



Interested in a **Vacation  
Scholarship, Honours,  
Masters or Doctorate**  
in Medical Research?

# **PHI Student** Handbook

**2012**

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# 1 Introduction to PHI

## Excellence in Research

Prince Henry's Institute (PHI) is recognised as a world leader in endocrinology, the study of hormones. Acknowledged as an eminent medical research institute in Victoria and in Australia, PHI is an independent not-for-profit organisation based at Monash Medical Centre in Clayton, Melbourne.

Affiliated with Monash University and Southern Health (Monash Medical Centre), PHI offers extensive postgraduate opportunities for students embarking on a research career. Our key areas of research include:

- bone, and joint disorders
- disorders of sex development
- heart disease
- hormones and ageing
- male and female fertility
- new contraceptive methods
- obesity
- ovarian, breast and bone cancer

## Overview

PHI currently has 38 students studying towards Honours, Masters, or PhD degrees.

PHI has a great reputation for postgraduate research and study, combining helpful and encouraging supervision with a high standard of research and expertise.

We encourage you to come and meet our researchers and take a tour of our facilities. Each August we hold an Open Day for prospective students however please contact us if you would like to come in for a chat and see what we can offer. We think you will be impressed!

## Research Projects

This handbook contains information about current research projects. The handbook also has details about studying at PHI and scholarships available.

## Further information:

For enquiries about projects please contact the supervisor listed with each project in this handbook.

As a student at PHI you will be enrolled through a university and your research project will be conducted predominately under the auspices of PHI.

Since Prince Henry's is an independent medical research institute there are no limitations as to which university you may enrol.

## Why Choose PHI?

Prince Henry's Institute provides students with an excellent start to their research careers, and past students have continued as high achievers in the research world.

Past postgraduate students have prestigious fellowships such as the NHMRC Overseas Training Fellowship and international research grants to work in leading laboratories around the world. We have an excellent record in the number of first class Honours degrees awarded to students, and have been fortunate to attract some of the most promising young scientists to study here, offering them a stimulating research environment conducive to developing their research careers.

## Scientific Environment

Collaborations between research groups are encouraged by a friendly work environment, exposing staff and students to a wide range of expertise and knowledge.

Since PHI is located at the Monash Medical Centre this provides strong clinical links and facilitates human research studies including clinical trials. We actively involve students in the life of the Institute and hold weekly seminars, including journal club and works in progress forums, to keep people updated on current research conducted within the Institute.

We also have weekly presentations from invited speakers from other research institutes keeping us up to date with current exciting research from Australia

and the rest of the world. Students have the opportunity to present their research annually at Student Presentation Day, providing experience of scientific presentation and a chance to follow the progress of other students.

All PhD students are given the opportunity to present their work at scientific meetings in their field of interest, including one international conference, usually in the final year of research. Students take this opportunity to visit internationally renowned laboratories where they may obtain postdoctoral positions as well as providing the student with the knowledge and some experience of the possible research directions he/she may wish to consider.

## Facilities

We have well equipped laboratories and facilities to undertake study and research. Students have access to the latest scientific technology, generally housed in shared facility rooms dedicated to specialised equipment.

As a student you will have access to both your University and Monash Medical Centre libraries. To keep up with the ever advancing scientific world we have the latest technologies and have expertise in specialist techniques including microspectrofluorimetry, real time PCR, microarray analysis, phosphoimaging, stereology and fluorescence, an animal behaviour suite, and substantial cell culture facilities including cell bio-analysis (xCELLigence).

Over the past year PHI has had substantial investment in enabling technologies. A new mass spectrometry suite has accelerated our proteomic research programs. Adding this capacity is a Typhoon multimode scanner which allows us to accurately measure proteins in a far more detailed and precise way than previously.

Shared facilities on site include Gandel Charitable Trust Sequencing Centre (NATA accredited). The Centre contains state-of-the-art genetic analysers for DNA sequencing and complementary genomic services which include fragment analysis, gene expression dHPLC, and DNA, RNA & protein analysis.

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

## University Links

Degrees undertaken at PHI are generally awarded by Monash University and students with students being enrolled through a particular department. However, we also have students enrolled at other universities. PHI researchers maintain close associations with university departments pertinent to their disciplines and hold adjunct appointments. PHI – they can provide expert supervision for your postgraduate degree.

Being just a 10 minute walk from Monash University, we can offer all the advantages of being an off campus dedicated research institute, whilst also having easy access to University facilities.

PHI researchers come from a diverse mix of backgrounds and we have a significant number of students who have come from overseas to study at the Institute.

# 2 Student Life

## Get to know us

### Student Life at PHI

At PHI, postgraduate research and study combines a friendly working atmosphere with helpful and encouraging expert supervision.

#### PHI offers you:

- **Experience** in an internationally renowned medical research institute
- **Expert supervision** from PHI researchers
- **The latest facilities** and technologies for research and study
- **A clinical setting** for human based research projects
- **Collaborations** between research groups
- **Weekly seminars and presentations**
- **Opportunities** to present at national and international scientific meetings
- **Annual PHI Student Symposium**

## PHI Students Excel

### Novo Nordisk Awards 2010

The 17th annual PHI Student Symposium was held in November 2010. This showcase, held over

2 consecutive days at Monash Medical Centre, offers students an opportunity to present their research in a formal environment to the wider research community. It also allows them to practise and develop their communication skills. Student awards at the Symposium were sponsored by our long standing partner Novo Nordisk. The presentations were judged by an independent panel of academic assessors comprised of PHI senior researchers.

### Results - 2010

#### Category - *PhD*

**Winner - 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- $\beta$  ligands in muscle wasting and cachexia"

#### Category - *Honours*

**Winner - Laura Bienvenu:** "Macrophage mineralocorticoid receptor mediated inflammation and fibrosis in the heart"

**Commended – Justine Olcorn:** "The regulation of sertoli cell micro-RNAs by TGF- $\beta$  superfamily members"

## PHI Student Society

### Prince Henry's Institute Student Society (PHISS)

The PHISS is a student run society that organises social events, facilitates student education and training, and represents students within the institute. The student society aims to create a positive social and academic environment, enabling PHI students to excel in their research degrees.

#### 2011 PHISS Committee

President: Daniel Czech (email: Daniel.Czech@princehenrys.org)

Secretary: Peter Nicholls

Treasurer: Jenna Haverfield

Honours Rep: Vlad Zuban

Social Events Rep: Kyren Lazarus

## Student Profiles



**Vlad Zuban** is an honours Student studying in the Metabolism & Cancer Lab

### Why did you choose research?

It sounded like an interesting and challenging year. It may also help me with my veterinary application for 2012.

### What do you enjoy about your research?

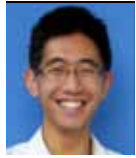
The mysteries and surprises of science, and trying to uncover some of them. Other fellow students and their inquisitive nature.

### Describe a typical day as a student at PHI:

I would plan out my day in the morning by writing a list of things to do, then, as efficiently as possible begin to complete all the set tasks during the day. For example; If I am running an immunohistochemical protocol in the lab for the day, all my tasks and work (ie. Meetings, presentations, thesis writing) is done during incubation times.

### Do you participate in any extracurricular activities?

Yes. I am on the student committee as the honours representative and we regularly organise events and functions for students at PHI. I am also a member at Healthwise Fitness Centre.



**Justin Chen** is a second year PhD student studying in the Growth Factor and Signalling Group.

#### Why did you choose research?

During my final year of undergrad, I wasn't sure what I really wanted to do. But I'm happy that I chose research in the end. There are new challenges all the time; figuring them out and succeeding is rewarding!

#### What do you enjoy about your research?

The good results! It is very fulfilling to get something after days of planning and lab work, and discussing with other researchers to see how it fits in with "the bigger picture". I also collaborate with other research groups around Melbourne, and it's always fun to work in their labs, meet other researchers and share ideas. We all have different expertise, and together it puts us in a better position to discover something new.

#### Why did you choose to study at PHI?

One of my lab demonstrators from undergrad started her post doc at PHI and encouraged me to study my Honours year here. Continuing on for a PhD was an easy choice. My supervisors are full of encouragement, support and motivation. As researchers within the Institute, they are always available to help out with any queries I have.

#### Describe a typical day as a student at PHI:

Every day is different. Some days are spent primarily in the lab. Others can be spent entirely at the computer analysing the results or planning for the next experiments – these are the days when I might be able to leave a little earlier. Then there are days where I need to stay later because of too many experiments going on at once! I also travel around Melbourne to other labs, and it's nice to get out and about. There is rarely ever a routine, which is what makes every day so different.

#### Do you participate in any extracurricular activities?

I try to make the most of my time when I'm out of the lab. I like catching-up with friends, playing tennis, running with my dogs, and learning to play my favourite songs on piano. As a student, the work hours are flexible, so it's easy to fit in other activities at the odd occasion.



**Justine Olcorn** is a first year PhD student studying in the Male Fertility Regulation Group.

#### Why did you choose research in reproduction?

After I concluded my undergraduate studies, I knew that I wanted to continue with research and that is why I choose to complete my honours year here at Prince Henry's Institute. Then towards the end of my honours year I also decided to undertake my PhD at Prince Henry's. I enjoy the atmosphere, environment and reputation that Prince

Henry's offered. I found reproductive research an interesting area of study that has a large amount of research potential and ultimately could have possible clinical outcomes.

#### What do you enjoy about your research?

I really enjoy the challenge of research itself and the excitement of discovering something new. It gives me the opportunity to develop and explore new ideas, which is very motivating. Research itself is very stimulating and offers a great variety in day to day work.

#### Why did you choose to study at PHI?

I wanted to escape the comfort zone that is present on a university campus. I also looked for a project that was interesting, that offered a variety of techniques and allowed me apply the skills that I have learned in university to a research environment. What also attracted me to Prince Henry's institute was that the institute has a fantastic reputation, world-class facilities and offers variety of different research areas.

#### Describe a typical day as a student at PHI:

At Prince Henry's Institute you are involved with every aspect of your research from planning to the final result. I usually spend my day carrying out experiments, analysing data, putting together results, reading the latest literature or planning future task. There are also supervisor meetings, lab meetings, research presentations, works in progress and seminars. Every day is different!

#### Do you participate in any extracurricular activities?

One of the best things about medical research it is very flexible, it allows you to undertake your research around your extra-curricular activities. The Institute offers a variety of social functions and sporting activities. Apart from the study and research experiments, I am actively involved in social aspects that are offered at PHI.



**Kyren Lazarus** is a second year PhD student studying in the Cancer Drug Discovery Group. He is investigating the role of the nuclear hormone receptor, LHR-1 in breast cancer.

#### Why did you choose research?

Pursuing a career in research was always on my mind throughout my undergraduate studies. I got the first taste of research while completing minor research projects at university and ever since then I love the journey between hypothesis generation and result presentation. Although the journey is filled with setbacks and disappointment, the beauty of research is that there always is another way. Choosing to do my PhD in breast cancer research was based on personal reasons that I came across during my undergraduate studies. Hopefully the research undertaken will open new insights into potential novel breast cancer treatments.

#### What do you enjoy about your research?

I really enjoy the concept of researching novel ideas in order to achieve a desired outcome. I enjoy the setbacks, failures and the euphoria from producing meaningful data.

Knowing that my research is contributing to the fight against breast cancer is also very satisfying.

#### Why did you choose to study at PHI?

Prince Henry's is renowned for its research in hormone related studies and clinical trials. It is centrally located within the research hub at Clayton due to its close proximity to Monash Medical Centre and Monash University. Most of the supervisors are affiliated with Monash University, with the added advantage of no lecturing time. They are always there to support me through my PhD career.

#### Describe a typical day as a student at PHI:

Prince Henry's encourages you to organise and direct your own research, from hypothesis to planning experiments. Most days are filled with experimental work, reading up on literature or analysing data. There are also lab meetings, supervisor meetings, seminars and journal clubs. This allows you to become more familiar with the advanced literature in various fields of research. Every day is as exciting as the next and sometimes you just can't wait to get to work.

#### Do you participate in any extracurricular activities?

The beauty about medical research is its flexible working hours, which sometimes may lead to long working days. However there is always time for extracurricular activities. I workout thrice a week, play basketball twice a week, and play in the PHI netball team. I also demonstrate undergraduate labs at Swinburne University. Organising your activities around your research is the key to a successful career.

## Quick Guide to research themes and laboratories

### CANCER

- Cancer Drug Discovery
- Metabolism & Cancer
- Ovarian Cancer Biomarkers
- Bone, Joint & Cancer
- Reproductive Development
- Steroid Receptor Biology

### CARDIOVASCULAR DISEASE

- Cardiovascular Endocrinology
- Steroid Receptor Biology
- Clinical Andrology

### GENES & HEALTHY DEVELOPMENT

- Sex Determination & Gonadal Development
- Bone, Joint & Cancer
- Reproductive Development & Cancer
- Embryo Implantation
- Implantation & Placental Development
- Endometrial Remodelling
- Brain & Gender
- Growth Factor Signalling
- Clinical Andrology

### MEN'S HEALTH

- Clinical Andrology
- Male Fertility Regulation
- Brain & Gender
- Reproductive Development & Cancer

### WOMEN'S HEALTH

- Cancer Drug Discovery
- Ovarian Cancer Biomarkers
- Reproductive Hormones
- Ovarian Biology
- Implantation & Placental Development
- Endometrial Remodelling
- Embryo Implantation
- Reproductive Development & Cancer

# 3 Research Projects

## BONE, JOINT AND CANCER

### Laboratory head

Professor Matthew Gillespie PhD

### About this laboratory

Bone diseases such as osteoporosis, arthritis and most cancers of bone all result in a reduction in bone mass, that can lead to fractures. We seek to identify the pathways that are required to build bone and/or limit bone destruction, and how the cells in the bone microenvironment communicate with each other. Ultimately, we aim to identify new factors or ways to promote bone formation.

### Related to research themes

Cancer, Genes & Healthy Development, Women's Health

## Current Research

### 1. Role of osteoprotegerin in breast cancer growth.

Osteoprotegerin normally blocks bone destruction very effectively, and can be used to stop the invasion of bone by cancer cells, a common problem in breast cancer patients. However we have found that if the breast cancer cells themselves make osteoprotegerin it has intracellular actions that enhances their growth in breast and bone. We aim to identify how osteoprotegerin enhances cell growth and what role the local stromal cells play in this process.

**Supervisors:** Prof Matthew Gillespie and Dr Julian Quinn

**Contact:** matthew.gillespie@princehenrys.org

**Suitability:** Honours or PhD student

### 2. Blocking cancer and inflammation induced bone loss by inhibiting formation of the bone-destroying osteoclasts.

We have defined several factors that inhibit osteoclast formation and wish to identify their mechanism of action and their function upon other cells in bone. We are also seeking factors that block osteoclast action without interfering with new bone formation and bone repair, as most current osteoclasts do. Advances in this area are critical for finding treatment for debilitating diseases such as osteoporosis, arthritis and cancer invasion of bone that affect millions of people.

**Supervisors:** Dr Julian Quinn and Prof Matthew Gillespie

**Contact:** julian.quinn@princehenrys.org

**Suitability:** Honours or PhD student

### 3. Identifying factors that drive new bone formation.

We are seeking factors affecting osteoblast differentiation. A clue to finding such factors is the action of PTH, a hormone is currently used as a drug (by daily injection) to build new bone.

However, its effects are unpredictable and can disappear on withdrawal, so identifying how it stimulates bone formation would allow design of better therapies. We have identified several osteoblast targets of PTH action and determined their ability to influence osteoblast differentiation and maturation and are assessing these for their ability to build new bone.

**Supervisors:** Dr Vicky Kartsogiannis and Prof Matthew Gillespie

**Contact:**  
vicky.kartsogiannis@princehenrys.org

**Suitability:** Honours or PhD student

## BRAIN AND GENDER

### Laboratory heads

Dr Joohyung Lee and Prof Vincent Harley

### About this laboratory

Our laboratory uses combined biochemical, anatomical, and behavioural approaches to determine the mechanisms underlying differences in the male and female brain. There are two areas of particular interest:

- The male sex-determining gene SRY, and the role it plays in the normal and diseased male brain such as Parkinson's disease and Schizophrenia
- The genetic basis of male and female gender identity.

### Related to research themes

Genes & Healthy Development, Men's Health

## Current Research

### 4. Cognitive effects of SRY inhibition in the brain.

The male sex determination gene SRY is widely expressed in the male brain, including the substantia nigra (SN), the ventral tegmental area (VTA), and the locus coeruleus (LC). We are interested in assessing the effect of SRY knockdown in these brain regions on cognitive function. This project will provide novel insights into the molecular neurobiology of sexually dimorphic behaviours.

**Supervisors:** Dr Joohyung Lee, Prof. Vincent Harley

**Contact:**  
joohyung.lee@princehenrys.org

**Suitability:** Summer Student; Honours or PhD student

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

We are testing the novel concept that the male sex-determination gene SRY is a factor involved in the susceptibility of males to Parkinson's disease. We will address this by determining i) whether SRY levels are altered in Parkinson's disease and ii) whether inhibition of SRY function can reduce the progression of Parkinson's disease using animal models.

**Supervisors:** Dr Joohyung Lee & Prof Vincent Harley

**Contact:**  
joohyung.lee@princehenrys.org

**Suitability:** Summer Student; Honours or PhD student

### 6. Sexual dimorphism in neurological disorders.

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

**Supervisors:** Dr Joohyung Lee, Prof. Vincent Harley

**Contact:**  
joohyung.lee@princehenrys.org

**Suitability:** Summer Student; Honours or PhD student

### 7. Genetics of gender identity.

Gender identity is the gender with which a person identifies. Studies suggest that gender identity is affected by genetic, prenatal hormonal or postnatal social determinants. We are investigating the role of genes in patients with gender identity disorders. Currently we are undertaking genetic association studies of steroidogenesis genes in a large cohort of male-to-female transsexuals.

**Supervisors:** Prof. Vincent Harley

**Contact:**  
vincent.harley@princehenrys.org

**Suitability:** Summer Student; Honours or PhD student

## CANCER DRUG DISCOVERY

### Laboratory head

Colin Clyne PhD

### About this laboratory

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

### Related to research themes

Cancer, Women's Health

## Current Research

### 8. Nuclear receptor pharmacology.

Oestrogen receptor blockers are very successful breast cancer treatments; however, not all patients respond to these drugs and many that do eventually become resistant to their effects. We are identifying alternative molecules related to the oestrogen receptor that could be exploited as novel breast cancer therapeutics.

### 9. Breast-specific anti-oestrogens.

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

**Supervisors:** Dr Colin Clyne, Dr Ashwini Chand

**Contact:** colin.clyne@princehenrys.org

**Suitability:** Summer Student; Honours or PhD student

## 10. Epigenetic regulation of oestrogen production in breast cancer.

While the genetic factors that contribute to oestrogen production in the stromal compartment are fairly well understood, epigenetic changes are less well characterised. This project will aim to identify genes epigenetically regulated in the stromal compartment of the breast that contribute to oestrogen production and tumour progression.

**Supervisor:** Dr Kevin Knower

**Contact:** kevin.knower@princehenrys.org

**Suitability:** Summer Student; Honours or PhD student

## CARDIOVASCULAR ENDOCRINOLOGY

### Laboratory head

Morag Young PhD

### About this laboratory

One of our major research goals is to provide a better understanding of cardiac failure and hypertension by studying the function of the mineralocorticoid receptor (MR) in these disorders. We aim to determine the cell types in the heart in which the MR is critical for the development of heart failure and identify the ideal features of tissue-selective blockers of the receptor.

### Related to research themes

Cardiovascular Disease

## Current Research

### Cellular localisation of mineralocorticoid receptor-mediated vascular inflammation and cardiac fibrosis.

We have used the Cre-Lox technique to delete MR expression (i.e. gene knockout) in a cell-specific manner in the cardiovascular system to identify the cell types critical for the development of vascular inflammation and cardiac fibrosis. Identification of the critical cell types will allow a focused investigation of the cellular mechanisms involved in the establishment and progression of this pathology. We have shown that MR signalling in the context of high salt leads to inflammation, fibrosis and ultimately heart failure. The cardiovascular remodelling is a direct effect of MR activation in the heart and blood vessels.

Our first study in tissue-selective MR knockout mice has shown that deleting the MR gene knockout in macrophages (immune cells) prevents the development of cardiovascular disease and surprisingly hypertension as well. A current research theme is to further investigate the novel role of MR in macrophages.

There are 3 specific projects in this section and each can be tailored for an honours or PhD project.

### 11. Does tissue-selective deletion of the MR in the heart protect against heart disease?

This will involve molecular and immunohistochemical analyses of hearts, aortas and kidneys from transgenic mice generated by a specific breeding program and subject to treatment that causes heart failure. Tissue selective knockout lines currently being investigated are endothelial cell (vessel

wall)-specific, macrophage-specific and cardiomyocyte-specific knockouts.

**Supervisor:** Dr Morag Young

**Contact:** morag.young@princehenrys.org

**Suitability:** Honours or PhD student

### 12. Identification of cell signalling pathways that regulate MR activation in response to pathological stimuli.

This cell culture-based project aims to determine and characterise, in those cell types shown to be critical in the development of cardiac fibrosis, the specific MR response to inactivation of the MR-protective enzyme 11bHSD2, oxidative stress, hypoxia and high salt. These studies aim to determine the important cellular signalling pathways that are regulated by the MR and other environmental factors that lead to cardiovascular disease.

**Supervisors:** Dr Morag Young, Professor Peter Fuller

**Contact:** morag.young@princehenrys.org

**Suitability:** Honours or PhD student

### 13. The role of the molecular clock in heart failure.

A diurnal rhythm has been shown for many physiological parameters including 24hr blood pressure and heart rate variation. It is well known that certain cardiac pathologies (e.g. Heart attack) occur more often in the early hours of the morning. An intrinsic molecular clock has now been described for virtually all mammalian cells include cardiomyocytes and that this is retained in primary

cultures of cells and include Cry, Per, CLOCK, Bmal and several other factors that are regulated in a cyclical manner. Dysregulation of the molecular clock has now been described for several models of heart, kidney and metabolic disease, highlighting the importance of this relatively recently described regulatory system. Our preliminary data suggests a role for cardiomyocyte MR signalling in regulating the intrinsic molecular clock. This project will investigate pathological signalling pathways in a model of heart failure in mice in which the molecular clock is not functioning.

**Supervisors:** Dr Morag Young

**Contact:** morag.young@princehenrys.org

**Suitability:** Honours or PhD student

## EMBRYO IMPLANTATION

### Laboratory head

Eva Dimitriadis PhD

### About this laboratory

This laboratory is working toward understanding how the embryo implants and a health placenta develop. A new initiative is to develop pharmacological strategies to treat endometrial cancer and ectopic pregnancy. Further, a major focus is on producing a non-hormonal contraceptive for women. Dr Dimitriadis' laboratory is the first study world-wide to demonstrate that pharmacological inhibition of uterine factors may be useful as a new contraceptive strategy.

### Related to research themes

Cancer, Genes & Healthy Development, Women's Health

## Current Research

**14. Human maternal-foetal interactions critical for a healthy pregnancy and baby.** The failure of a human embryo to implant in an adequately prepared maternal endometrium results in infertility, while impaired implantation leads to inadequate placentation. We aim to identify the critical molecules required for the establishment of pregnancy in women. We have identified 2 novel proteins expressed by placental cells as they invade into the endometrium to establish a functional placenta. This project will determine the cellular expression and regulation of these proteins in the endometrial-placental unit. Extension of the work will determine functions for these proteins in the establishment of a healthy pregnancy.

**Supervisors:** Dr Eva Dimitriadis, Dr Ellen Menkhorst

**Contact:** evdokia.dimitriadis@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

**15. Targeting cytokines as a new treatment strategy for endometrial cancer.** Endometrial cancer is the most common gynaecological malignancy. It typically affects postmenopausal women however a significant increased risk occurs in women over 40 years old. Current treatment options for advanced disease are inadequate. We have identified proteins that may be important in disease progression and are

determining the effect of targeting these proteins with specific inhibitors as novel treatments.

**Supervisors:** Dr Eva Dimitriadis, Dr Stefan Sonderegger

**Contact:** evdokia.dimitriadis@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

**16. Investigating how the human embryo interacts with the mother to ensure pregnancy success.** If the endometrium is not adequately prepared to accept an implanting embryo then this will result in infertility. Very little is known of how the embryo interacts with the endometrium in preparation for implantation. This project will investigate how human embryo secreted factors regulate the very early stages of implantation. This is a collaborative project with Monash IVF.

**Supervisor:** Dr Eva Dimitriadis

**Contact:** evdokia.dimitriadis@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

**17. Non-invasive pharmacological treatment options to cure ectopic pregnancies.** Tubal ectopic pregnancy remains the most common cause of maternal mortality in the first trimester of pregnancy particularly in the developing world. Treatment options are limited for

ectopic pregnancies and new non-invasive treatment options are urgently required. We have identified a number of proteins that may play a pivotal role in embryo implantation in the fallopian tube and this project will investigate their role in ectopic pregnancies using *in vitro* human and *in vivo* animal models.

**Supervisor:** Dr Eva Dimitriadis

**Contact:** evdokia.dimitriadis@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

## ENDOMETRIAL REMODELLING

### Laboratory head

Professor Lois Salamonsen PhD

### About this laboratory

The lining of the uterus, the endometrium, undergoes continual remodelling throughout a woman's reproductive years. It is shed and restored during each menstrual cycle in preparation for implantation of the embryo should the cycle be one in which conception occurs.

Disturbances to this remodelling can result in abnormal uterine bleeding, in infertility, endometriosis and endometrial cancer. We seek to understand the underlying causes for these disorders with a long term view on translation of our findings to the clinic in terms of diagnosis and treatments. Our focus is on women: our access to human material enables us to perform studies of direct relevance to women's health.

### Related to research themes

Genes & Healthy Development, Women's Health

## Current Research

### 18. The proteome of uterine fluid: importance for fertility in women.

Using state of the art proteomics techniques and multiplex analyses we have identified a number of proteins in the uterine cavity throughout the menstrual cycle and in women with infertility and other endometrial disorders. Validation by Western blot and immunohistochemistry will identify the cellular sources of these proteins. Extension of the work will determine functions for uterine fluid proteins on embryo development and uterine receptivity for implantation using our established *in vitro* cell culture systems.

**Supervisors:** Prof Lois Salamonsen, Dr Tracey Edgell

**Contact:** lois.salamonsen@princehenrys.org

**Suitability:** Honours or PhD student

### 19. Endometrial repair after menstruation: implications for bleeding problems in women.

Endometrial remodelling and repair occurs rapidly after the initiation of menstruation in the absence of steroid hormone support. Using tissues from both our mouse model of menstruation and repair and human endometrial tissues, we are determining the molecular mechanisms of repair of the endometrium immediately after menstruation. In order to understand the uterine micro-environment at

the time of repair we will assess the composition of menstrual fluid and its effect on repair. We hypothesise that disturbances of repair result in abnormal uterine bleeding. Furthermore, since the endometrium uniquely repairs without scarring, these studies are expected to provide leads and possible treatments for wound healing.

**Supervisors:** Prof Lois Salamonsen, Dr Jemma Evans

**Contact:** lois.salamonsen@princehenrys.org

**Suitability:** Honours or PhD student

## 20. Defining uterine receptivity for embryo implantation.

The endometrium allows implantation of an embryo for only a few days in each menstrual cycle: if this 'receptivity' is not established the woman will be infertile. It is also a major reason for failure of IVF. Our proteomics approach is defining the receptive endometrium and identifying discriminative markers for infertility. The functions of most markers we have identified are unknown in the endometrium: this project will use our in vitro cell culture/co-culture models for receptivity to determine functions and their importance to implantation.

**Supervisors:** Prof Lois Salamonsen, Dr Tracey Edgell, Dr Jemma Evans

**Contact:** lois.salamonsen@princehenrys.org

**Suitability:** Honours or PhD student

**21. Effects of IVF on the endometrium.** During IVF, exogenous hormones are given to women to

stimulate ovarian egg production. The effects these hormones have on endometrial receptivity are largely unknown. Assessment of potential markers of endometrial receptivity in addition to hormone receptor dynamics and function in endometrium stimulated for IVF will help to understand the effects of exogenous hormones on the endometrium and may assist in modifying clinical IVF protocols.

**Supervisors:** Dr Jemma Evans, Prof Lois Salamonsen

**Contact:** lois.salamonsen@princehenrys.org

**Suitability:** Honours or PhD student

## 22. Inside – out signaling: understanding regulation of endometrial epithelial cell polarity.

Dynamic alterations in epithelial cell polarity are involved in many physiological and pathological processes. Cancers show alterations in their epithelial cell polarity leading to loss of cell-cell adhesion and increased cell motility. In wound repair, such as that observed in the uterus after menstruation, epithelial cells must form tight junctions to re-establish an intact polarized epithelial monolayer. At the time of endometrial receptivity however, the uterine epithelium must later its polarity to allow implantation of the blastocyst. The factors and mechanisms governing endometrial epithelial cell polarity are little understood and represent an exciting research area with potential to modulate post-menstrual endometrial repair and endometrial receptivity.

**Supervisors:** Dr Jemma Evans, Prof Lois Salamonsen

**Contact:** lois.salamonsen@princehenrys.org

**Suitability:** Honours or PhD student

## GROWTH FACTOR SIGNALLING

### Laboratory head

Craig Harrison PhD

### About this laboratory

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

### Related to research themes

Cancer, Genes & Healthy Development

## Current Research

### 23. Inhibin A and B in the reproductive system.

Inhibin A and inhibin B, members of the TGF $\beta$  family, are essential regulatory factors in mammalian reproduction. This program aims to determine their mechanisms of action.

**Supervisor:** Dr Craig Harrison

**Contact:** craig.harrison@princehenrys.org

**Suitability:** Honours or PhD student

### 24. TGF- $\beta$ signalling pathway disorders.

Transforming growth factor- $\beta$ 2 (TGF- $\beta$ 2), plays important roles

in diverse developmental processes. Targeted disruption of TGF- $\beta$ 2 results in perinatal lethality and a wide range of developmental defects. In this project, we are focusing on the molecular interactions that mediate the assembly, secretion, ECM localisation and activation of TGF- $\beta$ 2.

**Supervisors:** Dr Craig Harrison, Dr Kelly Walton

**Contact:** craig.harrison@princehenrys.org

**Suitability:** Honours or PhD student

### 25. Myostatin and muscular dystrophy.

The use of broad-spectrum TGF- $\beta$  antagonists will be an effective strategy for promoting muscle growth in a variety of myopathies, including Duchenne muscular dystrophy.

**Supervisor:** Dr Craig Harrison

**Contact:** craig.harrison@princehenrys.org

**Suitability:** Honours or PhD student

## IMPLANTATION & PLACENTAL DEVELOPMENT

### Laboratory head

Guiying Nie PhD

### About this laboratory

The uterus provides a "fertile soil" for the embryo to grow. We are using a number of strategies to understand what makes the uterus receptive for embryo implantation and how the uterus regulates the development of a functional placenta. A particular emphasis is in translating these research outcomes into clinically useful discoveries.

**Related to research themes**

Cancer, Cardiovascular Disease, Genes & Healthy Development, Men's Health, Women's Health

**Current Research****26. PC6 as a potential target for dual-role female contraception: simultaneously blocking embryo implantation and HIV infection.**

Protein convertases (PCs) are a family of "master switch" serine proteases essential for activating numerous protein precursors of critical importance. We have identified that one member of this family, PC6, is critical for making the uterus receptive for embryo implantation. We propose that PC6 is a novel target to develop female contraception which could also protect women from HIV infection.

This project will investigate the molecular mechanism of PC6 action during embryo implantation in mice in vivo and in cell models relevant to human implantation, and explore various ways of inhibiting PC6 to prevent embryo implantation and HIV infection.

**Supervisor:** Dr Guiying Nie

**Contact:** [guiying.nie@princehenrys.org](mailto:guiying.nie@princehenrys.org)

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

**27. Role of PC6 and PC6-regulated proteins in uterine fertility/infertility and clinical implications.**

We have identified a group of proteins which are tightly regulated by PC6 in the human endometrium. These PC6 substrates

have never been characterised in the human endometrium and their contribution to normal and abnormal endometrial function is unknown. This project will determine the expression of these proteins in normal endometrium and establish their functions in uterine fertility and infertility. This project will also explore the clinical utility of PC6 and/or PC6-regulated proteins as biomarkers.

**Supervisors:** Dr Guiying Nie, Dr Sarah Paule

**Contact:** [guiying.nie@princehenrys.org](mailto:guiying.nie@princehenrys.org)

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

**28. Proprotein convertases and gynecological cancers: mechanisms and diagnostic potential.**

Our recent studies revealed that one class of proteins that are regulated by PCs are scaffolding proteins controlling cellular cytoskeleton-membrane interaction and polarity, changes of which are fundamental to cancer. This project will establish this mechanism in endometrial and ovarian cancers. One significant challenge in the management of these cancers is to diagnose them at early stages. We will explore whether local expression and/or secretion of PCs can provide clinically useful biomarkers for an early diagnosis of these cancers.

**Supervisor:** Dr Guiying Nie

**Contact:** [guiying.nie@princehenrys.org](mailto:guiying.nie@princehenrys.org)

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

**29. Role of HtrA3 in placental development, function and pregnancy disorders.**

We have recently discovered and cloned a novel gene, HtrA3, in the mouse and human, and identified that it is a previously unrecognized factor important for placental development and function. The current projects will investigate the molecular mechanisms of HtrA3 action during placental development in mice and human, and to determine the contribution of HtrA3 dys-regulation in pregnancy disorders such as pre-eclampsia.

**Supervisors:** Dr Guiying Nie, Dr Harmeet Singh

**Contact:** [guiying.nie@princehenrys.org](mailto:guiying.nie@princehenrys.org)

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

**30. The interface between aging and cancer: the role of HtrA3.**

More than 60% of new cancers and more than 70% of cancer deaths occur in people over the age of 65 years. HtrA3 knock out mice spontaneously develop a number of cancers as they age. This project will identify the biological reasons why older mice lacking HtrA3 are prone to develop cancer, and to identify the roles of HtrA3 in cancer development and progression with aging in the human population.

**Supervisors:** Dr Guiying Nie, Dr Harmeet Singh

**Contact:** [guiying.nie@princehenrys.org](mailto:guiying.nie@princehenrys.org)

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

**MALE FERTILITY REGULATION****Laboratory head**

Peter Stanton PhD

**About this laboratory**

Our overall aim is to identify how hormones control sperm production, or spermatogenesis. We approach this problem by first identifying the key hormone-regulated cell types in the testis, and then finding the key proteins and molecules within these cells. This research is central to finding new mechanisms of contraception in men and also in understanding causes of male infertility.

**Related to research themes**

Men's Health, Growth Factor Signalling

**Current Research**

**31. Regulation of Sertoli cell junctions.** We are investigating the ways in which hormones control junctions between cells in the testis, as these are potential sites of action of male hormonal contraception. This project will investigate how members of the TGF $\beta$  superfamily secreted by germ cells can regulate Sertoli cell junctions and Sertoli cell function.

**Supervisor: Dr Peter Stanton**

**Contact:** [peter.stanton@princehenrys.org](mailto:peter.stanton@princehenrys.org)

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

**32. Regulation of sperm release.** The final process of sperm release is an ideal target for male contraception, yet the molecular mechanisms governing this process are poorly understood. Our data shows that FSH and testosterone target specific microRNAs and proteins which may be important in sperm release. This project will focus on the relationships between hormones, miRNAs and cell junctions present at sperm release.

**Supervisors:** Dr Peter Stanton, Dr Liza O'Donnell

**Contact:** peter.stanton@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

### 33. Proteomic discovery programme in male reproduction.

We aim to identify protein markers useful for prediction of male fertility. This project will compare the proteomes of human testicular interstitial fluid collected from fertile and infertile men. Techniques include protein labelling, mass spectrometry, 1D and 2D SDS PAGE, western blotting, immunohistochemistry.

**Supervisors:** Dr Peter Stanton, Dr Andrew Stephens

**Contact:** peter.stanton@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

## METABOLISM AND CANCER LABORATORY

### Laboratory heads

Professor Evan Simpson PhD & Kristy Brown PhD

### About this laboratory

Our goal is to understand how dysregulation of metabolism leads to increased risk of breast cancer and specifically the role of obesity and aging in increased breast cancer risk. We believe that this association is mediated in large part through the regulation of aromatase expression within the human breast. This effort builds on our previous work to understand the regulation of aromatase expression within the postmenopausal breast, this being the major source of oestrogen driving breast cancer development in the postmenopausal woman.

### Related to research themes

Cancer, Genes & Healthy Development, Women's Health

## Current Research

### 34. Adipokines and Aromatase.

Obesity increases the risk of breast cancer in older women. Adipokines are factors produced by the adipose tissue. The focus of this project will be to characterise the effect of adipokines on oestrogen production within the breast.

**Supervisor:** Dr Kristy Brown

**Contact:** kristy.brown@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

### 35. Dysregulated metabolism in tumour-associated adipose.

Breast adipose stromal cells adjacent to a tumour display an increased rate of proliferation and secrete factors, including oestrogens, which in turn stimulate tumour cell growth. Dysregulated metabolism is a well-characterised occurrence in fat and tumour cells. This project aims to examine whether switches in energy metabolism (Warburg effect) also occur in breast adipose stromal cells.

**Supervisor:** Dr Kristy Brown

**Contact:** kristy.brown@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

### 36. Metformin as a breast-specific inhibitor of aromatase.

Aromatase expression within the breast stroma is a key mediator of tumour cell proliferation in response to many inflammatory mediators (prostaglandins, cytokines, etc). We have identified the commonly prescribed anti-diabetic drug metformin as a potent inhibitor of aromatase expression in the breast. This project will involve further characterising the effects of metformin to inhibit aromatase in vitro and in samples from a prevention and neo-adjuvant clinical trial.

**Supervisor:** Dr Kristy Brown

**Contact:** kristy.brown@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

## OVARIAN BIOLOGY LABORATORY

### Laboratory head

Professor Jock Findlay AO PhD DSc

### About this laboratory

Female fertility and age at menopause are determined by the number and quality of oocytes stored in the ovaries. For unknown reasons, two-thirds of all oocytes die soon after they are made during ovarian development. Furthermore, a serious side effect of anti-cancer treatment in young girls and women is oocyte death resulting in infertility and early menopause.

Our laboratory is investigating the genes and pathways involved in determining whether an oocyte will live or die. This understanding will help us develop novel strategies to preserve fertility during normal aging and anti-cancer treatment.

### Related to research themes

Cancer, Genes & Healthy Development, Women's Health

## Current Research

**37.** The life and death of female germ cells. This project utilises gene-targeted mice to investigate the role of proapoptotic BH3-only proteins in mediating germ cell and oocyte death during embryonic and postnatal ovarian development. The aim of this research is to understand the factors that determine how many oocytes a female will have and to evaluate the impact of initial oocyte number on fertile lifespan and age at menopause.

**Supervisors:** Dr Karla Hutt, Dr Michelle Myers and A/Prof Jeff Kerr

**Contact:** karla.hutt@princehenrys.org

**Suitability:** Projects can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

**38. Fertility preservation during anticancer treatment.** This project investigates the mechanisms by which oocyte apoptosis is induced as a side effect of anti-cancer treatment. This research also involves examining the potential of inhibiting BH3-only protein mediated oocyte apoptosis as a means to preserve fertility during cancer therapy.

**Supervisors:** Dr Karla Hutt, Dr Michelle Myers and A/Prof Jeff Kerr

**Contact:** karla.hutt@princehenrys.org

**Suitability:** Projects can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

## OVARIAN CANCER BIOMARKERS

**Laboratory head**  
Andrew Stephens PhD

**About this laboratory**  
Our laboratory is broadly interested in the development of new diagnostic and prognostic tools for ovarian cancer management. We use proteomic technologies to isolate proteins associated with tumour formation and progression, and subsequently evaluate their diagnostic efficacy and functional relevance. Our ultimate goal is to reduce cancer mortality through regular screening and early detection.

**Related to research themes**  
Cancer, Women's Health

## Current Research

**39. Proteomic analysis of uterine secretions from cancer patients.** Proteins secreted by (or in response to) ovarian tumours are present at very low levels in circulation, making them difficult to detect by conventional means. We have established that tumour-derived proteins can be detected in uterine secretions long before they appear in circulation. This project will identify proteins present in the uterine cavity that are derived from ovarian tumours, and evaluate their potential for diagnostic or prognostic clinical use. Techniques include protein labelling, mass spectrometry, 1D and 2D SDS PAGE, western blotting, immunohistochemistry, PCR, ELISA.

**Supervisors:** Dr Andrew Stephens, Dr Adam Rainczuk

**Contact:** andrew.stephens@princehenrys.org

**Suitability:** Honours student

**40. CXC-chemokine biology in ovarian tumours.** We have identified that some CXCR3-binding chemokines, small proteins with chemotactic and angiostatic properties, are over-expressed by early-stage ovarian tumours. Evidence suggests both the presence of multiple post-translationally modified forms as well as changes in localisation of these proteins in ovarian tumours. This project will evaluate the enzymes involved in processing these proteins and whether they or their

products might be used in a diagnostic capacity to detect early-stage ovarian disease. We will also attempt to identify new binding partners of the CXC chemokines by immunoprecipitation. Techniques include imaging mass spectrometry, 1D and 2D SDS PAGE, western blotting, immunohistochemistry, immunoprecipitation, PCR, ELISA.

**Supervisor:** Dr Andrew Stephens

**Contact:** andrew.stephens@princehenrys.org

**Suitability:** Honours student

**41. Analysis of biomarkers of early stage ovarian tumours.** Proteins produced by early stage, low volume ovarian tumours make ideal candidates as markers for diagnostic use. Our ongoing work has identified several proteins that appear to be elevated in early stage tumours and may be useful in a diagnostic or prognostic capacity. This project will continue to evaluate proteins already identified for their localisation, expression and potential for diagnostic efficacy in screening for epithelial ovarian cancers. Techniques include mass spectrometry, 1D and 2D SDS PAGE, western blotting, immunohistochemistry, immunoprecipitation, PCR, ELISA.

**Supervisor:** Dr Andrew Stephens

**Contact:** andrew.stephens@princehenrys.org

**Suitability:** Honours student

## REPRODUCTIVE CANCER & DEVELOPMENT

**Laboratory head**  
Kaye Stenvers PhD

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

**Related to research themes**  
Cancer, Genes & Healthy Development, Men's Health, Women's Health

## Current Research

**42. Mechanisms of ovarian cancer metastasis.** Our current work is determining the detailed mechanisms underlying the spread of cancerous ovarian granulosa cells in order to develop new therapeutic strategies to block tumour metastasis.

**Supervisors:** Dr Maree Bilandzic, Dr Kaye Stenvers

**Contacts:** maree.bilandzic@princehenrys.org or kaye.stenvers@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

**43. Mechanisms of foetal urogenital system development.** We study genetically modified mice to determine the roles of particular genes in the formation of the foetal ovary, testis, and kidney. Information gained from these studies is integral to the development

of better therapies and treatments for reproductive tract.

**Supervisors:** Dr Mai Sarraj, Dr Kaye Stenvers

**Contacts:** kaye.stenvers@princehenrys.org or mai.sarraj@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

## SEX DETERMINATION & GONADAL DEVELOPMENT

### Laboratory head

Professor Vincent Harley PhD

### About this laboratory

Disorders of sex development (DSDs), formerly intersex, are congenital conditions where development of chromosomal, gonadal, or anatomical sex is atypical. Our aim is to identify genes causing DSDs, and the molecular mechanisms underlying testis and ovary formation in the embryo. Approaches include human genetics, molecular, cell and developmental biology.

### Related to research themes

Genes & Healthy Development

## Current Research

**44. ATR-x syndrome & gonadal development.** The ATR-X syndrome, an X-linked recessive developmental disorder affecting males, belongs to a growing list of disorders of sex development (DSD) which affect 1% of all newborns. Clinical features

include mental retardation, alpha-thalassaemia and skeletal and genital abnormalities. The focus of our work is to investigate the role of ATRX in gonadal development.

**Supervisors: Prof Vincent Harley, Dr Anthony Argentaro, Dr Stefan Bagheri-Fam**

**Contacts:** vincent.harley@princehenrys.org or anthony.argentaro@princehenrys.org

**Suitability:** Honours or PhD student

**45. Genetic mechanisms underlying hypospadias.** Hypospadias is one of the most common birth defects in humans affecting 1 in 250 boys in which the opening of the urethra is not at the end of the penis but along the shaft. We are exploring the genetic mechanisms underlying hypospadias by the generation of mouse models.

**Supervisors:** Prof Vincent Harley, Dr Anthony Argentaro, Dr Stefan Bagheri-Fam

**Contacts:** vincent.harley@princehenrys.org or anthony.argentaro@princehenrys.org

**Suitability:** Honours or PhD student

**46. Identification of novel genes required for gonadal development.** Our aim is to identify the underlying molecular and cellular events that cause human disorders of sexual development.

As one approach, we are undertaking an ENU mutagenesis screen to identify novel genes involved in gonad development. We have identified several mutant strains affecting testis

development which are currently under investigation.

**Supervisors:** Prof Vincent Harley, Dr Stefan Bagheri-Fam

**Contacts:** vincent.harley@princehenrys.org stefan.bagheri-fam@princehenrys.org

**Suitability:** Honours student

**47. Discovering new genes responsible for disorders of sex development.** Our project aims to identify new genetics factors involved in rare disorders of human gonadal development using Array Comparative Genomic Hybridization (CGH).

**Supervisors:** Prof Vincent Harley, Dr Pascal Bernard

**Contacts:** vincent.harley@princehenrys.org pascal.bernard@princehenrys.org

**Suitability:** Honours or PhD student

**48. Wnt/beta-catenin, SOX signaling & sex determination.** While male and female gonadal development have been considered as independent, sex determination is regulated by opposing signals, (XY) tipped toward maleness by the presence of SRY. In females R-Spondin 1 (a Wnt agonist) is the earliest driving force. Using cell and molecular biology techniques, this project aims to understand the mechanisms of action of these two opposing pathways.

**Supervisors:** Prof Vincent Harley, Dr Pascal Bernard

### Contacts:

vincent.harley@princehenrys.org  
pascal.bernard@princehenrys.org

**Suitability:** Honours or PhD student

**49. Functional characterisation of the chromatin-remodelling protein, ATRx.** The ATR-X syndrome is a severe developmental disorder resulting in a mental retardation, characteristic facial and skeletal abnormalities, alpha thalassaemia and urogenital abnormalities. The ATRX protein comprises two highly conserved domains; an N-terminal PHD-like domain and a C-terminal helicase-like domain which shares homology to the SNF2 family of chromatin remodelling proteins. The functional importance of these domains is highlighted by the fact that the majority of the clinical mutations are located within these domains. Mutations which arise in a third domain located in the extreme C-terminus almost always result in complete XY sex reversal in patients suggesting that this region plays an important role in urogenital development.

This project will focus on identifying and characterising proteins which interact with the C-terminal domain of the ATRX protein which will elucidate the functional role of ATRX in urogenital development.

**Supervisors:** Dr Anthony Argentaro, Prof Vincent Harley

### Contact:

vincent.harley@princehenrys.org  
anthony.argentaro@princehenrys.org

**Suitability:** Honours or PhD student

### 50. The genetics of gender

**identity.** Transsexualism is a medical condition where individuals of one sex identify as the other. Studies found increased responses to androgen in the hypothalamus in male-to-female transsexuals, implicating that transsexuality may be associated with sex-atypical physiological responses in specific brain circuits. We have completed a genetic study investigating SNP polymorphisms in three genes - androgen receptor, oestrogen receptor beta, and aromatase - and their profiles in pre-and post-operative male-to-female transsexuals. We observed a small, but significant difference in a CAG repeat length polymorphism in the AR gene. Future studies aim to expand the sample sizes and number of genes to be tested.

**Supervisor:** Prof Vincent Harley

**Contact:** vincent.harley@princehenrys.org

**Suitability:** Honours or PhD student

### 51. The molecular genetic pathways in human sex determination.

Intersex disorders are surprisingly common with estimates as high as 1% of all live births. These disorders usually result in infertility, genital abnormalities, gender misassignment and long-term psychological trauma. The cause of these problems is the failure of the network of gene regulation that is responsible for the proper development of testes or ovaries in the embryo.

This project aims at understanding how the key sex-determining transcription factors, SRY, SF1 and SOX9, regulate target genes required for the development of testes, and

how mutations in these genes lead to aberrant sexual development in humans.

**Supervisor:** Prof Vincent Harley

**Contact:** vincent.harley@princehenrys.org

**Suitability:** Honours or PhD student

## STEROID RECEPTOR BIOLOGY

### Laboratory head

Professor Peter Fuller MBBS, PhD, FRACP

### About this laboratory

The group is currently focussed on two principle themes that of the mechanism of action of the adrenal steroid hormone aldosterone, and the molecular pathogenesis of granulosa cell tumours of the ovary. The laboratory uses the techniques of molecular biology and mouse genetics to address these topics.

### Related to research themes

Cancer, Cardiovascular Disease

## Current Research

### 52. Structure - function relationships of the mineralcorticoid receptor.

The mineralcorticoid receptor (MR) is an important therapeutic target in cardiovascular disease. We have identified interactions of the receptor that differ between the physiological hormones, aldosterone and cortisol. Understanding these interactions and their structural basis will lead to the development of new therapeutic agents. The studies involve the use of

yeast-2-hybrid screens, transactivation assays, structural analysis, mutation detection and transgenic mouse models.

**Supervisor:** Professor Peter Fuller

**Contact:** peter.fuller@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

### 53. Mineralcorticoid receptor regulation of gene expression.

The mineralcorticoid receptor (MR) principally acts by regulating the expression on its target genes. We have identified a number of genes that are directly regulated by the MR and are seeking to understand the mechanism of that regulation *in vitro* and *in vivo*.

**Supervisor:** Professor Peter Fuller

**Contact:** peter.fuller@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

### 54. Molecular pathogenesis of granulosa cell tumours of the ovary.

Granulosa cell tumours (GCT) of the ovary are endocrine tumours that both make hormones and respond to hormones. The group seeks to understand the molecular events that lead to the development of the tumours. Areas of current focus include the role of nuclear receptors including Estrogen Receptor- $\beta$  (ER $\beta$ ), the significance of the activation of the NF- $\kappa$ B pathway observed in two GCT derived cell lines, the exploration of novel therapeutic strategies and the use of microarray analysis to identify paths and profiles of gene expression.

**Supervisors:** Prof Peter Fuller, Dr Simon Chu

**Contact:** peter.fuller@princehenrys.org or simon.chu@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

### 55. Hormonal regulation of folliculogenesis.

Our current work is determining the detailed mechanisms of how hormones and local ovarian factors interact to regulate ovulation. Our goal is to elucidate the local control of ovarian follicular development in order to obtain a better understanding of, and treatments for, infertility, premature menopause and ovarian cancer.

**Supervisor:** Dr Ann Drummond

**Contact:** ann.drummond@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

### 56. Role of ER $\beta$ in folliculogenesis.

It is our hypothesis that oestrogen action, via ER $\beta$ , limits GC proliferation by opposing pro-proliferative, anti-apoptotic signals such as the NF- $\kappa$ B pathway and by promoting their differentiation into luteal cells. Thus activation of ER $\beta$  may contribute to the selection of the dominant follicle and/or recruit follicles to enter the FSH-dependent differentiation phase. We plan to identify genes and proteins specifically activated by ER $\beta$  and elucidate their biological role in ovarian function.

**Supervisors:** Dr Ann Drummond, Dr Simon Chu

**Contact:** ann.drummond@princehenrys.org or Simon.chu@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

### 57. Ovarian phenotype of the IKK $\beta$ conditional knockout mouse.

These studies will investigate the importance of the NF- $\kappa$ B signalling pathway to ovarian function. By deleting IKK $\beta$  from the ovarian cells of mice we prevent activation of the NF- $\kappa$ B signalling pathway. These conditional knockout mice are a unique model now established in the laboratory. Histological analyses of ovaries at different stages of development, serum hormone analyses and gene expression studies will be undertaken to characterise their novel ovarian phenotype. We expect these studies to yield novel data regarding ovarian function.

**Supervisor:** Dr Ann Drummond

**Contact:** ann.drummond@princehenrys.org

**Suitability:** Project can be tailored to suit student (Vacation Scholar, EPRD, Honours, PhD)

# 4 Scholarships

## PHI Scholarships

Initial enquiries to study at Prince Henry's Institute of Medical Research should be directed to the relevant research project supervisor, or research group leader. This handbook summarises each research project and includes contact details for the relevant supervisor.

### Application forms

Application forms can be found on our website at:

[www.princehenrys.org/students](http://www.princehenrys.org/students)

### Vacation scholarships

Vacation scholarships are available for students to carry out a research project at the institute over the summer vacation. The scholarship provides a stipend for up to 6 weeks at \$250.00 per week. Applications close on October 16.

### Graduate Excellence Awards

These scholarships are available to students newly arrived at PHI and who have recently enrolled in a postgraduate research degree (typically a PhD).

PHI Graduate Excellence scholars receive additional support on top of an existing scholarship stipend (at APA level).

Please visit the Graduate Excellence Awards on our website for more information. Applications close October 14.

## Other Postgraduate Scholarships

From time to time special scholarships are also available through Prince Henry's Institute. Up to date information about these can be obtained only by direct contact with the Director of the Institute.

For information relating the following scholarships please go to our website.

### Australian Postgraduate Award (APA)

This scholarship is awarded through Monash University and is awarded for a period of 3 years.

For study at Prince Henry's Institute, the application must be filled out in consultation with a Prince Henry's Institute supervisor. Overseas students are not eligible. Applications close October 31.

### Monash Graduate Scholarship (MGS)

This scholarship is awarded through Monash University for a period of 3 years. For study at Prince Henry's Institute,

the application must be filled out in consultation with a Prince Henry's Institute supervisor. Overseas students are eligible. Applications close October 31.

### **Cancer Council of Victoria Postgraduate Scholarship**

Prince Henry's Institute is an approved institution to carry out a project in a cancer related area under the Anti Cancer Council of Victoria Scheme. Applications usually close in early November. Contact the Cancer Council for the current closing date for applications.

## **Further Study options**

### **Education Program in Reproduction and Development (EPRD)**

The Education Program in Reproduction and Development (EPRD) aims to foster education and research into reproductive biology, embryology and developmental biology for domestic and international postgraduate students.

The EPRD program is located in the Department of Obstetrics and Gynaecology in the Southern Clinical School on Level 5 in Monash Medical Centre. The program is a joint venture between the Monash University Department of Obstetrics and Gynaecology and Prince Henry's Institute in association with the The Ritchie Centre, Monash University Departments of Physiology, Pharmacology, Paediatrics and Anatomy & Cell Biology and the Monash Institute of Medical Research (MIMR). The program has a close relationship with Monash IVF and is

supported in its teaching and research activities by staff from Melbourne IVF, the University of Melbourne, Victorian Assisted Reproductive Treatment Authority, Family Planning Victoria, and many IVF centres around Australia and New Zealand

The Graduate Diploma & Master of Reproductive Sciences and the Master of Clinical Embryology are run by the EPRD through the Department of Obstetrics and Gynaecology. EPRD courses attracted enrolments from 52 students, including 24 international students in 2011.

PHI plays a key role in the coordination and teaching of the EPRD program and helps to promote its activities. Many of the Institute's scientists assist in the development of course units, lecturing, facilitate practical sessions, unit assessment activities and supervising students in minor research projects for the Graduate Diploma in Reproductive Sciences.

PHI researchers also supervise students undertaking research projects in the Master of Reproductive Sciences.

For more information on courses and open days contact Penny Chen (EPRD Administrator) on +61 3 9902 4772, +61 3 9594 7462 or +61 3 9594 7100, email penny.chen@monash .edu or eprd@monash.edu, or visit the EPRD website at [www.med.monash.edu.au/eprd](http://www.med.monash.edu.au/eprd).



