Centre for Reproductive Health

Student Research Projects 2019
The Translational Research Facility is connected via a link bridge to Monash Health, and provides a crucial link between our scientific discoveries and medical treatments. The facility houses nine world-leading technology platforms and an eight-bed, 21-chair Clinical Trials Centre supporting the transition of discoveries from initial Phase I testing through to Phase IV primary health trials.
About Hudson Institute

Hudson Institute specialises in discoveries in three areas of medical need
- Cancer
- Inflammation
- Reproduction and development

Our 478 scientists and students focus on laboratory discovery science, plus translational research – taking discoveries to patients and industry for real world impact.

Students at a glance 2017

- 290 Staff
- 188 Students
- 55 Research Groups
- 309 Research Publications

2017

We educate and train more than 180 students through our academic affiliation with Monash University. Our postgraduate training is predominantly through the School of Clinical Sciences at Monash Health, part of the Faculty of Medicine, Nursing and Health Sciences at Monash University.

Our students
- Get exposure to university, institute and hospital research
- Attend national and international conferences
- Publish their research (50 student first author publications in 2017)
- Are mentored by leading supervisors and their teams
- Regularly win prestigious prizes and awards
- Have continuous opportunities for networking, learning and development

All work and no play...

Hudson Institute is not all about work. Our students are encouraged to join in a range of student networking and social events organised by the Hudson Institute Student Society (HISS).

Our Precinct

Hudson Institute is a partner in the Monash Health Translation Precinct (MHTP), a major medical and scientific research hub at Monash Medical Centre in Clayton.

Our location at Monash Medical Centre means our research is informed by patient need and our discoveries are rapidly transitioned into practical treatments.

With our precinct partners, Monash University and Monash Health, our site brings together world-leading scientists, clinicians and educators to collaborate on innovative discoveries that advance human health.

Our Transitional Research Facility (TRF) is connected to Monash Health via a walkway and provides a crucial link between our scientific discoveries and medical treatments.

The facility houses laboratories alongside nine state of the art technology platforms and an eight-bed, 21-chair Clinical Trials Centre supporting the transition of discoveries from initial Phase I testing to Phase IV primary health trials.
Reproductive health is a key global challenge that affects every individual, as it both reflects and determines the health of present and future generations. Recent breakthroughs in our discipline have provided unequivocal proof that an individual’s lifelong health is determined by events which occurred prior to their conception; their effects are transmitted by both mother and father via the placenta, oocyte and sperm. Using basic and translational science, Reproductive Health and Biology researchers are making discoveries about sperm and egg development, formation of the embryo and its implantation into the womb, formation of the placenta and its impact on fetal development. We study how each of these affects human development and health, and use animal and cell culture models to reveal the cellular, molecular and biochemical mechanisms involved. With an increasing number of couples seeking the use of assisted reproductive technologies and the rapidly increasing world population, new approaches are needed in the field of fertility research. Advances in reproductive sciences translate to allied fields: cancer biology, animal food production, and conservation of endangered species. In addition, proteins involved in the regulation of reproduction have wider actions, influencing inflammation and tissue repair in a variety of organs. Due to our focus on clinical problems, we expect our studies to lead to new approaches for improved diagnosis, prevention or treatment of disease.
Uterine and Placental Biology

Research group: Embryo Implantation

Project: Embryo non-coding RNAs required for IVF success

**Suitability:** Honours, PhD/Doctorate  
**Project leader:** Prof Eva Dimitriadis  
**e:** evdokia.dimitriadis@hudson.org.au

**Project description:** This project will investigate epigenetic biomarkers of embryo development. It will utilise techniques including cell culture, in vivo animal and human models and functional assays.

**Keywords:** embryos, implantation, infertility, IVF, biomarkers, microRNA

Project: Is IVF associated with pregnancy complications and how can we prevent them?

**Suitability:** Honours, PhD/Doctorate  
**Project leader:** Prof Eva Dimitriadis  
**e:** evdokia.dimitriadis@hudson.org.au

**Project description:** We have identified epigenetic mechanisms by which human embryos may regulate their fate to implant. This project will investigate the effect on these factors on facilitating embryo development and implantation into the uterus. It will use innovative cell culture models and in vivo mouse models to determine the function of the epigenetic regulators we identified. This work has the potential to be used as a treatment to facilitate implantation in women with implantation failure associated infertility, or the development of biomarkers of an uncomplicated pregnancy.

**Keywords:** human embryos, IVF, infertility

Project: Nanoparticles targeting the uterus and placenta to treat infertility and preeclampsia

**Suitability:** Honours, PhD/Doctorate  
**Project leader:** Prof Eva Dimitriadis  
**e:** evdokia.dimitriadis@hudson.org.au

**Project description:** The World Health Organisation has reported that infertility is the third most severe disease worldwide. We have identified factors that may be targeted to treat infertility and pregnancy disorders including preeclampsia and intrauterine growth restriction. This project will investigate specific targeting of the uterus and placenta to treat these disorders and investigate whether potential off target effects can be eliminated. The project will investigate sustained release of the agents using FDA approved nanoparticles and nano fibres both in vitro using cell culture. In addition, it will investigate the use of nanoparticle delivery of agents to target the uterus to treat or prevent infertility and diseases associated with abnormal placentaion such as preeclampsia.

**Keywords:** infertility, treatments, preeclampsia, placenta, IVF, female fertility, clinical

Project: Secreted microRNA as biomarkers of preeclampsia, miscarriage and infertility

**Suitability:** Honours, PhD/Doctorate  
**Project leader:** Prof Eva Dimitriadis  
**e:** evdokia.dimitriadis@hudson.org.au

**Project description:** This project will use gene arrays to investigate biomarkers in human serum and tissue to determine the use of microRNA as predictive biomarkers of preeclampsia and infertility. It will also investigate the function of identified secreted microRNA on placental function to determine their utility as treatment targets. The methods are already established in our laboratory. The candidate will use both primary cell culture and culture of cell lines to undertake functional studies. The will also undertake array analysis using a number of different platforms.

**Keywords:** preeclampsia, clinical biomarkers, microRNA, epigenetic, miscarriage, infertility, non-coding RNA, biomarkers
Research group: Implantation and Placental Development

Project: Blood vessel endothelial aging and pregnancy disease preeclampsia

Suitability: Honours, Masters by Research, PhD/Doctorate
Project leader: Prof Guiying Nie
e: guiying.nie@hudson.org.au

Project description: Preeclampsia is a life-threatening disorder of pregnancy, characterized by a sudden increase in blood pressure and urine protein after 20 weeks of gestation in previously normotensive women. Preeclampsia is a medical emergency as it can progress to multi-organ failure. One key characteristic of preeclampsia is widespread and systemic blood vessel endothelial dysfunction. Abnormal release of placental factors into the maternal circulation is known to cause endothelial injury in preeclampsia. Our current studies strongly suggest that preeclamptic placentas also release factors that cause premature aging of endothelial cells. Furthermore, these factors may prevent endothelial progenitor cells from repairing the injured/aging endothelial cells. This project will explore these new concepts to investigate endothelial homeostasis in preeclampsia. This study will provide crucial knowledge in the understanding of preeclampsia and shed new light on developing novel treatment for this disorder.

Keywords: pregnancy, women's health, placenta, preeclampsia, aging, blood vessel, endothelial cells

Project: Molecular understanding of placental development and preeclampsia

Suitability: Honours, Masters by Research, PhD/Doctorate
Project leader: Prof Guiying Nie
e: guiying.nie@hudson.org.au

Project description: Preeclampsia is a life-threatening disorder of pregnancy that is characterised by a sudden increase in blood pressure and urine protein after 20 weeks of gestation in previously normotensive women. Preeclampsia is a medical emergency as it can progress to multi-organ disorder associated with renal failure, seizures and stroke. Currently the only effective “cure” for this condition is to deliver the baby prematurely to save the mother's life. Although causes of preeclampsia are multi-factorial, it is well established that the placenta is sufficient and necessary to cause preeclampsia. It is also emerging that placental stress contributes to preeclampsia development. This project will investigate a placenta-specific enzyme in placental development, placental stress and preeclampsia. It will use a number of approaches including the latest molecular biology technologies and unique cell models. The long-term goal is to develop novel early diagnosis and personalized treatment of preeclampsia.

Keywords: placenta, pregnancy, placental stress, preeclampsia

Project: Uterine surface remodeling for embryo implantation and IVF success

Suitability: Honours, Masters by Research, PhD/Doctorate
Project leader: Prof Guiying Nie
e: guiying.nie@hudson.org.au

Project description: Embryo implantation is a critical step in establishing pregnancy, and implantation failure is a bottleneck in IVF treatment to overcome infertility. The uterus acts as “fertile soil” for the embryo to implant and grow. However, for implantation to succeed, the uterus must remodel substantially to become “receptive”, as the surface of the uterus is normally non-receptive to embryo attachment. Defective uterine receptivity is a major cause of implantation failure in IVF treatment. We study the mechanisms that govern uterine remodelling for embryo implantation. This project will investigate a group of cell-surface proteins that are pivotal for uterine receptivity and IVF success. The study will use a number of approaches including the latest molecular biology technologies, cell culture, unique embryo implantation models and clinical samples. The goal is to establish the functional importance of these proteins in uterine receptivity and their clinical utility in IVF treatment.

Keywords: uterus, embryo implantation, fertility, infertility, IVF

Research group: Endometrial Remodelling

Project: CSF3 role in fertility and pregnancy

Suitability: PhD/Doctorate, Masters by Research, Honours, BMedSci (Hons), Short projects
Project leader: Dr Tracey Edgell
e: tracey.edgell@hudson.org.au

Project description: We have identified changes in CSF3 concentrations within the uterus are related to infertility and pregnancy loss. This project aims to understand how CSF3 influences the interaction of endometrium and embryo, identifying changes in inflammatory, angiogenic and immunological profile elicited by elevated CSF3.

Keywords: CSF3, endometrium, embryo

Project: Endometrial proliferative phase as a determinant of embryo
implantation

Suitability: PhD/Doctorate, Masters by Research, Honours, BMedSci (Hons)
Project leader: Dr Tracey Edgell
e: tracey.edgell@hudson.org.au
Project description: This project builds on our earlier studies to identify changes, associated with unexplained infertility, in cytokine/chemokine and proteome of the endometrium during the proliferative phase. This project will examine the identified factors for their influence on known factors involved in the later secretory phase of the menstrual cycle when embryo implantation occurs. This project will further refine and use our developed 3D model of endometrial gland formation.
Keywords: endometrium, proliferative phase, embryo implantation

Research Group: RNA Biology in Health and Disease
Project: How platelets are produced to maintain haemostasis throughout life

Suitability: Honours, PhD/Doctorate
Project leader: Dr Minna-Liisa Anko
e: Minni.Anko@monash.edu
Project description: Platelets are an essential component of the haemostatic system and low platelet counts are harmful, more so in situations such as pregnancy where platelets conduct important functions supporting the developing embryo and the mother. Platelets are produced by specialised cells called megakaryocytes that undergo a complex differentiation and maturation before they are capable of releasing platelets into blood circulation. We have identified a novel regulator of megakaryocyte maturation which is an RNA binding protein and essential for the production of platelets. This project investigates the underlying mechanisms of megakaryocyte maturation, in particular the role of RNA processing that we have discovered plays a novel and crucial role in providing the body with sufficient amount of platelets.
Keywords: platelet, cell differentiation, RNA biology, maternal and embryonic health

Project: Tapping the power of pluripotency: The role of HMGA1 in stem cell self-renewal and cell fate transitions

Suitability: Honours, PhD/Doctorate
Project leader: Dr Minna-Liisa Anko
Project description: Embryonic stem cells are pluripotent stem cells derived from an early-stage pre-implantation embryo. They provide an excellent model to investigate the events taking place during early development. Pluripotent stem cells also hold almost limitless potential to improve cell replacement therapies and regenerative medicine. However, if we are to reliably and safely generate and utilise these cells, we must first gain a comprehensive understanding of their pluripotency or ‘stemness’. We have found that one key player in RNA control of pluripotent cells could be HMGA1, a known DNA binding protein and central molecular switch required for stem-cell-like states during normal but also in malignant transformation. This project investigates HMGA1’s RNA binding properties in pluripotent stem cells and address how the HMGA1-RNA interaction supports self-renewal and cell fate transitions. Uncovering HMGA1 functions will help understanding early development but could also help the design of highly specific HMGA1 inhibitors or activators, with broad applicability in fields ranging from regenerative medicine to cancer therapeutics.
Keywords: early development, stem cell biology, RNA, cell fate
Male Reproductive Biology

Research group: Testis Development and Germ Cell Biology

Project: Growth factor signalling and pathway crosstalk in testis development and disease

Suitability: PhD/Doctorate, Masters by Research, Honours
Project leader: Prof Kate Loveland
e: kate.loveland@hudson.org.au

Project description: Signalling through many distinct pathways drive normal testis development and are essential for normal fertility in males. Research projects are available examining the functions of activins, Wnts, Snail transcription factors and importin proteins, each using mouse models and human clinical materials. These projects examine how communication between the germ cells and their supporting somatic cells mediates normal spermatogenic progression (focussing on spermatogonial stem cells) and study how these signalling pathways may contribute to testicular cancer and infertility. Our culture models allow us to reveal how crosstalk between different signalling pathways governs the cellular processes that underpin fertility.

Keywords: cell signalling, spermatogenesis, nucleocytoplasmic transport, cell differentiation

Project: The contribution of TGFbeta superfamily signalling crosstalk to male fertility

Suitability: PhD/Doctorate, Masters by Research, Honours
Project leader: Prof Kate Loveland
e: kate.loveland@hudson.org.au

Project description: Mammalian spermatogenesis involves the differentiation of sperm precursor cells from a diploid, stem cell state, through a progressive series of developmental stages involving mitosis, meiosis and haploid germ cell differentiation. These processes require the correct and timely cues provided by testicular somatic cells, mediated by growth factors, hormones and cytokines. This project is focused on gaining knowledge of how proteins in the Transforming Growth Factor-beta (TGFb) superfamily interact to control the development of sperm within the complex milieu of the testes. Published studies by our lab, and by others, have defined key stages at which specific TGFbeta superfamily ligands perform crucial signalling roles.

To understand its relevance to male fertility and how disruptions to this pathway can lead to male infertility, we undertake cellular and biochemical analyses using primary organ cultures of testes (in which the cellular communication processes are intact). This work also uses cell lines and isolated cells, to directly interrogate signalling crosstalk between members of this complex family which shares receptors, ligands, inhibitors and transcription factors is coordinated to achieve normal and pathological outcomes. Their potential to interact with immune cells is also considered as part of the normal environment of the testis that is required to sustain fertility.

Keywords: male fertility, infertility, cell signalling, TGFbeta biology, immunology

Research group: Endocrinology and Immunophysiology

Project: Discovering therapies to prevent inflammatory diseases of the male reproductive tract and infertility

Suitability: Honours, Masters by Research, PhD/Doctorate
Project leader: Prof Mark Hedger
e: mark.hedger@hudson.org.au

Project description: Inflammation in the testis and epididymis can impair male fertility, and epididymal obstruction is a major cause of infertility following infection and inflammation of the male tract. Activin has both proinflammatory and immunoregulatory functions, but until now, the role of activin in testicular and epididymal inflammation has been very poorly investigated. This project examines activin and its binding protein, follistatin in regulating inflammation and fibrosis caused by infection and autoimmunity in the male tract. These studies will also assess the potential for exogenous follistatin to serve as a therapeutic intervention for these conditions. Students undertaking this project at postgraduate level may also have the opportunity to undertake 6 – 12 months collaborative research at the Justus Liebig University in Giessen, Germany, with the option of studying for a joint degree award from both Universities.

Keywords: inflammation, men's health, infertility, testis, epididymis, immunoregulation

Project: Exploring the functional regulation of the male reproductive tract in health and disease

Suitability: Honours, Masters by Research, PhD/Doctorate
Project leader: Prof Mark Hedger
e: mark.hedger@hudson.org.au

Project description: Disorders of the epididymis and vas deferens contribute to infertility, recurrent
infections, chronic inflammation and pain. Evidence suggests that interactions between the inflammatory cytokine, activin and its binding protein, follistatin, play fundamental roles in creating the unique functions of the epididymis and vas, and that defects in activin-follistatin interactions underlie disease in these tissues. In this project, the student will investigate activin and its regulation by follistatin in control of the development and mature functions of the epididymis and vas deferens. This project could also include studies of the role of activin in controlling inflammation and immunity in the male tract. Students undertaking this project at postgraduate level may also have the opportunity to undertake 6 – 12 months collaborative research at the Justus Liebig University in Giessen, Germany, with the option of studying for a joint degree award from both Universities.

**Keywords:** inflammation, men's health, fertility, chronic pain, epididymis

**Project: Uncovering the novel phenotype of macrophages in the testis**

**Suitability:** Honours, Masters by Research, PhD/Doctorate

**Project leader:** Prof Mark Hedger  
**e:** mark.hedger@hudson.org.au

**Project description:** Mouse testicular macrophages have several unique functional properties associated with testicular immune privilege. These cells have an alternatively activated phenotype that creates an environment whereby cell-mediated immune responses are tightly controlled. The intratesticular mechanisms responsible for directing the maturation of the testicular macrophages, and their functional consequences need to be investigated. In this project, monocytes isolated from blood will be matured in culture in the presence of putative testicular macrophage-regulating factors, such as activin and testosterone, in order to understand the relative importance of the testicular environment in creating the unique testicular macrophage phenotype. Students undertaking this project at postgraduate level may also have the opportunity to undertake 6-12 months collaborative research at the Justus Liebig University in Giessen, Germany, with the option of studying for a joint degree award from both Universities.

**Keywords:** inflammation, men's health, fertility, testis, immunoregulation, macrophages

**Research group: Germ Cell Development and Epigenetics**

**Project: Defining the epigenetic origins of maternally inherited disease**

**Suitability:** Honours, PhD/Doctorate

**Project leader:** Dr Patrick Western  
**e:** patrick.western@hudson.org.au

**Project description:** The notion that non-genetic factors in oocytes (eggs) and sperm can alter development and postnatal health in offspring is gaining traction with our increased understanding of epigenetic programming in male and female germ cells. Epigenetics provides an interface between the environment and DNA function through the ability of epigenetic modifications to regulate gene expression. Primary epigenetic modifications involve methylation of the DNA or chemical modifications, such as methylation, acetylation, phosphorylation, of the histones that facilitate DNA organisation and packaging. These modifications regulate the combination of genes that are switched on or off in a cell, and can provide a “long-term memory” of the transcriptional state for that cell and its progeny, substantially contributing to the maintenance of the cell’s specialized function. Epigenetic modifiers have been widely studied in somatic tissues, but their roles in the germline are poorly understood. Germ cells are unique in that they undergo the most extensive epigenetic reprogramming of any in vivo cell type, a process that ultimately results in establishment of specialized epigenetic information in oocytes and sperm. Some of this information is transmitted via the oocyte and sperm to the next generation, and disruption of this inherited epigenetic information can lead to developmental defects and disease in offspring. The Germ Cell Development and Epigenetics group aims to understand how epigenetic modifiers acting in germ cells, alter development and health in offspring. One such modifier is EED which establishes methylation on lysine 27 in histone 3 (H3K27me3), thereby repressing gene expression (turning genes off) in animal cells, including in humans. To understand the role of EED in epigenetic programming of oocytes and in inheritance, we developed a model for deleting Eed only from growing oocytes in mice. This model provides a unique opportunity to study epigenetic inheritance in genetically identical offspring in the absence of maternally contributed confounding factors. Our studies demonstrate that EED-mediated epigenetic programming in oocytes is important for offspring development, but the mechanisms remain unclear. This project will examine: (i) how the loss of EED activity impacts on gene transcription and programming in oocytes, and (ii) how EED-mediated programming in oocytes affects development and postnatal health in offspring, with focusses on preimplantation development, skeletal development, neural development and behaviour. This research will involve application of genome-wide RNA sequencing, immunofluorescence and confocal imaging and a range of molecular and cell biological approaches. The project will also provide extensive opportunities for student collaboration with experts in preimplantation development, brain development and behaviour/psychology and skeletal growth and development. Determining how epigenetic programming in oocytes and sperm regulates outcomes offspring is highly topical and of direct...
relevance to understanding the impacts of environmental impacts, such as drugs, diet and toxins, on health and developmental outcomes in humans.

**Keywords:** epigenetics, germ cells, inherited disease, development, ovary

**Project: Signalling in male germ cell development, pluripotency and germ cell tumour formation**

**Suitability:** Honours
**Project leader:** Dr Patrick Western  
e: patrick.western@hudson.org.au

**Project description:** Germ cells are specialised cells found in the developing testes and ovaries that form sperm in males, or oocytes (eggs) in females. Germ cell development underpins reproductive health and fertility throughout an individual’s life, while sperm and oocytes transmit the parent’s genetic and epigenetic information to the offspring. Germ cells therefore play multiple central roles in biology of the individual and the species. This project aims to determine the role of signalling in male germ cell development, stem cell pluripotency and germ cell tumour formation (testis tumours). Inhibitors that block specific signalling pathways will be used in vivo and in an ex-vivo organ culture system to determine the role of specific signalling pathways in male germ cell differentiation, pluripotency and germ cell tumorigenesis. By exploring germ-line development and the establishment and function of epigenetic information in the germ line, our research will contribute to understanding human disease, including various cancers and the development of novel drugs targeting epigenetic processes.

**Keywords:** germ cell, pluripotency

**Research group: Male Fertility Regulation**

**Project: Developing better tests and treatment for male infertility**

**Suitability:** Honours, PhD/Doctorate
**Project leader:** Dr Peter Stanton  
e: peter.stanton@hudson.org.au

**Project description:** Infertility affects 1 in 20 men, but in most cases there are no known molecular reasons why spermatogenesis has failed. We found that the fluid which surrounds testicular tubules where sperm are made contains numerous proteins which could be important in their production. Hence, the aim of this project will be to use proteomics to identify protein markers useful for the prediction of male fertility. Methods include ELISA, SDS PAGE, western blotting, immunohistochemistry, mass spectrometry, cell culture.

**Keywords:** infertility, spermatogenesis

**Project: How does activin regulate adult testis function?**

**Suitability:** Honours, Masters by Research, PhD/Doctorate
**Project leader:** Dr Peter Stanton  
e: peter.stanton@hudson.org.au

**Project description:** Mature, differentiated Sertoli cells are essential for spermatogenesis to occur in the adult. We recently found that activin A can cause Sertoli cells, which ‘nurse’ the developing germ cells, to revert to an immature de-differentiated phenotype, suggesting a novel role for activin in testicular disease. This project will use in vitro and in vivo models to determine the molecular mechanisms of activin action on mature Sertoli cell function.

**Keywords:** male reproduction, growth factors, cell-cell communication, fertility, spermatogenesis

**Project: Male germ cells and the blood testis barrier**

**Suitability:** Honours, Masters by Research, PhD/Doctorate
**Project leader:** Dr Peter Stanton  
e: peter.stanton@hudson.org.au

**Project description:** During spermatogenesis, early male germ cells (spermatocytes) cross the blood-testis barrier into a protected environment in order to complete their maturation. This migration step is critical for sperm output but its regulation is poorly understood. We have found a new mechanism by which particular types of germ cells can directly regulate blood-testis barrier function, which includes the expression of novel tight junction proteins. This project will investigate this new mechanism with aims to identify the factor(s) and tight junction proteins involved, and their relevance to male fertility. Methods include in vitro and in vivo models of blood-testis barrier function, qPCR, western blotting, and confocal immunocytochemistry.

**Keywords:** testis, fertility, reproduction, cell-cell communication
Contact our supervisors

Students are encouraged to contact our supervisors to discuss projects, arrange a time to visit the lab and view our facilities. Simply email the supervisor to arrange a time.

**STEP 1:** Find a project you are interested in.
**STEP 2:** Email the supervisor, "I am interested in your student project. Could I please arrange a time to visit you in your lab?"

All the information you need to enrol is on our website, or your supervisor can help you
w: hudson.org.au/students/courses-available/