. A key aim of our ongoing work is to relate these changes to the changing pattern of follicles produced by the ovary. We suspect that a major cause for the clinical difficulties associated with menopause is the unpredictable development of follicles by the ovary when the reduction in follicle numbers disturbs plasma hormone patterns. In collaboration with researchers at the University of Saskatchewan, Canada, we are now working to relate these plasma hormone changes to the pattern of ovarian follicle development as women approach menopause.

Endocrinology of menopausal transition

The pituitary gland produces follicle stimulating hormone (FSH) and luteinising hormone (LH) to stimulate ovarian production of follicles containing eggs. The ovary produces hormones such as inhibin and estradiol to suppress these pituitary hormones and control the formation of multiple eggs. As women age, the number of available eggs falls, altering the balance between pituitary and ovarian hormones.

We have conducted several studies of changes in hormone levels during menstrual cycles in women in their late reproductive years and women undergoing the transition to menopause. The changes we have observed, including decreased inhibin and increased FSH, appear largely due to age-related decline in the number of egg follicles.

In particular, we have shown that inhibin B is an important inhibitor of FSH as well as a contributor to the regulation of LH. Anti-Müllerian hormone (AMH), which helps to control follicle formation, is negatively associated with FSH, but not as a direct relationship. We also established that the ratio of FSH to inhibin B and the level of anti-Müllerian hormone both have potential as early indicators of approaching menopause.

Our current investigations in this area involve detailed ultrasound imaging in association with our studies of age-related changes in fertility hormones.

Anti-Müllerian hormone and fertility

In 2010, ongoing investigations of changes in hormone levels during the menstrual cycle revealed that when AMH levels become substantially reduced and more highly variable in a woman's late reproductive years, they are much less reliable as markers of ovarian follicle reserves.

We will continue to examine the influence of AMH on fertility at different ages and during different stages of the menstrual cycle.

Understanding ovarian hyperstimulation syndrome

Ovarian hyperstimulation syndrome is a rare but important consequence of hormonal stimulation of ovaries in women engaged in *in vitro* fertilisation programs. Symptoms can range from mild bloating to severe abdominal pain.

In 2010, we used proteomic methods to identify several blood proteins with potential to be used as predictors or indicators of ovarian hyperstimulation syndrome. We are now assessing these proteins to determine whether they have the required sensitivity and specificity to act as clinical markers.

REPRODUCTIVE DEVELOPMENT AND CANCER

The processes by which the ovary and testis are formed during foetal life are poorly understood. Research into these processes points the way to a better understanding of fertility and new therapies for ovarian and testicular cancer.

Our research focuses on identifying key factors that govern the formation and maintenance of healthy ovaries and testes with the aim of applying our discoveries to the treatment of disorders of the reproductive organs.

Proper formation of the adult ovary and testis requires precise regulation at the molecular and cellular levels. The adult capacity for reproduction is determined during foetal and neonatal development with the establishment of populations of primitive sperm and egg cells and essential supporting cells.

Gonad development is influenced by a family of multifunctional growth factors known as transforming growth factor-beta (TGF-β). We are studying betaglycan, a cell-surface receptor protein that facilitates the actions of several members of the TGF-β family. We have previously demonstrated that betaglycan and the factors that interact with it are essential for successful development of the foetal gonads and kidneys. Current research is revealing how betaglycan regulates cell growth, survival and migration during foetal development, and how this affects the health of the gonads and fertility in adulthood. Our aim is to improve our knowledge of the causes of urogenital birth defects and their impact on human health.

Another major research focus is the emergence and progression of ovarian cancer. Most deaths by cancer result from metastasis, a process by which malignant cancer cells move away from the primary tumour site and spread to distant parts of the body.

Previously, we found that loss of betaglycan expression allows normal ovarian cells to become cancerous and metastatic – and that reintroducing betaglycan to ovarian cancer cells may be able to halt or prevent metastasis. We are currently investigating the detailed mechanisms underlying betaglycan's actions in normal and cancerous ovarian cells in order to determine the clinical importance of betaglycan in human reproductive cancers and develop therapeutic strategies based on this key protein.

Defects in the development of the foetal testis

In 2010, we established that betaglycan is essential for 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 – suggesting that loss of betaglycan during foetal development may adversely affect adult male fertility.

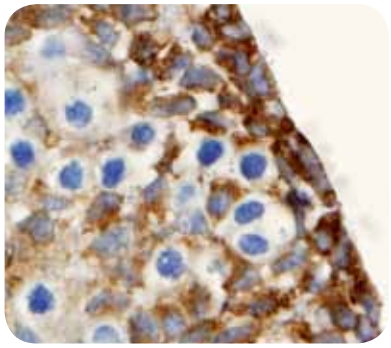
Identification of molecules that regulate ovarian cancer metastasis

In 2010, we also showed that betaglycan blocks the motility (mobility) and invasiveness of ovarian cancer cells by reducing the expression of the matrix metalloproteinases, which are key regulators of tissue remodelling. Ongoing studies will exploit this finding to investigate methods of blocking the spread of ovarian cancer cells.

Understanding how to kill a cancer cell

We have previously shown that the TGF-β pathway regulates the survival of cancerous ovarian granulosa cells, which would normally support egg development in the ovary. In 2010, we identified an additional signalling molecule, NFκB, which interacts with the TGF-β pathway to promote cancer cell survival over cell death. With the aim of discovering better ways to target cancer cells, we are currently investigating agents that counter the pro-survival signal and enhance the cell death signal.

We are broadening our focus to examine other common types of ovarian cancers and assist the development of clinical applications, in collaboration with the Royal Women's Hospital.



Expression of laminin protein in the extracellular matrix of a foetal ovary section. Image: Mai Sarraj

Men's Health

Research into men's health has lagged compared to many other areas of medical health. It is true that there have been improvements, such as in the treatment of cardiovascular disease and increased survival rates of men with prostate cancer. However little is known of the effects of age on men's health including metabolic diseases and the basis for male infertility, an area of scientific and clinical interest for us. One in 20 men are infertile, half of those for reasons unknown - a clear challenge for our medical scientists.

SEX DETERMINATION AND GONADAL DEVELOPMENT

As many as one in 100 babies are born with a disorder of sexual development (DSD). DSDs encompass a wide range of abnormalities, including hypospadias (abnormal urinary opening in males), gonadal dysgenesis (underdeveloped or imperfectly formed gonads), ambiguous genitalia, and sex reversal.

We are using human genetics and molecular, cellular and developmental biology approaches to identify genes associated with disorders of sexual development to improve diagnosis and uncover the molecular mechanisms underlying testis and ovary formation in the embryo.

A key focus is the SOX9 protein which plays the central role in embryonic testis development in animal species ranging from humans to birds and fish. In mammals, the sex-determining region Y gene (*SRY*) codes for a protein that binds to a section of DNA (the 'testis enhancer of SOX9' or TES region) that turns up *SOX9* gene activity in the testes.

In 2010, we identified a smaller region within TES that is present (evolutionarily conserved) in all four-limbed vertebrates indicating that they share common aspects of SOX9 regulation in the testis. Our finding has had a significant impact world-wide, and has prompted researchers who work with other species such as frogs and birds to investigate this region. This will provide new insights into the evolution of sex determination mechanisms.

Also in 2010, we concluded from a human study of XY female DSD individuals that mutations in TES are not a common cause of gonadal dysgenesis. This suggests that regions in the *SOX9* gene outside TES could be important in human gonadal development.

New technique speeds up gene analysis

As part of demonstrating that genes believed to be contributing to DSDs are actually implicated in these disorders, researchers must show the impact of deleting or over-expressing them in animal models. These techniques are costly, can take years to complete and can fail.

We have now developed an alternative highly specialised technique called whole organ nucleofection that enables several genes to be evaluated in just three to four days. The concept has successfully been demonstrated with mouse gonads, for example the delivery of the *SRY* gene into an XX cultured gonad changed the fate of pre-ovarian cells to become testicular.

The molecular battle between the sexes

Recent studies by us and others have shown that sex determination in males and females is complex and regulated by both positive and opposing signals. In XX females, the Wnt/β-catenin pathway is involved in ovarian differentiation – and also inhibits *SOX9* gene expression. In XY individuals, *SRY* expression up-regulates SOX9 and inhibits Wnt/β-catenin signalling.

Having identified key mechanisms *in vitro*, we have begun working with mouse models to prove that these mechanisms are relevant *in vivo*.

Identification of novel genes causing DSDs

We have been preparing material for a major mutagenesis screening project, which has involved using N-ethyl-N-nitrosourea (ENU) to induce inheritable mutations in mice. This high-throughput screening project will enable us to identify novel genes involved in gonad development.

An important regulator of spermatogenesis

Infertility affects about one in 20 Australian men, and it is a common experience for men with DSDs. Studies of the molecular action of the *ATRX* gene are providing a better understanding of some underlying causes of male infertility. We have discovered that the ATRX protein is an important co-regulator of androgen receptor activity, as well as playing a key role in the survival of testicular cells.

- *The NHMRC Program Grant on Disorders of Human Sexual Development held by Associate Professor Vincent Harley was renewed for 2010-14.*

- *Dr Stefan Bagheri-Fam and Dr Anthony Argentaro have been awarded New Investigator Grant funding from the NHMRC for 2011-13 to study ATRX function in the testis.*

MALE FERTILITY REGULATION

Identifying the hormonal mechanisms that control sperm production in the testis will improve our understanding of the causes of male infertility and assist the future development of treatments to regulate fertility in men.

A highlight of 2010 was our discovery that certain micro-RNAs in the testis are regulated by hormones (follicle stimulating hormone, FSH and androgen) and are important for the release of mature sperm.

Our broad approach in this area involves identifying the key cell types in the testis that are regulated by hormones and then finding the key genes and proteins within these particular cells.

In previous research, we investigated the processes by which the Sertoli cells in the testis nurture immature sperm cells and release them at the end of their maturation. We have also studied the so-called tight junctions between Sertoli cells. These junctions form part of the blood-testis barrier that protects sperm from the body's immune system.

In 2010, our work focussed on exploring hitherto-undescribed mechanisms of action by FSH and androgen (primarily testosterone), in particular the influence of these hormones on short, gene-regulating ribonucleic acid molecules, known as micro-RNAs, within the Sertoli cell.

We are also seeking to identify protein markers that would form the basis of a blood test for certain types of male infertility and would avoid the need for a testis biopsy, which is intrusive and may not produce conclusive results.

Hormonal regulation of micro-RNA expression

We have now demonstrated that micro-RNAs - small non-coding RNAs that regulate protein translation - are themselves regulated by FSH and androgen in the testis. An important finding from our research is that FSH and testosterone exert hormone-specific effects on micro-RNAs in the testis that influence the absorption of tight junction proteins and intracellular signalling.

Our view is that these micro-RNAs coordinate cell adhesion pathways in the Sertoli cell that are important for the release of mature sperm. If correct, control of micro-RNA transcription offers a new model for understanding the hormonal dependence of spermatogenesis and provides new targets for inhibiting or restoring male fertility.

Regulation of Sertoli cell junctions

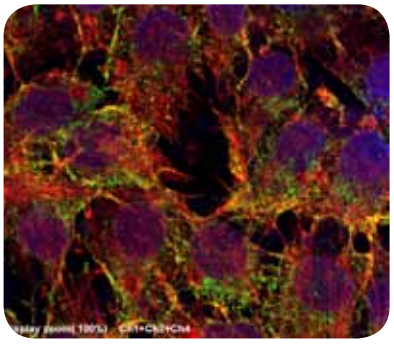
Animal studies we have conducted have shown that the blood-testis barrier, which involves the tight junctions between Sertoli cells, is controlled by FSH and androgen. As the blood-testis barrier is essential for the production of viable sperm, we have focussed our efforts on determining if the tight junctions are regulated in a similar way in humans.

Proteomic discovery in male reproduction

In earlier research we identified several serum proteins that vary between men with normal sperm production and men whose sperm production is impaired. In 2010, we continued using proteomic methods to see if we could identify any protein that could act as a marker for a cellular process in the testes such as germ cell differentiation. If we can find such a marker, it may offer potential as a simple diagnostic test for testicular function as an alternative to biopsy.

- *Dr Peter Stanton and Dr Craig Harrison, have been awarded an NHMRC Project Grant for 2011-13 to investigate how micro-RNA molecules transmit the signals from FSH and testosterone to the cellular machinery of the testis, particularly at cell junctions.*

- *PhD student Peter Nicholls won the Society for Reproductive Biology's prestigious New Investigator Award in 2010 for a presentation on aspects of this work.*



Sertoli cell monolayer EPS15 actin 2. Image: Peter Nicholls

BRAIN AND GENDER

Genetic differences between the male and female brain offer clues to understanding the causes of neurological disorders that are more prevalent in one gender than the other.

Our research is primarily focussed on studying the role of gender-specific genes in neurological disorders such as Parkinson's disease, schizophrenia, attention deficit hyperactivity disorder (ADHD) and autism. These diseases are more prevalent in men than in women, and men typically experience earlier onset, faster progression, more severe symptoms, and a less effective response to medication.

Of particular interest to us is the sex-determining region Y gene (*SRY*), which is responsible for maleness in mammals. In the brain, the *SRY* gene is involved in the production of neurotransmitters such as dopamine that control movement and coordination, as well as mood, motivation and the level of mental attention. We are investigating the links between abnormalities in SRY, abnormal regulation of the relevant neurotransmitters and susceptibility to male-biased brain diseases.

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

Parkinson's disease is a common neurological disorder, affecting an estimated 70,000 Australians. The disease appears when more than 70 per cent of the dopamine-producing cells in the brain region called the *substantia nigra* die. Men are about 50 per cent more likely to be diagnosed with the condition than are women.

We have found from post-mortem analyses that SRY is expressed in dopamine-producing cells in the *substantia nigra* in the male brain, but not in the female.

Our cell and animal research have uncovered strong evidence that the *SRY* gene regulates the dopamine pathway in the brain and therefore influences the control of movement in males. Using human male cell lines, we found that SRY regulates two enzymes: one that controls the synthesis of dopamine and one that degrades dopamine. These findings follow animal studies in which we were able to show that inhibiting expression of the *SRY* gene in the substantia nigra leads to an impairment of motor function in males.

Recent research has investigated impacts on the level of SRY protein. Using an *in vitro* model of Parkinson's disease, we have shown that human dopamine-producing cells dramatically increase their SRY expression in response to stress or injury. Current studies are exploring a potential avenue towards therapeutic application; by inhibiting SRY levels in the *substantia nigra*, it may be possible to slow the progression of Parkinson's in men or reduce their susceptibility to this debilitating disease.

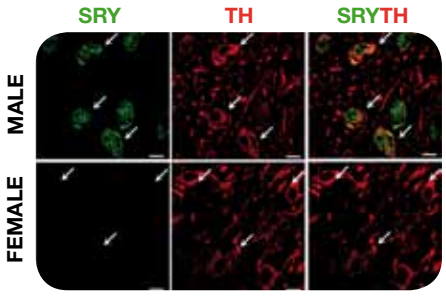
Cognitive effects of SRY inhibition in the brain

SRY also plays a role in cognitive function. Our research has established that SRY protein is expressed in the locus coeruleus, part of the brain involved in alertness, stress and memory.

The presence of the SRY protein in the locus coeruleus might explain differences between men and women in disorders such as ADHD, autism and anxiety. We aim to elucidate the role of SRY in this brain region.

Genetics of gender identity disorders

Transsexuals often feel they are trapped in a body with the wrong gender, a condition that appears to be related to how strongly the brain's hypothalamus responds to testosterone. A major genetic study of male-to-female transsexuals previously undertaken at PHI was the first to identify a small difference in the androgen receptor gene, located on the X-chromosome, which occurs more frequently among transsexuals. Research is continuing to identify other genes that may be associated with this condition.



SRY protein co-localises with dopamine neurons in the male substantia nigra. SRY (green) and TH (red) expressing neurons in the human male (upper panels) and female (lower panels) substantia nigra (scale bar = 30µm). Images: Daniel Czech

CLINICAL ANDROLOGY

Our research into how testosterone and pituitary hormones influence sperm production is assisting in the development of an effective and reversible male contraceptive. Other current studies include an assessment of testosterone as a potential therapy for obesity and diabetes in older men and an investigation of the genetic basis of male infertility.

A better understanding of the mechanisms regulating sperm production offers hope of an easy-to-reverse alternative to vasectomy and new treatments for male infertility, which is implicated in a third of infertile couples.

In 2010, we completed our second randomised clinical trials of testosterone in older men, and established a service at Southern Health to assist men who experience medically-induced testosterone deficiency as part of their treatment for prostate cancer.

Reversible male contraception
We are participating in an international, multicentre clinical trial of a reversible male contraceptive conducted internationally by the World Health Organisation and CONRAD, a US-based reproductive health organisation.

The phase IIb trial involves several hundred couples in seven countries. We are studying the safety and efficacy of a two-monthly injection of testosterone and a synthetic hormone, progestin. The formulation lowers production of the pituitary hormones that initiate spermatogenesis in the testis, but does not affect the normal testosterone levels in the blood needed for sexual function and general health.

During 2010, many couples completed a full year of the trial. Sperm output was seen to fall within a few months and remain suppressed throughout the trial. This major project is scheduled to conclude in 2013.

Approximately five per cent of the men taking part in this clinical trial do not achieve full suppression of sperm production. To understand this problem, we are conducting animal studies to explore how pituitary hormones control sperm production and release from the sperm-producing tubules of the testis.

Genetics of male infertility
Most male infertility is likely to have a genetic basis. Our research involves assessment of candidate infertility genes and chromosomal defects. We are using animal models and correlative data from DNA studies, and clinical information from over 2,000 infertile men. The importance of DNA and oxidative damage to sperm DNA is also being assessed. Our work will aid in the clinical management of infertility.

Klinefelter's syndrome is a common chromosomal disorder, and is the subject of special attention. This condition, which is caused by an additional X-chromosome, affects about one in every 650 men, and is characterised by infertility, testosterone deficiency and learning problems. We are collaborating with the Murdoch Children's Research Institute to study the psychosocial status in men with Klinefelter's. As most cases currently go undiagnosed, we are assessing the possible risks and benefits of introducing genetic screening programs at different ages.

Testosterone replacement therapy
Testosterone, or androgen deficiency can profoundly affect males at all stages of life. Its effects not only include sexual function, but also mood and cognition and muscle, bone and cardiovascular health. Testosterone replacement has a proven role in testosterone-deficient men, but it may also ameliorate some of the physical and psychosexual aspects of ageing, and assist the management of diabetes and obesity.

We are undertaking clinical studies to investigate the efficacy and safety of testosterone replacement therapy in obese men. Our analysis of testosterone replacement in 40 middle-aged and older men with obesity showed a reduction in body fat and improved muscle mass, but few other benefits. Our research in this area will continue.

In 2010, we introduced a clinical research service for men undergoing androgen deprivation therapy for prostrate cancer. This therapy uses a chemical that drastically reduces blood testosterone levels in order to slow tumour growth, but patients may then suffer the consequences of severe testosterone deficiency. Our service aims to reduce symptomatic and physical problems in patients experiencing androgen deficiency.


Translation

ENABLING TECHNOLOGIES

Prince Henry's Institute, in conjunction with our MHTP collaborators is contributing to innovation and improving clinical care through our technology platforms that accelerate our rate of fundamental discovery and our understanding of the role that DNA and proteins play in health and disease.

Two key facilities are the mass spectrometry suite and the Gandel Charitable Trust Sequencing Centre. Together they provide complementary technologies and are state-of-the-art in the instrumentation and service they offer.

Proteomics is helping medical researchers and clinicians to identify causes, improve methods of diagnosis and develop new treatments for a range of conditions including cancer, cardiovascular disease and infertility in men and women. Proteins are the fundamental building blocks of life and too much, too little or incorrect proteins lead to many of the diseases we know. Proteomics is the technology that understands these proteins.

During 2010 PHI installed a new mass spectrometry suite allowing acceleration of our proteomic research programs.

The **Mass spectrometer** ($680,000 through a grant from the Ovarian Cancer Research Foundation) can analyse samples, molecule by molecule as they fly through a vacuum at high speed. It allows us to identify proteins even if they are unknown, but requires sophisticated and specialised equipment that few research institutes can directly access.

This mass spectrometry is the first new generation technology in Australia to be solely dedicated to medical research and biotechnology innovation. It will be used to identify protein signatures for ovarian cancer, which may then be used as the basis of a medical test to detect the cancer at an early stage.

Adding to our proteomics suite is the Typhoon ($136,000) which allows us to accurately measure proteins in a far cheaper and more detailed and precise way than previously. For example, we can accurately measure the amount of that component made by the cells when they are exposed to hormones or chemotherapy drugs. We previously used a film-based system, which is much slower, less sensitive and more expensive.

The Gandel Charitable Trust Sequencing Centre continues to expand its range of services and technology. Users of the Centre's services now include 500 medical researchers and clinicians from the Monash Health Translation Precinct, the Peter MacCallum Cancer Centre, Ludwig Institute of Medical Research and Commonwealth Serum Laboratories, as well as facilitating diagnostic results at the Austin and Burnet campuses.

A recent gift from the Gandel Charitable Trust has enabled the introduction of a genetic microbial identification system using DNA sequencing.

This new system provides a rapid and accurate method of identifying bacteria and fungi causing disease and illness. Considered a superior diagnostic method, bacterial and fungal DNA are analysed and the unique sequence profile is matched against a validated library, containing the known sequence of thousands of bacterial and fungal strains.

The Rebecca L Cooper Medical Research Foundation supported the purchase of a second Real-Time PCR 7900HT instrument that permitted an increase in gene expression and DNA sequencing output.

An adjunct to our sequencing capabilities will be the Centre for Genomic Cancer Research, which is to be supported by a $1.6 million equipment allocation from the Australian Cancer Research Foundation to Monash Institute of Medical Research and Prince Henry's Institute. This Centre will provide a next generation sequencing service which will benefit medical researchers throughout Australia.

COMMERCIALISING OUR DISCOVERIES

The commercialisation of research discoveries delivers products and patents which can be translated into new drugs, preventative treatment therapies and technologies. It positively impacts on Australia's ability to innovate and leads to major global advances in health care.

Three new patents were granted in 2010. Two patents related to our epitopic antibody patent and the other for the *SRY* (sex-determining) gene in Parkinson's disease.

Importantly, the royalties we receive from licensed patents fund future discovery.

We are presently liaising with the US-based licensee for PHI's epitopic antibody patent regarding development of a commercial scale diagnostic cancer test, and supply of reagents for our research. Our researchers presented the licensee with new research data and proposals for additional research.

Seven divisional patent applications covering four patent families in various jurisdictions are also under examination. A new provisional application was filed in collaboration with the Walter and Eliza Hall Institute of Medical Research and Monash University. PHI currently holds nine patents in total.

In the past year, we executed 16 new agreements for collaborative research, materials transfer and confidential disclosures.

Our intellectual property (IP) and commercialisation initiatives are overseen by the Intellectual Property and Commercialisation Committee which is a subcommittee of the Board. Members provide expert guidance on issues such as corporate governance of IP-related functions and strategies for managing our licensing relationships. We greatly appreciate the contribution made by members of this committee.

Enhancing our procedures for managing intellectual property and related functions has been a priority for us in 2010. We developed a rigorous protocol to assess the suitability of applications for IP protection and reviewed all our executed agreements to identify possible exposure to risk.

The new IP assessment procedure enables our researchers, Intellectual Property and Commercialisation Committee and external advisors to review whether inventions would comply with the basic requirements of a patent application. It also helps would-be inventors to better understand the patenting process and its costs.

Mass spectrometer at PHI: Research Assistant Jessica Gathercole and Research Officer Adam Rainczuk

CLINCIAL SERVICES

Prince Henry's Institute has a 50 year history of engagement with the provision of clinical services.

Traditionally, senior scientific staff have been active clinicians contributing to the provision of consulting endocrinology services in the affiliated health service. Currently, our staff are involved in leadership and service development roles in several clinics in conjuction with Southern Health.

The Southern Health General Endocrinology Clinic was originally headed by Professor Henry Burger and is currently headed by Professor Peter Fuller with a number of other clinicians, both qualified and trainee consultant endocrinologists contributing to the provision of endocrine care for the south-east corridor of Melbourne, a population base approaching 1.6 million.

As the demand for this service has increased, so has the evolution of more specialised clinics.

The Androgen Replacement Clinic is a joint initiative of Prince Henry's Institute and the Southern Health Endocrinology Unit. The clinic advises on the management of men with androgen deficiency, for education of clinicians in this aspect of endocrinology, and also provides a basis for a number of research studies. This clinic is primarily led by Drs. Carolyn Allan and Kati Matthiesson. Dr Matthieson also provides the andrology expertise to the Reproductive Biology Unit Clinic at Monash Medical Centre.

L - R: Elise Forbes RN, Clinical Research Fellow Dr Carolyn Allan, Anna Zamojska RN

In the 1970's, Professor Henry Burger, with the late Jean Hailes, established Australia's first Menopause Clinic. That Clinic continues at Southern Health as a collaboration between the Endocrinology Unit and the Gynaecology Units of Southern Health.

The Endocrinology component is headed by Dr. Amanda Vincent who then has several research collaborations with members of the Institute and Dr. Fran Milat, who is a Clinical Fellow within PHI, contributes her expertise in the management of osteoporosis. Fran has been instrumental in 2010 in the establishment of our most recent specialist clinic, the Metabolic Bone Disease Clinic, a collaboration with the Paediatric Endocrinology Unit. The clinic manages the care of osteoporosis patients in particular, but also other diseases of bone in younger patients, many of whom are transitioning from paediatric care. This has involved both service development and the provision of protocols in areas for which there have not previously been management guidelines. Several research studies have arisen from the development of this clinic.

Professor Rob McLachlan maintains his active engagement with Monash IVF heading their andrology laboratories and andrology services.

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EDUCATION

Prince Henry's Institute undertakes a strong teaching role in research. Students are enrolled through our affiliated universities and are completing higher degrees at Honours, Masters and Doctoral level.

Research education primarily centres on teaching the discipline of laboratory science, ethics and research communication. This is reflected in regular presentations at a laboratory group level, annual presentations to the Institute and at a national scientific meeting, and in the case of PhD students once internationally during their candidature.

We also offer regular scientific seminars and more recently at the instigation of the education committee and the newly formed student society we have introduced student technical seminars enabling students to learn the latest techniques.

With a focus on the translation from laboratory to the clinic, we offer a stimulating learning envrionment for medically qualified PhD students with regular and continuing clinical practice in Southern Health clinics, integrated with training in basic science and research technical skills.

We recognise that a career in research, while rewarding, is a challenging career path and that education and mentoring across both scientific and professional areas are important facets for success.

Practical support for graduate excellence

Due to the demands of research and study, many students are unable to take on employment to supplement their PhD scholarship. In 2010, with support from the corporate sector, we increased practical support available for early career researchers. Three award winners were announced in 2010 following a competitive selection process, bringing the total to five who receive $15,000 each over three years

Social and academic support

At the instigation of the Education committee and Student welfare committee, we are delighted that the Prince Henry's Institute Student Society was re-established in 2010.

Novo Nordisk Awards - Student Symposium - PhD Awards
L - R: Stacey Jamieson, Peter Nicholls, Justin Chen

The society aims to create a positive academic and social environment for students at PHI by advocating for and being the representative voice of its members, organising social events, and facilitating student education and training.

Students 2010:

PhD	31
Masters	4
Honours	14
Total	49

Prince Henry's Institute Student Society 2010

Committee members:
Stacey Jamieson (President)
Daniel Czech
Peter Nicholls
Hamish Morgan
Jenna Haverfield

Graduate Excellence Awards 2011

Justin Chen
Jenna Haverfield
Rajini Sreenivasan

17th annual PHI student symposium awards 2010

Novo Nordisk Presentation Awards

PhD
Peter Nicholls: "Hormonally regulated miRNAs target the tubulobulbar complex in the testis"

Commended - **Stacey Jamieson**
"The FOXL2 C134W mutation is pathognomonic for adult granulosa cell tumours of the ovary"

First Year PhD Award
Justin Chen
'The role of TGF-β ligands in muscle wasting and cachexia'

Novo Nordisk Awards - Student Symposium - Honours Awards. L - R: Justine Olcorn, Laura Bienvenu

Honours
Laura Bienvenu
"Macrophage mineralocorticoid receptor mediated inflammation and fibrosis in the heart"

Commended - **Justine Olcorn**
"The regulation of sertoli cell micro-RNAs by TGF-β superfamily members"

University affiliations:

MONASH University

THE UNIVERSITY OF MELBOURNE

SWINBURNE

DEAKIN UNIVERSITY

LA TROBE UNIVERSITY AUSTRALIA

Education supporters:

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Student List

PhD Graduates

Jenny Chow BBiomedSci (Hons) PhD
'The role of estrogen in triglyceride homeostasis'
Supervisors: Dr Wah Chin Boon; Professor Evan Simpson

Emily Yan Mei Lam
BBiomedSci (Hons) PhD
'Differential regulation of the mineralocorticoid receptor by corticosteroids and high salt in cardiovascular disease'
Supervisor: Dr Morag Young

Michelle Van Sinderen BSc (Hons) PhD
'The role of sex hormones in adiposity and insulin resistance in the aromatase knockout (ArKO) mouse model'
Supervisors: Dr Margaret Jones; Dr Wah Chin Boon; Professor Evan Simpson

Jyothsna Rao BScMSc PhD
'Effect of fat-derived hormone adiponectin on pancreatic beta cell function in Type 2 diabetes'
Supervisors: Assoc. Professor Helena Parkington, Professor Lois Salamonsen,

Hasnawati Saleh MSc PhD
'The influence of lymphocytes on the metabolism of bone'
Supervisors: Professor Matthew Gillespie; Dr Julian Quinn

PhD Students

Dimuthu Alankarage
BBiomedSci (Hons)
'Novel genes in sex determination'
Supervisor: Assoc. Professor Vincent Harley

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

Justin Chen BSc (Hons)/BA
'The role of TGF-β ligands in muscle wasting and cachexia'
Supervisors: Dr Craig Harrison; Dr Kelly Walton

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

Davina Cossigny BSc, GradDip Reprod Sci
'The role of TGF-β superfamily members: TGF-β1 and activin A in early folliculogenesis'
Supervisors: Professor Jock Findlay; Dr Ann Drummond

Daniel Czech BSc (Hons)
'Investigating the role of SRY in dopamine regulation and gender bias in neurological pathology'
Supervisors: Assoc. Professor Vincent Harley; Dr Joohyung Lee

Damien Eeles BBiomedSci (Hons)
'The roles of IL-33 and galanin in bone'
Supervisor: Dr Julian Quinn; Dr Brian Grills; Dr John Schuijers

Jenna Haverfield BSc (Hons) 'Hormonal regulation of Sertoli cell function *in vivo*'
Supervisors: Dr Sarah Meachem; Dr Peter Stanton

Amy Herlihy BSc GradDipGeneticCounselling
'An exploration of the prevalence and psychosocial aspects of Klinefelter Syndrome in the context of population-based genetic screening'
Supervisors: Professor Rob McLachlan; Assoc. Professor Jane Halliday; Assoc. Professor Lynn Gillam; Dr Megan Cock

Hui Ting Ho BSc (Hons)
'Proprotein convertase 6: role in embryo implantation and clinical implications'
Supervisor: Dr Guiying Nie

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

Stacey Jamieson BA/BSc (Hons)
'Molecular mechanisms in the pathogenesis of granulosa cell tumours of the ovary'
Supervisor: Professor Peter Fuller

Kyren Lazarus BSc (Hons)
'Role of LRH-1 in breast cancer'
Supervisors: Dr Colin Clyne; Dr Ashwini Chand

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

Michael Mond MBBS FRACP
'Defining the molecular pathogenesis of thyroid tumours'
Supervisors: Assoc. Professor Chris Gilfillan; Professor Peter Fuller

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

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

Nirukshi Samarageewa BBiomedSci (Hons)
'Elucidating of the role of CRTC co-activation of CREB in regulating promoter II-driven aromatase expression in human breast adipose stromal cells'
Supervisors: Professor Evan Simpson; Dr Kristy Brown

Courtney Simpson BSc (Hons)
'Structure and Function of Growth and Differentiation Factor 9 (GDF9)'
Supervisors: Dr Craig Harrison; Dr Peter Stanton

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

Sarah To BSc (Hons)
'TNFα in the development and progression of breast cancer'
Supervisors: Dr Colin Clyne; Dr Kevin Knower

Gabrielle van der Kraan BBiomedSci (Hons)
'The potentiating effects of cell stress on pathological bone loss'
Supervisors: Dr Julian Quinn; Dr John Price; Professor Matthew Gillespie

Rajini Sreenivasan BSc, PGDipSc, MSc
'Genetic Regulatory mechanisms in mammalian sex determination'
Supervisors: Assoc. Professor Vincent Harley; Dr. Robb de Longh

Kenneth Walker BSc (Hons)
'The development and function of high nephron endowment'
Supervisors: Professor John Bertram; Dr Kaye Stenvers

Phillip Wong MBBS FRACP
'Thalassaemia and bone'
Supervisors: Professor Peter Fuller; Professor Matthew Gillespie; Dr Fran Milat

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

Masters Students

Seungmin Ham BSc, Grad Dip Drug Evaluation Pharma Sc, Grad Dip RSc
'The regulation of aromatase by the LKB1/AMPK pathway in the testis'
Supervisors: Dr Kristy Brown; Dr Sarah Meachem

Lorraine Lin BSc
'The role of Leukemia inhibitory factor in endometrial stromal cell decidualization (Human and mice).'
Supervisor: Dr Eva Dimitriadis

Rim Nour BSc
'Ovarian Phenotype of the IKKβ knockout mouse'
Supervisors: Professor Peter Fuller; Dr Ann Drummond

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

Honours Students

Laura Bienvenu BSc (Hons)
'Macrophage mineralocorticoid receptor mediated inflammation and fibrosis in the heart'
Supervisor: Dr Morag Young

Karen (Ying Jie) Chua
'SRY in the locus coeruleus'
Supervisors: Dr Joohyung Lee; Assoc. Professor Vincent Harley

Paige Everingham BSc (forensics)/BA
'Mutational analysis of hTES, the human homologue of the testis specific enhancer of SOX9'
Supervisor: Assoc. Professor Vincent Harley

Tamara Howard BA/BSc (Hons)
'Identification of LRH-1 antagonists for breast cancer therapy'
Supervisors: Dr Colin Clyne; Dr Ashwini Chand

Justine Olcorn BSc (Hons)
'The regulation of sertoli cell micro-RNAs by TGFβ superfamily members'
Supervisor: Dr Peter Stanton

Agustinus Prijanto
'Genetic mechanisms underlying hypospadias'
Supervisor: Assoc. Professor Vincent Harley

Li Tsan Tai BSc (Hons)
'The role of proprotein convertases in cancer through targeting scaffolding proteins EBP50 and ezrin'
Supervisor: Dr Guiying Nie

Han Lin Tan BSc (Hons)
'The effects of betaglycan on SMAD signalling balance in granulosa tumour cells'
Supervisors: Dr Kaye Stenvers; Maree Bilandzic

Dhilushi Wijayakumara BSc (Hons)
'Exploring the relationship between LRH-1 and estrogen target genes using GREB1 and pS2'
Supervisors: Dr Colin Clyne; Dr Ashwini Chand

Mei Yun Yong (Jacy)
'Functional analysis of FGFR2 in testis development'
Supervisors: Assoc. Professor Vincent Harley; Dr Stefan Bagheri-Fam

Deborah John
'Molecular pathogenesis of granulosa cell tumours'
Supervisors: Dr Simon Chu; Dr Cenk Suphioglu

Emily Kelly BSc (Hons)
'Regulation of nodal synthesis and signalling'
Supervisors: Dr Craig Harrison; Dr Kelly Walton

Virginia Lay BSc (Hons)
'Interleukin 11 and endometrial cancer'
Supervisor: Dr Eva Dimitriadis

Hamish Morgan
'The role of PUMA in germ cell death during ovarian development: impact on the fertile lifespan'
Supervisor: Dr Karla Hutt; Assoc. Professor Jeff Kerr

Vacation Students

Abdul Aziz Al-Helou
Xylia Chan
Calvin Chee
Cameron Ewert
Samuel Hawthorne
Rachel Howe
Justine Olcorn
Daniel Payne
Hoi Teng Pun
Asvini Subasinge
Jessica Truong
Lixian Wang
Joyee Yeung
Maria Zaldivia
Shen Zhao
Zhe Zhao

INVITED PRESENTATIONS

Carolyn Allan
- Invited Speaker, Endocrine Society of Australia Annual Scientific Meeting/Australasian Branch of Women in Endocrinology Symposium
- Invited Speaker, Blackmores Research Symposium: Fertility to Frailty, Sydney

Maree Bilandzic
- Invited Speaker, Department of Biomedical Science Deakin University, Melbourne Campus

Kristy Brown
- Invited Speaker, Tohoku Medal Award Lecture, Tohoku University, Sendai, Japan
- Invited Speaker, Xth International Aromatase Conference, Edinburgh, UK
- Invited Speaker, Réseau Québécois en Reproduction (RQR) Lecture Series, Université de Montréal, St-Hyacinthe, Canada
- Invited Speaker, ANZ Breast Cancer Trials Group Annual Scientific Meeting, Sydney
- Invited Speaker, MODI (Monash Obesity and Diabetes Initiative) Workshop, Melbourne
- Invited Speaker, VBCRC Annual Scientific Meeting, Melbourne
- Invited Speaker, Southern Health Breast Interest Group, Melbourne
- Invited Speaker, MCCC Cancer Research Seminar Series, Monash University, Melbourne

Henry Burger
- Invited Speaker, St Vincents Hospital Clinical School Centenary Symposium, Melbourne
- Invited Speaker, 4th meeting of the Asia Pacific Menopause Association and 14th Australasian Menopause Society Conference, Breast Cancer and Hormone Replacement Therapy, Sydney
- Invited Speaker, The Jean Hailes Educational Program – Hormone Replacement Therapy Update, Melbourne

Ashwini Chand
- Invited Speaker, Xth Aromatase Conference, Edinburgh, Scotland
- Invited Speaker, Victorian Breast Cancer Consortium Annual Scientific Meeting, Melbourne

Evdokia Dimitriadis
- Invited Speaker, SRB RCRH Award Lecture, Annual Meeting of the Society for Reproductive Biology, Sydney
- Invited Chair, World Congress of the International Society for the Study of Hypertension in Pregnancy, Melbourne
- Invited Chair, Joint SRB/ESA Symposium, AH & MR Congress, Melbourne

Peter Fuller
- Invited Speaker,16th World Congress of Basic and Clinical Pharmacology, Copenhagen, Denmark
- Invited Speaker, 14th International Congress of Hormonal Steroids and Hormones & Cancer, Edinburgh, Scotland
- Invited Speaker, American Society of Nephrology, Renal Week 2010, Denver, Colorado

John Funder
- Invited Speaker, World Congress of Internal Medicine, Melbourne
- Invited Speaker, Disorders of Sexual Development and Hot Topics in Steroid Biology, Miami, USA
- Invited Speaker (plenary lecture), Primary Aldosteronism and Low Renin Hypertension, Sendai, Japan
- Invited Speaker (plenary lecture), International Congress of Endocrinology, Kyoto, Japan
- Invited Speaker (plenary lecture), Cardiovascular Endocrinology and Metabolism, Nara, Japan
- Invited Speaker (plenary lecture), International Aldosterone Forum, Japan
- Invited Speaker (plenary lecture), The Endocrine Society, San Diego, USA
- Invited Speaker, International Society of Hypertension, Vancouver, Canada

Matthew Gillespie
- Invited Speaker, 14th Congress of Asia Pacific League of Associations for Rheumatology (APLAR 2010), Hong Kong

Craig Harrison
- Invited Speaker, Department of Cell Biology, New York University Medical Center, New York, USA
- Invited Speaker, Department of Biochemistry at the University of Texas Health Science Center, San Antonio, USA
- Poster Presentation, 92nd Annual meeting of the Endocrine Society, San Diego, USA
- Invited Speaker, University of Melbourne RMH/WH Academic Centre Seminar

Vincent Harley
- Invited Speaker, IOC-convened US Pediatric Endocrinology Meeting: 2nd World Congress on the Hormonal and Genetic Basis of Sexual Differentiation and Hot Topics in Endocrinology, Miami, Florida
- Invited Speaker, Necker Institute, Paris, France
- Invited Speaker, Dept Human Genetics, New York University, New York, USA
- Invited Speaker, 14th Human Genome Meeting (HGM) 2010: Next Generation Genomics and Medicine (HUGO), Montpellier, France
- Invited Speaker, Genetics 2010: Model Organisms to Human Biology (MOHB), Boston, USA (Plenary Speaker)
- Invited Speaker, APEG Satellite meeting on DSD Adelaide
- Invited Speaker, MCRI Seminar Series, Royal Childrens Hospital, Melbourne
- Invited Speaker, MCRI Seminar, Royal Children's Hospital, Melbourne

Kevin Knower
- Invited Speaker, Tohoku University Memorial Lecture, Sendai, Japan

Sarah Meachem
- Invited Speaker, Andrology Society of America, Houston, TX, USA
- Invited Speaker, Health Summit, Melbourne University, Parkville
- Facilitator, Mid career Professional Development Day, Australian Health and Medical Research Congress, Melbourne
- Invited Speaker, Senior Schools Program, Melbourne Museum, Tall Poppy Campaign, Australian Institute of Policy and Science

Rob McLachlan
- Invited Speaker, US Endocrine Society, Clinical Case Management forum, San Diego, USA
- Invited Speaker, Australasian Epidemiological Association Annual Conference, Sydney
- Invited Speaker, European Meeting on the Psychosocial Aspects of Genetics. Gothenburg, Sweden
- Invited Speaker, International Workshop on Klinefelter's Syndrome. Copenhagen, Denmark
- Invited Speaker, Human Genetics Society of Australasia Annual Scientific Meeting, Melbourne
- Invited Speaker, Australian Sonographers Association Annual National Conference, Melbourne

– Invited Speaker, Andrology Australia Annual Forum, Sydney
– Invited Speaker, Endocrine Society of Australia, Fertility Society of Australia Annual Scientific Meetings, Sydney
– Invited Speaker, Victorian Urology trainees annual weekend retreat, Daylesford
– Invited Speaker, Monash Division of General Practice, Melbourne

Guiying Nie
– Invited Speaker, 1st International Conference on Enzymes and Biocatalysis, Shanghai, China
– Invited Chair, 1st International Conference on Enzymes and Biocatalysis, Shanghai, China
– Invited Speaker, Shanghai Institute of Planned Parenthood Research, Shanghai, China
– Invited Speaker, ARC Centre of Excellence in Biotechnology Workshop, Melbourne

David Robertson
– Invited Speaker, Society for Reproduction and Fertility, Nottingham, UK

Lois Salamonsen
– Invited Speaker, IX International Congress of Reproductive Immunology, Palm Cove, Cairns, Queensland
– Invited Speaker, Society for Reproduction and Development Annual Meeting, Towada, Japan
– Invited Speaker, International Symposium for Immunology of Reproduction, Osaka, Japan
– Invited Speaker, Dept of Obs–Gyn, Tokyo University, Japan
– Invited Speaker, MIMR / Monash IVF, SHAPE Meeting, Melbourne

Mai Sarraj
– Invited Speaker, Departmental Seminar, Virginia University, USA
– Platform presentation, Society for the Study of Reproduction (SSR), Milwaukee, USA

Evan Simpson
– Invited Speaker, Breast cancer Think Tank 20, Barbados
– Invited Speaker, 14th International Congress of Endocrinology, Kyoto, Japan
– Invited Speaker, 14th World Congress of Gynecologic Endocrinology, Florence, Italy
– Invited Co-Chair Chinese Endocrine Society, Beijing, China
– nvited Speaker, Estrogens, SERMS and TSEC Meeting (Pfizer sponsored), Pennsylvania PA, USA

Kaye Stenvers
– Invited Speaker, Monash Comprehensive Cancer Consortium Seminar Series, Australia
– Invited Speaker, 43rd Annual Meeting of the Society for the Study of Reproduction, Milwaukee, USA

Andrew Stephens
– Invited Speaker, 4th Annual Biomarker Discovery and Development Conference, San Francisco, USA
– Invited Speaker, 2nd Annual Cancer Targets and Therapeutics Conference, San Francisco, CA, USA
– Invited Speaker, OzBio2010: The Molecules of Life – From Discovery to Development, Melbourne
– Invited Speaker, Australian Society for Medical Research, Careers in Biomedical Research, Melbourne

Sarah To
– Invited Speaker, 53rd Annual meeting of the Endocrine Society of Australia, Sydney

Morag Young
– Invited Speaker, Cardiac Society of Aust & NZ with the International Society for Heart Research, Adelaide, Australia
– Invited Speaker, 3rd International Aldosterone Forum, Tokyo, Japan
– Invited Speaker, International Congress of Endocrinology, Kyoto, Japan
– Invited Speaker, Cardiovascular Endocrinology and Metabolism, Nara, Japan
– Invited Speaker, 58th Annual Scientific Meeting of the Cardiac Society of Australia and New Zealand, Adelaide

SEMINARS

Hormones in Health & Disease: 50 Years of endocrine research at PHI

Dr Carolyn Allan
Postdoctoral Clinical Research Fellow, Clinical Andrology, PHI
"Androgens, adiposity and the ageing male"

Dr Bill Bremner
Director, Center for Research in Reproduction and Contraception, University of Washington
"Tissue steroid levels: Not necessarily what would be predicted from blood levels"

Professor Henry Burger AO
Emeritus Director and Senior Fellow, PHI
"An endocrine odyssey"

Professor Iain Clarke
Chair, Department of Physiology
Monash University
"Baaaa graphs"

Professor Judith Clements
Hormone Dependent Cancer Program Leader, Institute of Health and Biomedical Innovation
Queensland University of Technology
"From mice to men - kallikreins in hormone-dependent cancers"

Professor David de Kretser AC
Governor of Victoria
"The role of activins and follistatin in inflammation and tissue repair"

Professor Jock Findlay AO
Head, Ovarian Biology Laboratory, PHI
"Exploring the secrets of the ovary"

Professor John Funder AO
Senior Fellow, PHI, Director of Research Strategy, Southern Health and Professorial Associate, Centre for Neuroscience, The University of Melbourne
"A tale of three cities"

Professor Matthew Gillespie
Director of PHI
"PHI in 2020"

Associate Professor Vincent Harley
Head, Molecular Genetics & Development Laboratory, PHI
"Disorders of sex development"

Professor Adrian Herington
Director of Mathematical, Information and Physical Sciences, Faculty of Science & Technology
Queensland University of Technology
"Ghrelin gene-related peptides in hormone dependent cancer"

Professor Khalid Kadir
Professor of Medicine, Monash University, Malaysia & Head of the Clinical School, Johor Bahru & Head of the Clinical School, Johor Bahru & Head of the Clinical School, Johor Bahru
"Metabolic stress and the epidemic of diabetes"

Gab Kovacs AM
International Medical Director, Monash IVF
"How to combine a state of the art clinical service with research output"

Professor Harry Majewski
Head, School of Medical Sciences, RMIT University
"Diabetes is an elevated PGE_2 condition: clues for protective therapy"

Associate Professor David Robertson
Head, Reproductive Hormones, PHI
"Development of diagnostic tests for the early detection of ovarian cancer"

Professor Lois Salamonsen
Head, Uterine Biology Program and Endometrial Remodelling Laboratory, PHI
"A life with the womb"

Professor Evan Simpson
Metabolism and Cancer Group Leader, PHI
"Obesity increases the risk of breast cancer – a role for estrogens?"

Professor Helena Teede
Director Research, Jean Hailes Foundation for Women's Health
"Female reproductive health, insulin resistance and obesity"

MHTP Seminars

Dr Lyn Airey
CSIRO Education, CSIRO
"Science in Schools"

Professor R. John Aitken
University of Newcastle
"Cell biology of germ cells, fertilization and early embryonic development"

Professor Claude C.A. Bernard
Deputy Director, Immunology and Stem Cell Laboratories (MISCL), Monash University
"The promise of stem cells as a regenerative approach for the treatment of multiple sclerosis"

Professor Paul Bonnington
Director, Monash e-Research Centre, Monash University
"e-Research"

Professor Henry Burger
Emeritus Director, Prince Henry's Institute
"Clinical research – a cautionary tale"

Dr Nicholas Clemons
Surgical Oncology Laboratory, Peter MacCallum Cancer Centre
"Using 3-D tissue reconstitution models to study Barrett's oesophagus and adenocarcinoma"

Professor Kim Cornish
School of Psychology and Psychiatry, Faculty of Medicine
"When being "fragile" takes on a whole new meaning: exploring gene to behaviour in fragile X syndrome"

Professor Susan Davis
Department of Medicine, Monash University
"Should women receive androgen replacement therapy, and if so, how?"

Associate Professor Lea Delbridge
Head, Cardiac Phenomics
Department of Physiology
The University of Melbourne
"Perinatal origins of adult primary cardiac hypertrophy – a story of angiotensin II and cardiomyocyte autophagy"

Dr Rod Dilley
O'Brien Institute of Microsurgery, Melbourne
"Engineering cardiac tissue for heart repair"

Ms Phyllis Di Palma &
Dr Jennifer Scott Research Degrees Office, Faculty of Medicine, Nursing & Health Sciences
"Confirmation of candidature and progress reviews"

Ms Kangi Donaldson &
Dr Jennifer Scott
Research Degrees Office, Faculty of Medicine, Nursing & Health Sciences, Monash University
"Scholarships and awards"

Associate Professor Xiao-Jun Du
The Baker IDI Heart and Diabetes Institute
"Cardiovascular actions of the reproductive hormone relaxin: from basic science to clinical therapy"

Associate Professor Sam El-Osta
Baker IDI
"Development of diabetic complications as a result of prior poor glycemic control are mediated by persistent activating epigenetic changes of methyl-writing and -erasing enzymes"

Dr Kelly Ewen-White
Applied Biosystems
"See the difference - the SOLiD 4 system and beyond"

Professor Mark Febbraio
Head, Cellular & Molecular Metabolism Laboratory, Head of Basic Science, Division of Metabolism & Obesity, Baker IDI Heart and Diabetes Institute
"Activation of heat shock protein 72: a panacea for disease prevention?"

Professor John Funder AO
Director of Research Strategy, Southern Health
"Hypertension and heart failure: lessons for basic biology from clinical studies"

Professor Michael Gale
Department of Immunology
The University of Washington School of Medicine, Seattle, Washington, USA
"Triggering and control of innate immune defenses against RNA virus infection"

Professor David Gardner
Head of Zoology, University of Melbourne
"The ART of 'OMICS: how the 'OMICS are shaping the future of human IVF"

Dr Christine Gicquel
Epigenetics in Human Health and Disease Laboratory, Baker IDI Heart and Diabetes Institute
"Human 11p15-related fetal growth disorders: a model to study genomic imprinting"

Professor Tom Gonda
Diamantina Institute for Cancer, Immunology and Metabolic Medicine, The University of Queensland
"MYB in myeloid transformation and breast cancer"

Professor David Handelsman
Director, ANZAC Research Institute
"Androgens and male ageing"

Associate Professor Mark Hedger
Deputy Director, Centre for Reproduction and Development, MIMR
"Spermatogenesis, inflammation and testicular immunity: common mechanisms for diverse outcomes"

Associate Professor Michael Hickey
Centre for Inflammatory Diseases
Department of Medicine (MMC)
Monash University
"Leaving the mainstream – leukocyte navigation of the inflamed microvasculature"

Professor John Hodges
University of New South Wales
"What's new in grontotemporal dementia: from FUS to fibs"

Dr Levon Khachigian
Director, UNSW Centre for Vascular Research
"Development of DNAzymes as novel "first-in-human" therapeutics"

Professor Charles Mackay
Monash University
"New roles for chemo-attractant receptors in inflammation, metabolism and fibrosis"

Professor Richard Martin
Cape Western Reserve University, Cleveland, Ohio
"Intermittent hypoxic episodes in preterm infants - do they matter?"

Associate Professor Grant McArthur
Peter MacCallum Cancer Centre
"Therapeutic targeting of oncogene addiction"

Professor Fredrick Mendelsohn
Director of the Howard Florey Institute
"Neural Plasticity: implications for development, memory, rehabilitation and regeneration"

Professor George Muscat
Institute for Molecular Bioscience, The University of Queensland
"Orphan nuclear receptors and the Ski gene in skeletal muscle: insights into the regulation of adiposity and insulin signalling"

Dr Tony Panenfuss
Bioinformatics Division, The Walter and Eliza Hall Institute of Medical Research
"New approaches to genome searching reveals novel MHC class I genes in mammals and insights into malaria?"

Dr Philippe Rigault
Président Directeur Général – President & CEO GYDLE
"Bioinformatics solutions for complex integrative biology"

Dr Karen Schindler
University of Pennsylvania, USA
"Protein kinases and phosphatases that control chromosome dynamics during meiosis in oocytes"

Professor Andrew Sinclair
Early Development and Disease, Murdoch Childrens Research Institute, Department of Paediatrics, The University of Melbourne
"Insights into disorders of testis development using whole genome analysis"

Dr Margareta Sutija
Drug Discovery & Assay Development Specialist, PerkinElmer Australia
"The power of the alpha screen technology"

Dr Matt Sweet
Institute for Molecular Bioscience, The University of Queensland
"The good, the bad and the ugly of innate immunity: macrophage inflammatory and anti-microbial pathways"

Dr Anne Thompson
Executive Officer, Victorian Cancer Biobank,
"The Biobank: how do we support research?"

Dr Anne Thompson
Executive Officer, Victorian Cancer Biobank
& Ms Zdenka Prodanovic
Tissue Bank Manager, Southern Health
"Digital microscopy to support biomarker analysis"

Professor Dominic Thyagarajan
Director of Neurology, Monash University
"Impaired transcription termination in the human mitochondrial genome: novel mechanism of disease"

Dr Alex Veldman
Research Clinician, The Ritchie Centre
"Molybdenum Cofactor Deficiency: from desperation to commercialisation"

Ms Livia Vo
Technical Sales Specialist, Cell Systems, Invitrogen
Cell imaging: "From chaos to order: introducing the attune, the first acoustic flow cytometer and its applications"

Dr Tony White
Senior Research Fellow, Monash Cardiovascular Research Centre in association with Monash Heart
"Cardiac regeneration: Realistic possibility or pipedream?"

Dr Carol Wicking
University of Queensland
"The primary cilium in trafficking, development and disease"

Associate Professor Mary Wlodek
Head, Fetal, postnatal & adult physiology and disease laboratory, Department of Physiology, The University of Melbourne
"Solving the developmental programming puzzle – windows of opportunity for offspring born small"

Engagement

SERVICE TO THE SCIENTIFIC COMMUNITY

Awards and Prizes

Carolyn Allan
- Monash University Medical Research Students' Society Outstanding Supervisor Award: Honours Degree of Bachelor of Medical Science

Maree Bilandzic
- Poster Prize Winner, 14th International Congress on Hormonal Steroids and Hormones & Cancer Edinburgh, Scotland

Kristy Brown
- Career Development Award (CDA1), NHMRC
- Tohoku University Medal

Eva Dimitriadis
- Research Centre for Reproductive Health - SRB Award for Research Excellence in Reproductive Biology

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

John Funder
- Degree of Doctor of Laws honoris causa (Monash University)
- Research Australia Leadership and Innovation Award

Peter Nichols
- Winner, New Investigator Award, 41st Meeting of the Society for Reproductive Biology, Sydney
- Highly Commended, Male Endocrinology category, Southern Health Research Week Poster Competition

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

Service to the Scientific Community

Carolyn Allan
- Member, Andrology Australia Forum 2010: The Healthy Male, Sydney
- Thesis Assessor, Honours Degree Bachelor of Medical Science, Monash University

Stefan Bagheri-Fam
- Member, The Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB)

Maree Bilandzic
- Chair, ESA /SRB 2010 Cancer basic orals session

Henry Burger
- Member, Jean Hailes Foundation for Womens Health Board
- Chair, Research Committee, Jean Hailes Foundation for Womens Health
- Member, Faculty of 1000 Physiology
- Member, Council of Past Presidents, International Menopause Society
- Member, VARTA Advisory Panel
- Member, Biomedical Specialist Panel, World Health Organisation Reproduction Research Program, Geneva

Colin Clyne
- Member, Editorial Board, Endocrinology

Davina Cossigny
- Trainee Volunteer, Society for the Study of Reproduction Volunteer Committee, Annual Meeting, Milwaukee, USA

Evdokia Dimitriadis
- Member, Reviewing Board, Journal of Reproductive Immunology
- Member, Editorial Board Reproductive Biology and Endocrinology
- Member, Organizing Committee, XI International Congress of Reproductive Immunology, Palm Cove, Cairns, Queensland
- Awards judge, XI International Congress of Reproductive Immunology, Palm Cove, Cairns, Queensland
- Chair, Awards Committee, Society for Reproductive Biology
- ANZPRA Awards judge, SRB Annual Scientific Meeting, Sydney

Jock Findlay
- Chair, Scientific Committee of the Victorian Breast Cancer Research Consortium Inc.
- Member, Board of the Victorian Breast Cancer Research Consortium Inc.
- Co-Director, Ovarian Workshop, (USA)
- Member, Hospital Research Directors' Committee, Bio21 Cluster
- Director of Research, Royal Women's Hospital, Carlton Victoria
- Chair, Scientific Advisory Council, Bio21 Cluster
- Member, Bio21 Cluster Board
- Member, Melbourne Health Biobank Management Committee
- Member, Board of the Robinson Institute, University of Adelaide
- Director, Society for Study of Reproduction (USA)
- Chair, Embryo Research Licensing Committee of the NHMRC (the NHMRC Licensing Committee)
- Member, Patient Review Panel, Government of Victoria
- Chair, Grant Review Panel, NHMRC, Canberra

Peter Fuller
- Member, Council; Member, Executive Committee, Cancer Council, Victoria
- 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
- Co-Editor, Hormone and Metabolic Research
- Editor, Endocrine and Metabolic Section, Expert Opinion on Investigational Drugs
- Member, Editorial Board, Steroids
- Member, Editorial Board, Endocrinology
- Member, Faculty of 1000, Medicine
- Associate Editor, Endocrinology
- Member, Organising Committee, Annual Scientific Meeting of the Southern Health Care Network
- Member, Southern Health Tissue Bank Steering Committee
- Member, Research Affairs Core Committee of the Endocrine Society (USA)

John Funder
- Chair, Drug Policies Modelling Program Review Committee
- Chair, Liggins Institute Review Committee
- Chair, Orygen Review Committee
- Chair, Pfizer Australian Senior Research Fellowship Selection Committee
- Chair, Schering Plough/Merck Science Alliance
- Chair, Scientific Advisory Board, National Research Centre for Growth and Development, New Zealand
- Chair, Scientific Advisory Committee, Liggins Institute, New Zealand
- Secretary-Treasurer, International Aldosterone Conference
- Founding Member, Board of International Aldosterone Forum, Japan
- Member, Finkel Foundation Board
- Member, The Freemasons Foundation Centre for Men's Health, Scientific Advisory Committee

– Member, Garnett Passe and Rodney Williams Memorial Foundation Board
– Member, Harold Mitchell Foundation Board
– Member, Schering Plough/ Science Alliance

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, Monash Health Research, Precinct Pty Ltd
– Member of Board of Prince Henry's Institute
– Program Committee, ANZBMS Annual Scientific Meetings, Adelaide 2010
– Member, Research Committee, Faculty of Medicine, Nursing and Health Science, Monash University
– Member of Professorial Promotions Committee, Faculty of Medicine, Nursing and Health Science, Monash University.
– Member, Australian Synchrotron Clinical Advisory Panel
– Member, Australian Synchrotron Monash University, Therapeutic Beamline Implementation Committee
– Member, Science Policy Committee of the American Society for Bone and Mineral Society.
– Member, Advisory Board Centre for Physical Activity and Nutrition Research, Deakin University
– Member, RGMS User Group, National Health and Medical Research Council
– Chair, GRP National Health and Medical Research Council
– 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
– Editor, Directed Issue of International Journal of Biochemistry and Cell Biology: Sox genes
– Judge of Abstracts, 92nd Annual Meeting of The Endocrine Society, ENDO 2010
– Member, NHMRC Genetics Grant Review Panel
– Medical Research Council review of the MRC NIMR Genetics & Development Group, Mill Hill [London], UK
– Co-convenor: APEG Satellite meeting on DSD, Adelaide
– International Olympic Committee-convened meeting on the genetics of gender, Florida
– Member, American Society for Biochemistry and Molecular Biology (ASBMB)
– Member, Australian Neuroscience Society
– Member, The American Society of Human Genetics (ASHG)
– Member, US Endocrine Society
– Member, Lorne Genome Conference Inc. (Vice-president)

Craig Harrison
– Member, Organising Committee Committee, TGF-β Down Under Meeting

Rob McLachlan
– Associate Editor, International Journal of Andrology
– Associate Editor, Journal of Clinical Endocrinology and Metabolism
– Editor, Male Endocrinology Section, ENDOTEXT– Endocrinology text
– Member, Reviewing Board, Clinical Endocrinology
– Member, Reviewing Board, Biology of Reproduction
– Member, Reviewing Board, Endocrinology
– Member, Reviewing Board, Journal Clinical Endocrinology and Metabolism
– Member, Reviewing Board, Journal of Andrology
– Member, Reviewing Board, Human Reproduction
– Member, Reviewing Board, International Journal of Andrology
– Member, Reviewing Board, Acta Pediatrica
– Member, Reviewing Board, New England Journal of Medicine
– Member, World Health Organisation 'Research on Methods for the Regulation of Male Fertility Sub-committee'
– Chairman, Monash IVF Research and Education Foundation
– Co-chair, Longitudinal Male Health Study sub-committee
– Chairman, Medical undergraduate curriculum committee: developing a proposal for a male health curriculum for consideration by the Deans of Medicine of Australian medical schools.
– Member, Infertility Treatment Authority, now Victorian Assisted Reproduction Treatment Authority (VARTA) Public Education Reference Group
– Scientific adviser, Infertility Treatment Authority
– Chairman: LOC: International Society of Andrology, Melbourne 2013

Sarah Meachem
– Immediate Past President, The Australian Society for Medical Research
– Chair, Advisory Group to the board, Australian Society for Medical Research
– Ambassador, Victorian Tall Poppy Campaign, Australian Institute of Policy and Science

Ellen Menkhorst
– Chair, Society of Reproductive Biology Conference

Peter Nicholls
– Member, Student Representative Board, Society of Reproductive Biology

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

Lois Salamonsen
– Member, Editorial Board, Journal of Reproductive Immunology
– Member, Editorial Board, Endocrinology
– Member, International Advisory Panel, Reproduction, Fertility and Development
– Associate Editor, Biology of Reproduction
– Associate Editor (Pacific region), Reproductive Sciences
– Faculty member, Faculty of 1000 Medicine (Women's Health)

Mai Sarraj
- Member, judging panel for the "New Investigator Award", Society of Reproductive Biology (SRB)
- Volunteer, Society for the Study of Reproduction Volunteer Committee, Annual Meeting, Milwaukee, USA

Harmeet Singh
- Member, Reviewing Board, Reproductive Biology and Endocrinology, Fertiliy and Sterility

Evan Simpson
- Member, IOC, International Congress of Hormonal Steroids, Edinburgh
- Member, IOC, Aromatase 2010 Meeting, Edinburgh
- Member, Executive Council, International Congress of Endocrinology, Kyoto, Japan
- Member, Executive Committee, International Society for Endocrinology
- Member, Committee for Governance Affairs, Endocrine Society (USA)
- Member, Society for Endocrinology (UK) Council
- Chair, Advisory Panel on International Outreach, Endocrine Society (USA)
- Member, Council, Endocrine Society of Australia

Kaye Stenvers
- Guest editor, Molecular and Cellular Endocrinology, Special Issue, Activins and Inhibins

Andrew Stephens
- Member, Reviewing Board, Proteomics, Journal of Proteome Research, Reproductive Sciences, Expert Reviews in Proteomics, Molecular and Cellular Proteomics, BMC Bioinformatics

Sarah To
- Australasian Women in Endocrinology-Novo Nordisk New Investigator award
- Best poster presentation – 5th Australian Health and Medical Research Congress, Melbourne
- Endocrine Trainee Day Award – The Endocrine Society

Morag Young
- Member, Australian Society for Medical Research
  Chair, Careers Subcommittee, Victorian Branch ASMR
- Member, High Blood Pressure Research Council of Australia
- Member, Editorial Board, Endocrinology
- Member, Faculty of 1000, Physiology

PHI IN THE COMMUNITY

During 2010, we increased our commitment to engaging with the community to promote understanding of medical research and how our discoveries translate into prevention of disease, better treatments, and improved diagnosis that advances the health of all Australians.

Celebrating 50 years of service to science and the Victorian community in 2010

Our 50th anniversary provided an added impetus for us to renew and extend relationships and research collaborations. We invited PHI research alumni, who are now contributing through leadership roles in leading scientific and medical research institutions around the world, to meet with our current staff and students.

On 26 October 2010, over 250 researchers and supporters of PHI came together at the Arts Centre in Melbourne to survey and celebrate an extra-ordinarily productive half century's research discoveries of hormones in health and disease. The one-day symposium, entitled *'Hormones in health and disease: 50 years of endocrine research at PHI'* was a resounding success, scientifically and socially.

The symposium was opened by Professor Richard Larkins, and presenters included Professor David de Kretser AC, Professor Gab Kovacs AM, Professor Iain Clarke, Professor Henry Burger AO (Emeritus Director of PHI), eminent endocrinology researchers and current research staff.

It is also important to pay tribute to those individuals who have made significant financial contributions to funding of research. Following our 50th anniversary scientific symposium, we gathered at Government House for a reception hosted by the Governor of Victoria, Professor David de Kretser AC and Mrs Jan de Kretser. In acknowledging the important scientific and medical contributions by Prince Henry's Institute and our collaborators, Professor de Kretser made special mention of Mr Trevor Montgomery for his contributions to the Board and philanthropy at PHI.

'Ride 4 PHI' cycle challenge (L - R): Bruce Watson, Andrew McCallum, Michael Cooper, Grant Barry, Sam Micken, Kara Britt, Peter Wilson, Kath Backholer, Mark Roberts, Natalie Hannan, Matthew Gillespie, Vince Harley

Dr Sarah Meachem, Victoria's Tall Poppy Ambassador (and PHI researcher) with Dr Natalie Hannan, winner of a 2010 Victorian Young Tall Poppy Award

2010 Victorian Young Tall Poppy Science award

Dr Natalie Hannan, who recently completed her doctoral training at Prince Henry's Institute, was recognised in 2010 for her research and community education work. Natalie's Young Tall Poppy award from the Australian Institute of Policy and Science acknowledges her research on how a healthy pregnancy is established and also her public speaking engagements over the last five years to thousands of Victorian school students.

Dr Sarah Meachem, a PHI researcher, maintains active support for the awards in her role as Tall Poppy Campaign Ambassador for Victoria.

Engaging with the business community

Mr Harold Mitchell AO, businessman and philanthropist, was a guest of honour at the PHI 50 year dinner in October which brought together Melbourne business leaders and our partner organisations to raise awareness of our research into breast cancer and ovarian cancer. PHI researchers, Dr Kristy Brown and Ms Stacey Jamieson provided compelling insights for guests into their research and their driving motivations to translate their research into new treatments and clinical care for women and their families.

The evening, which was held at AAMI Park and included a fundraising auction, was successfully staged by the PHI Foundation, a volunteer fundraising committee of the Board.

Scientists and patent attorneys take a challenge

For the fifth consecutive year, a team of PHI researchers and business executives from the intellectual property sector have undertaken a challenging 520 kilometre ride to raise awareness and funds for research. Riding through rural Victoria provides an opportunity to join with thousands of other researchers, health workers and community members for a common cause – improving health care for Australians. Over the course of the Ride for PHI, our riders and their sponsors have raised more than $150,000 which has funded new equipment purchases.

Raising awareness and public support for ovarian cancer

In partnership with the Ovarian Cancer Research Foundation, our researchers have provided scientific expertise at numerous major community, business, education functions, as well as fundraising campaigns such as the NAB Silver Ribbon Appeal and other major public events such as L'Oreal Melbourne International Fashion Week.

At PHI's 50 year dinner: Gareth Delve (far left) from Melbourne Rebels, Matthew Gillespie and guest of honour, Harold Mitchell AO

Media engagement

To reach as broad an audience as possible in the community, our research discoveries are promoted through local, Victorian, national and international media outlets.

Major coverage in 2010 of our science discoveries included an ABC TV Catalyst feature on the male pill, and a Women's Weekly extended feature on the search for an early detection test for ovarian cancer.

In honour of the eminent contribution to science by Professor Henry Burger, PHI's Emeritus Director, we were delighted that the Australian Academy of Science invited him to contribute to their 'Interviews with Australian Scientists' series. A stimulating two hour filmed interview with Professor Burger was filmed in 2010, and is to be available for viewing from the Academy's website, and will be distributed on DVD to Australian schools.

Utilising social media for science and medical research

As consumers of information, Australians are increasingly choosing to access information directly using social media.

In a crowded information market-place, PHI provides a credible and trusted information service through our website and published newsletters, and in 2010 we expanded our information platforms to include Facebook and Twitter.

Community support of clinical research

Translation of our research into improved health care and treatments simply would not be possible without the participation and willingness of the Australian community to join our clinical studies and trials. Over 600 women have now participated in a unique ovarian cancer research program by making a simple tissue donation. The Melbourne collection program expanded during the year to include Sydney and will soon operate from Brisbane.

Researchers in the community

PHI researchers remained active in school education initiatives, which encourage students to consider a career in medical research and innovation. Some researchers have been matched through the CSIRO's Scientists in Schools scheme, and other researchers have visited schools throughout regional Victoria as part of the Australian Society for Medical Research education program.

GRANT FUNDING COMMENCED / ANNOUNCED IN 2010

Research Support

Commenced

NHMRC

- Disorders of Human Sexual Development. CIC Vincent Harley, $5,000,000 (2010-14)
- Crosstalk between Wnt/β-catenin and SOX signalling in mammalian sex determination. Pascal Bernard, $547,500 (2010-12)
- Role of PC6 in uterine-epithelium for embryo implantation and clinical implications. Guiying Nie, $620,925 (2010-12)
- The role of Interleukin-33 and T cells in the maintenance of bone mass. Julian Quinn, $571,500 (2010-12)

Bill and Melinda Gates Foundation - Grand Challenges Exploration Grants

- Women-controlled contraception that also prevents HIV. Guiying Nie, USD100,000
- Novel and very early detection of preeclampsia. Guiying Nie, USD100,000

Cancer Council Victoria

- Role of LHR-1 in breast cancer proliferation. Colin Clyne, $196,500 (2010-12)

CASS Foundation - Proof of Concept

- Extension to "Male susceptibility to Parkinson's Disease: A role for SRY?" Jooyung Lee, $20,000

Heart Foundation

- Identification of Ligand-Discriminant Interactions of the Mineralocorticoid Receptor. Peter Fuller, $129,000 (2010-11)

Helen Macpherson Smith Trust

- SRY in Parkinson's Disease - Proof of Concept & Beyond. Jooyung Lee, $30,000

Medical Advances Without Animals (MAWA)

- Human explant models to study the link between obesity and breast cancer in postmenopausal women. Kristy Brown, $30,000

Ovarian Cancer Research Foundation

- Operation of the OCRF Ovarian Cancer Tissue Bank. Andrew Stephens, $174,300
- Discovery and development of screening markers for the early detection of ovarian cancer. Andrew Stephens, $521,000
- Molecular pathogenesis of high grade serous ovarian cancer and molecular pathogenesis of granulosa cell tumours. Simon Chu, $155,000

The Clive and Vera Ramaciotti Foundation

- When good eggs go bad: Identification of genes associated with the loss of oocyte quality with age. Karla Hutt, $50,000

Announced

NHMRC

- A pivotal role for mineralocorticoid receptor Receptor signalling in cardiomyocytes. Morag Young, $591,732 (2011-2013)
- ATR-X in spermatogenesis. Stefan Baheri-Fam, $628,416 (2011-2013)
- BH3 proteins in the ovary: the balance between life and death of oocytes. Karla Hutt, $264,182 (2011-2013)
- Fat and Breast Cancer: Aromatase, p53 and HIF-1alpha. Kristy Brown, $586,732 (2011-2013)
- Ligand-discrimination at the aldosterone receptor. Peter Fuller, $521,706 (2011-13)
- Modulation of micrRNA activity in the tesits: a new paradigm for male fertility? Peter Stanton, $404,615 (2011-2013)
- Therapeutic potential of a modified activin A propeptide. Craig Harrison, $486,706 (2011-2013)

In partnership with:

St. Vincent's Institute

- Influence of osteocytes on anabolic bone therapies. CIC Julian Quinn (2011-2013)

Walter and Eliza Hall Institute

- Mechanisms of DNA damage induced oocyte apoptosis and infertility: examination of the role of BH3-only proteins. CIB Karla Hutt (2011-2013)

People Support

Commenced

NHMRC

Biomedical Training Award - Australian

- Endometrial-trophoblast interactions: identifying critical regulators of implantation and placentation. Ellen Menkhorst, $285,000 (2010-13)

Biomedical Scholarship

- PC6 as potential target for developing dual-role female contraception by blocking embryo implantation and HIV infection. HuiTing Ho, $74,750 (2010-12)

The Lalor Foundation

- Jemma Evans, Postdoctoral Basic Research Fellowship, USD 35,000

USA Department of Defense

- Ashwini Chand, Postdoctoral Fellowship, USD 315,000 (2010-12)

Announced

NHMRC

Senior Principal Research Fellowship

- Peter Fuller, $855,805 (2011-2015)
- Lois Salamonsen, $855,805 (2011-2015)

Career Development Award

- Kristy Brown, (Level 1), $384,160, (2011-2014)
- Craig Harrison, (Level 2), $424,920, (2011-2014)

Overseas Biomedical Training Fellowship

- Amanda Rickard, INSERM Fellow, $333,904 (2011-2014)
- Yogeshwar Makanji, $347,736 (2011-2014)

Ovarian Cancer Research Foundation

- Stacey Jamieson, Post Doctoral Fellowship, $77,508 (2011)

Philanthropic Trusts and Foundations

Philanthropic support from trusts and foundations is most gratefully acknowledged, and provides support for research projects and staff, purchase of essential equipment and travel to present at international scientific meetings. We sincerely thank all trusts and foundations for their generous support.

We also thank the following learned societies for their support: Endocrine Society of Australia, Marine Biological Laboratory, and the Society for Reproductive Biology.

Commenced

Ovarian Cancer Research Foundation
- Bruker UltrafleXtreme III MALDI Mass Spectrometer, equipment purchase, $679,000

Clive and Vera Ramaciotti Foundation
- Typhoon multimode scanner, equipment purchase, $50,000

The Marion & E.H. Flack Trust
- Typhoon multimode scanner, equipment purchase, $35,000

Harold Mitchell Foundation
- Maree Bilandzic, Postdoctoral travel award, $5,000
- Davina Cossigny, PhD travel award, $5,000

Montgomery Foundation
- Courtney Simpson, Postgraduate Scholarship

The Trust Company
- Fran Milat, The Michael, John and Phoebe Jones Memorial Fellow

Announced

Harold and Cora Brennen Benevolent Trust
- xCELLigence system, equipment purchase, $20,000

CASS Foundation
- Mai Sarraj, Travel award, $5,000

Prince Henry's Institute Awards

TM Ramsay Fellowship

The TM Ramsay Fellowship was first established in 2007, from a bequest by the late Lady Ramsay as a perpetual memorial to her late husband, Sir Thomas Ramsay. The fellowship is a significant award, and enables us to attract a talented researcher to Australia to build on their career success.
- Dr Michelle Myers (2011-2012)

PHI Career Enhancement Award
- Joohyung Lee, Level 1 ($5,000 over two years)
- Kristy Brown, Level 1 ($5,000 over two years)
- Julian Quinn, Level 2 ($10,000 over two years)

Infrastructure support

These funds support costs associated with infrastructure – from utilities, to support services, through to commercial and clinical translation of the institute's research endeavours, and equipment maintenance. Such support is not directly provided for by competitive grants.

Department of Business and Innovation
- The Victorian Government's Operational Infrastructure Support Program (OIS)
- OIS provides infrastructure support for the 13 independent medical research institutes based in Victoria. Funds are allocated on a performance basis that is tied to research funding investment attracted into Victoria as well as a range of commercial, clinical and international excellence outcomes.

National Health and Medical Research Council
- Independent Research Institute Infrastructure Support Scheme:

  Funds are provided annually to NHMRC accredited institutes for overhead infrastructure costs based on a proportion of competitive research funding awarded by the NHMRC.
- Equipment Grant:

  Funding is allocated on a pro rata basis to NHMRC administering institutions according to their share of the total funding awarded by the NHMRC for research each year.

SUPPORTERS AND DONORS

We are sincerely grateful to our donors and supporters for their generosity past, present and future. We express our continued gratitude to the PHI alumni for your support.

We wish to acknowledge and thank everyone who has made a gift to support our medical research. All gifts, no matter the size, are most gratefully received and wisely stewarded.

In 2010, donors and supporters contributed to our annual appeals, our annual Ride 4 PHI cycle relay, and to our special 50 year celebratory events and sponsorships. This support has enabled us to acquire major equipment and technology purchases, to accelerate planned research priorities, and to investigate new avenues of research which otherwise would remain unfunded.

Thank you.

Major donors

Ms Maria Alexiadis
Mrs Jean Armstrong
Mr John Bate
Mr Peter Best
Mr Edward Billson
JS Bonnington & Assoc
Mrs Margaret Bowman
Dr Kara Britt
Mrs Marian Brookes
Professor Henry Burger
Mr Maurice and Mrs Jean Cahill
Mr Peter Chalk
Churchill Park Golf Club
Mrs Florence Clarridge
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Miss Joan Covey
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Mrs & Mrs BC Randall
Mr Mark Roberts
Mr Edward Russell
Mr Ian Shimmin
Mr Dylan Simmons
Ms Melanie Sloss
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Hormones in Health and Disease 50 years of endocrine research at PHI sponsors

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Southern Health
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Invitrogen by life technologies

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STRATEGIC PARTNERS

Prince Henry's Institute acknowledges the support of the following organisations

Affiliated Partners

Southern Health

MONASH University

MHTP Monash Health Translation Precinct

MHTP Monash Health Translation Precinct

A partnership between Southern Health, Monash University, Prince Henry's Institute and Monash Institute of Medical Research translating scientific discoveries into world's best healthcare.

Southern Health

MONASH University

phi science for better life

MONASH INSTITUTE OF MEDICAL RESEARCH

Research Funding Partners

Australian Government National Health & Medical Research Council

Victoria The Place To Be

Australian Cancer Research Foundation

Victorian Breast Cancer Research Consortium

Cancer Council Victoria

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Heart Foundation

Helen Macpherson Smith Trust

MAWA Medical Advances Without Animals

Harold Mitchell Foundation

National Breast Cancer Foundation

ovarian cancer research foundation nab www.ocrf.com.au

The Trust Company

Clive and Vera Ramaciotti Foundations
The Gandel Charitable Trust
Harold and Cora Brennen Benevolent Trust
The Lalor Foundation Inc.
The Marian and E.H. Flack Trust
United States Department of Defense

THE BOARD

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

Chairman
Dr Robert (Bob) Edgar
BEcon(Hons) PhD(Econ) FAICD

Experience and expertise: Non-executive director and Chair. Extensive experience in financial services including 25 years at ANZ Bank where his final role was that of Deputy Chief Executive Officer.

Other current directorships: Asciano Group, Linfox Armaguard Pty Ltd, Nufarm Limited, Transurban Ltd, AMMB Holdings Berhad, Shanghai Rural Commercial Bank and Bank of Tianjin.

Special responsibilities: Chair of the Board, Member of the Finance and Audit Committee and Chair of the Investment Committee.

Chief Executive Officer
Professor Matthew Gillespie
BSc (Hons) PhD

Experience and expertise: Matt brought over 20 years research and leadership experience to the Institute when he became its CEO and fourth director in 2008, including nearly 20 years with St Vincent's Institute of Medical Research with the last 9 as Associate Director. He is an internationally renowned researcher in the fields of bone, joint and cancer and a member of the Research Committee of the National Health Medical Research Council.

Other current directorships: Ovarian Cancer Research Foundation, Australian and New Zealand Bone and Mineral Society and Monash Health Research Precinct Pty Ltd.

Special responsibilities: Chief Executive Officer, Member of Intellectual Property and Commercialisation Committee, Investment Committee and of the Foundation.

Treasurer
Ms Jay Bonnington
BCom MBA FCPA FAICD

Experience and expertise: Jay started her career as an accountant and worked overseas before working in the construction, engineering and manufacturing, electricity and financial services sectors. She was the CFO/Finance Director of Yallourn Energy and the CEO of the Make-A-Wish Foundation Australia until 2005. Jay now serves as a non-executive company director on a number of boards.

Other current directorships: HESTA Superannuation Fund, St John of God Health Care Group, Port of Melbourne Corporation, AgServices Victoria, Metropolitan Fire and Emergency Services, the Royal Botanic Gardens. Jay is a Trustee of The Queens Fund and the Lord Mayor's Charitable Foundation, and a member of the Deakin University Council.

Special responsibilities: Treasurer of the Board and Member of Finance and Audit Committee and Member of the Investment Committee.

Mrs Jane Bell BEcon LLB LLM FAICD

Experience and expertise: A Board member of the Company's predecessor since 2002, Jane brought her experience and knowledge across to the Company including over 20 years legal experience in corporate treasury and financial services operations in Australia, UK, USA and Canada.

Other current directorships: Melbourne Health, WorkSafe Victoria, Westernport Water Corporation.

Special responsibilities: Chair of Intellectual Property and Commercialisation Committee.

Ms Jennifer Joiner BEcon CPA

Experience and expertise: Currently Customer Care Lead Asia Pacific for Life Technologies Jennifer has an extensive background in Australian and global life sciences businesses including senior executive positions at Idexx Labs, Bayer AG and GE Medical Systems Australia Pty Ltd.

Special responsibilities: Member of Intellectual Property and Commercialisation Committee.

Associate Professor Wayne Ramsey AM CSC MBBS MHA FRACMA

Experience and expertise: Wayne was a Board member of the Company's predecessor since 2007. Following a successful military career, including the role of Director General Defence Health Service, Wayne moved into research, clinical and medical services and is currently Executive Director of Medical Services and Quality for Southern Health. He has Board experience in companies involved in medical research and clinical service delivery.

Other current directorships: Kitya Board responsible for Jesse McPherson Hospital.

Professor Steve Wesselingh BMBS PhD FRACP

Experience and expertise: Steve is currently Dean of the Faculty of Medicine, Nursing and Health Sciences, Monash University. Prior to taking up the Deanship in October of 2007, he was Director of the Burnet Institute. He is recognised internationally as an expert in viruses that affect the human brain.

Other current directorships: Anex, Australian Centre for Health Innovation, Baker IDI, Centre of Excellence in Intervention and Prevention Science, Lucid.

Mr John Weste MBA BSc

Experience and expertise: Over 25 years general and line management and management consulting experience and expertise gained whilst working within global corporations and as a Partner/ Vice President in some of the world's leading management consulting firms, most recently as the founder of the Richelieu Group Pty Ltd.

Other current directorships: Hocking Stuart Pty Ltd.

Special responsibilities: Chair of the Foundation.

COMMITTEES

PHI Board Committees

PHI Foundation

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

Members:
Mr John Weste (Chair)
Mr Ronnie Atlas
Professor Matthew Gillespie
Mr Graeme Goldman
Ms Lyn Moorfoot
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 Richard Condon
Professor Jock Findlay
Professor Matthew Gillespie
Mr Martin O'Meara
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)
Mr Grant Fisher
Prof Matthew Gillespie
Ms Jennifer Joiner
Dr Michael Panaccio
Assoc. Prof David Robertson
Prof Lois Salamonsen
Mr Andrew McCallum (Secretary)

Internal PHI Committees

Authorship & Data Audit Committee

The Authorship & Data Audit Committee manages the guidelines for authorship, publication and storage of scientific data at PHI to meet the requirements of the *NHMRC Code for the Responsible Conduct of Research*. This is done via a mechanism to audit all data prior to publication in scientific journals and maintenance of a complete and readily accessible bibliography of publications by Institute members.

Members:
Dr Peter Stanton (Chair)
Dr Neil Owens (co-Convenor)
Ms Dianne Arnold
Ms Claudette Thiedeman

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

Education Committee

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

In 2010 the committee included initiated a new "PHI Student Technical Seminar" series, aimed at helping students to acquire practical knowledge about commonly applied laboratory techniques.

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
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
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. All other committees report at ISG.

Members:
Dr Kaye Stenvers (Chair)
Dr Anthony Argentaro
Dr Stephan-Bagheri-Fam
Dr Pascal Bernard
Dr Maree Bilandzic
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
Dr Karla Hutt
Dr Vicky Kartsogiannis
Dr Joohyung Lee
Professor Rob McLachlan
Dr Sarah Meachem
Dr Katie Meehan (Secretary)
Dr Ellen Menkhorst
Dr Guiying Nie
Dr Liza O'Donnell
Dr Neil Owens
Dr Julian Quinn
Dr Adam Rainczuk
Assoc. Professor David Robertson

Professor Lois Salamonsen
Dr Mai Sarraj
Professor Evan Simpson
Dr Peter Stanton
Dr Andrew Stephens
Dr Morag Young

Higher Degrees Committee
The Higher Degrees Committee was established in 2010, and its charter and function established (01/06/2010)

Achievements included:
- Introducing guidelines for mentors of HDR students
- Establishing clear lines of communication between the student welfare committee, the Student society and HDR
- Overseeing preparation of a starter pack for provision to each new student by HR
- Ensuring complete details/ files are maintained for all students at PHI.

Members:
Prof. Lois Salamonsen (Chair),
Professor Matthew Gillespie
Dr Peter Stanton

Invitees:
Dr Neil Owens
Ms Christina Matisons (HR)
Dr Kristy Brown (Student Welfare Committee)

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

In 2010 the committee introduced policies on First Aid, Manual Handling, the OH&S Charter, Occupational Allergies, Occupational Exposure, Pregnancy and Breast Feeding in the Workplace, Poison Schedule, Radiation Management, Visitor Information Pack and Waste Policy.

Members:
Prof Matthew Gillespie (Chair)
Dr Steve Bouralexis
Ms Francine Brennan
Ms Cassie Hincks
Ms Ileana Kuyznierewicz (HSR)
Dr Yogeshwar Makanji
Mr Charles Pritchard

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
Dr 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.

In 2010 a major change was made to the timing of the staff review process. This was to enable processing of requests for promotion/reclassification to be made before the start of January when the new employment contracts start.

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

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.

Achievements incuded:
- Establishment of the PHI-Student Society (PHISS)
- Re-establishment of the student mentoring scheme
- Advanced governance of student candidature at PHI by contributing to development of the Higher Degree by Research Committee (HDC)
- Re-vitalising induction of HDR students to PHI

Members:
Dr Kristy Brown (chair)
Ms Davina Cossigny
Mr Daniel Czech*
Assoc. Professor Vincent Harley
Ms Stacey Jamieson*
Dr Neil Owens
Dr Kelly Walton
* denotes student representatives

External Committees
The responsible conduct of research underpins all activities undertaken by Prince Henry's Institute. We comply with the NHMRC Australian Code for the Responsible Conduct of Research, and we have also adopted our own Code of Research Conduct. Our active promotion of these codes establishes the ethos at PHI which guides all areas of the Institute from governance, through to the conduct, management and reporting of our research.

Prince Henry's Institute complies with all legislative and regulatory requirements for the safe and ethical conduct of research. Institutional biosafety and Ethics committees are external, and our researchers apply to these committees for approval to conduct their nominated research.
The external committees used by Prince Henry's Institute are:
Southern Health
– Human Research Ethics (HREC)
Monash University
– Animal Ethics Committee A and B (AEC)
Monash University
– Institutional Biosafety Committee (IBC)

STAFF LIST

1/1/10 – 31/12/10

Director
Matthew Gillespie BSc (Hons) PhD

Associate Director
Peter Fuller BMedSci MBBS PhD FRACP NHMRC
Senior Principal Research Fellow

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

Senior Fellow
John Funder AO MD BS PhD FRACP FRCP LLD(Hon)

Research Advisory Group
Jock Findlay AO PhD DSc NHMRC Senior Principal Research Fellow

Peter Fuller BMedSci MBBS PhD FRACP
NHMRC Senior Principal Research Fellow

Matthew Gillespie BSc (Hons) PhD

Vincent Harley PhD NHMRC Senior Research Fellow

Rob McLachlan MBBS FRACP PhD
NHMRC Principal Research Fellow

Guiying Nie PhD
NHMRC Senior Research Fellow

David Robertson PhD NHMRC Principal Research Fellow

Lois Salamonsen PhD NHMRC Principal Research Fellow

Evan Simpson BSc (Hons) PhD FAA
NHMRC Senior Principal Research Fellow

Laboratory Heads
Colin Clyne PhD - Cancer Drug Discovery

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

US Department of Defense Fellow
Kevin Knower PhD

Witchery & Madison Research Fellow
Katie Meehan PhD

The Lalor Foundation Fellow
Ellen Menkhorst PhD (until May)

CDMRP Department of Defense Postdoctoral Fellow
Ashwini Chand PhD

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

NAB OCRF Research Fellow
Andrew Stephens PhD

Witchery Research Fellow
Adam Rainczuk PhD

Clinical Research Fellows
Carolyn Allan MBBS (Hons) PhD DRCOG(UK) FRACP PhD

Jonathan Cohen MBBS (Hons) (until Jan)

Kati Matthiesson MBBS FRACP PhD

Kishani Kannangara MBBS BSc (Hons) (from Feb)

NHMRC Post-Doctoral Fellows
Karla Hutt PhD

Ellen Menkhorst PhD

Clinical Research Nurses
Marie Burley RN

Nicole Fairweather RN

Elise Forbes RN

Judi Hocking RN

Anna Zamojska RN

Senior Research Officers
Anthony Argentaro PhD

Stefan Bagheri-Fam PhD

Pascal Bernard PhD

Anne Corbould MBBS (Hons) PhD FRACP

Ann Drummond PhD

Vicky Kartsogiannis PhD

Sarah Meachem PhD

Liza O'Donnell PhD

Julian Quinn DPhil MSc

Helena Sim PhD

Research Officers
Mohamad Aljofan, PhD

Maree Bilandzic PhD

Jemma Evans PhD

Nicholas Fleming PhD (until July)

Louisa Ludbrook PhD (until Aug)

Chantal Magne Nde PhD

Yogeshwar Makanji BAppSci (Hons) PhD

Sarah Paule PhD

Jyothsna Rao PhD (from Sept)

Amanda Rickard PhD

Nana Saleh PhD

Mai Sarraj MSc PhD

Harmeet Singh MSc PhD

Stefan Sonderegger MSc PhD (from March)

Kelly Walton PhD

Senior Research Assistants
Maria Alexiadis BSc (Hons)

Francine Brennan BSc (Hons)

Maria Docanto BSc (Hons)

Kemperly Dynon BSc (Hons)

Ruth Escalona BSc (Hons) MSc

Caroline Foo BAppSc

Ming Yee Lee BBiomedSci, BSc (Hons)

Ying Li BSc GDipMicroBio

Melissa Solano BSc (Hons) (until Sept)

Yao Wang BSc

Yizhou Yao MD

Senior Technical Assistant
Anthony Sutherland (from Nov)

Research Assistants

Georgia Balourdos BSc (Hons)
Karen Chan BAppSc
Greg Cranston BSc (Hons)
Pei Leng Chong BSc (Hons)
Cameron Ewert (until July)
Jessica Gathercole BSc (Hons) (from Oct)
Lauren Hare BA/BSc (Hons)
Guy Harris MSc
Sophy Heng BSc (Hons)
Kerrie Herridge BSc (Hons)
Cassandra Hincks BSc (Hons)
Tamara Howard BA/BSc (Hons) (from June)
Ileana Kapic BAppSc (Hons)
Virginia Lay BSc (Hons)
Priscilla Li BSc (Hons) (until Sept)
James Morgan BSc (Hons)
Charles Pritchard BSc (Hons)
Enid Pruysers
Michelle Puryer BSc (Hons)
Belinda Quenette (until May)
Janelle Ryan BSc MSc
Saw Eng Tan BVet MedTech (until Feb 10)
Maggie Soliman BSc (Hons) (from Dec)
Alex Umbers BSc (Hons)
Elizabeth Verghese BSc (Hons) (until June 10)
Wendy Yang MBioMedSci (from Oct)
Joanne Yap BSc (Hons) MCE

Laboratory Technicians

Robin Leuba BA Dip Ed
Susan Taleh BA

Administrative Support

Chief Financial Officer

Peter Murray FCA BSc (Econ) (Hons)

Development & Commercialisation Services Manager

Andrew McCallum BE (Met) MEngSc GAICD

Laboratory & Technical Services Manager

Steve Bouralexis PhD BSc B Hlth Sci (Hons) B Comp Sci

Marketing & Communications Manager

Katrina Wilkins (until May)
Lyn Moorfoot EMFIA, Dip. T, Dip. OpMusTh (from July)

Accounts Officer

Jennifer Watson

Biomedical Engineer

Bruce Watson DipEng

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 Officers

Shilo Desira (until April)
Hsien Teh (from June)

Purchasing and Facilities Officer

Henry Wos

Science Communications Officer

Ian Muchamore BSc (Hons) (until Dec)

Sequencing Manager, The Gandel Charitable Trust Sequencing Centre

Vivien Vasic BSc

Executive Assistant

Diane Yallop (until Oct)

Personal Assistants / Administrative Officers

Dianne Arnold BSc
Jeanette Birtles BSc (Hons)
Sue Elger
Jacqueline Harrison
Claudette Thiedeman
Jeana Thomas

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
Director, ARC Centre of Excellence in Biotechnology & Development, University of Newcastle, New South Wales

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

Professor Iain Clarke
Chairman, Department of Physiology, Monash University, Victoria

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

Professor David de Kretser AC
The Governor of Victoria

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

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

Associate Professor Tom Jobling
Chairman, Ovarian Cancer Research Foundation

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

Professor Gab Kovacs AM
International Medical Director, Monash IVF, Victoria

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

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

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

Dr Luk Rombauts
Monash IVF, Victoria

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

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

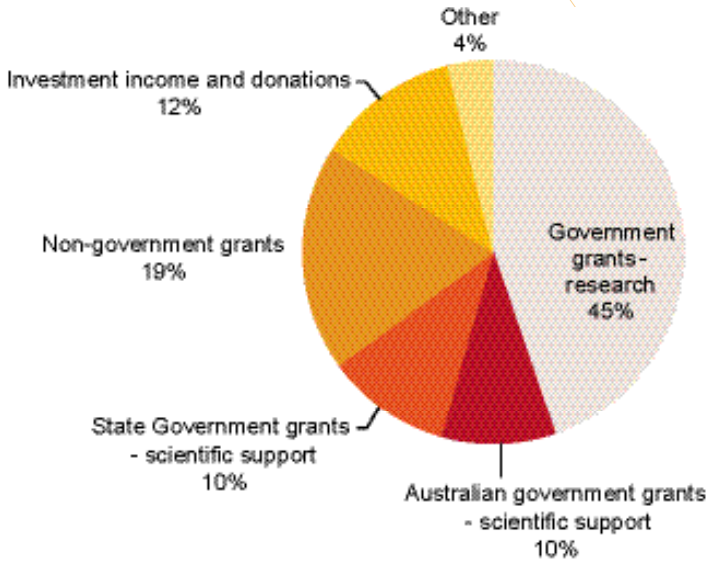
Dr Greg Tesch
Department of Medicine, Faculty of Medicine, Nursing & Health Sciences, Monash Medical Centre, Victoria

Honorary Research Associates

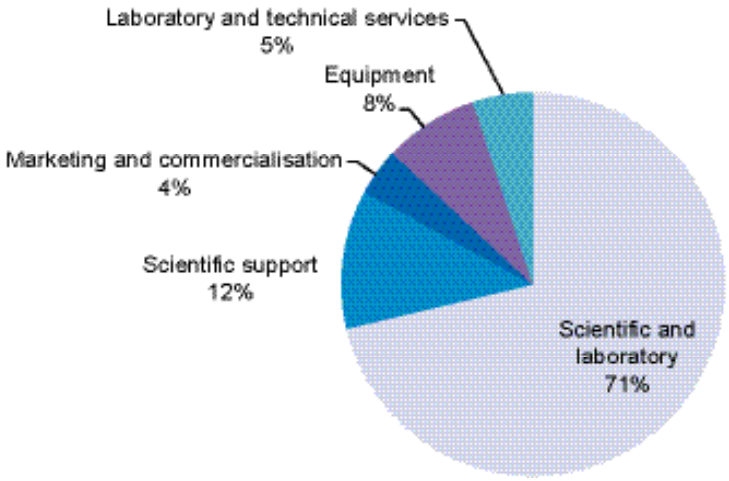
Dr Wah Chin Boon
Dr Tu'uhevaha Lino

FINANCIAL YEAR AT A GLANCE

Income



Expenditure



The year in brief	**2010**	**2009**
Income for research	8330958	8259470
Income for scientific support	2646124	2602865
Investment income and donations	1572491	845107
Other income	500987	573860
Expenditure on research	10202789	10221474
Expenditure on scientific support	1879732	1653279
Total surplus	968039	406549
Number of NHMRC fellows	8	8
Number of staff	156	155
Number of students	49	42
Number of PhD students	31	22
Capital expenditure	937196	186585

SUPPORT US

Our important research would not be possible without the support of individuals, business and community groups. Have you considered how you can support Prince Henry's Institute?

Donations

You can make a donation to PHI by using the attached slip. Donations can be made as a memorial gift in memory of a friend or loved one, or as a celebration gift in lieu of birthdays, weddings or anniversaries.

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Capital donations or named funds are a vital component of the Institute's funding and can be in memory of a loved one or on behalf of a business or community group.

Your named fund can be established as a fellowship, scholarship or award for students, scientists or administrative staff and underpins a celebration of excellence through your support.

Bequests

Bequests can be made to contribute to a specific area of research you choose. In addition, bequests can support a fellowship program, scholarship or award, or go to purchase important laboratory equipment.

Support medical research beyond your lifetime by making a bequest to PHI. An easy to use bequests brochure is available upon request.

Corporate Support

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Our Integrity

PHI operates on the mandate of ensuring that 100% of proceeds from donations fund important research discoveries, new cutting edge technologies and contribute to the education of our students who are our future. In all we do, we strive to ensure that your support makes the difference you intended.

For more information please contact:

Prince Henry's Institute
PO Box 5152
Clayton VIC 3168 Australia
Tel: 61 3 9594 4372
Fax: 61 3 9594 6125
Email: reception@princehenrys.org

Yes, I would like to support research at Prince Henry's Institute

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Email

Date of Birth

Donation Amount

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Donations over $2 are tax deductable. ABN 48 132 025 024

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Signature Expiry Date /

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Clayton, VIC 3168

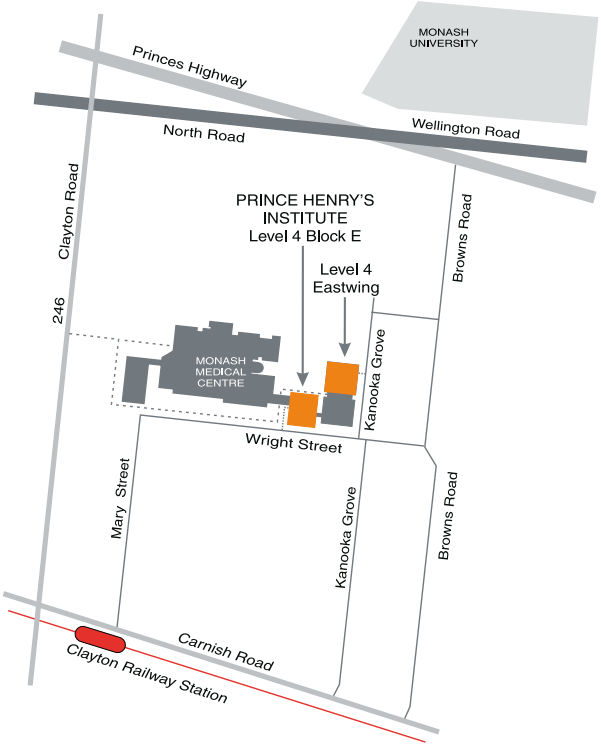
Prince Henry's Institute is a health promotion charity. Donations $2 and over are tax deductible. Prince Henry's Institute respects your privacy and complies with the Privacy Act, 1988 (Cth) and amendments. Your details remain confidential and we do not pass on any data to third parties.

HOW TO CONTACT US

Prince Henry's Institute
Level 4, Block E
Monash Medical Centre
246 Clayton Road
Clayton, VIC 3168
T 03 9594 4372
F 03 9594 6125
E reception@princehenrys.org

website www.princehenrys.org

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



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Tel. 03 9594 4372

www.princehenrys.org