HUDSON
INSTITUTE OF MEDICAL RESEARCH

CENTRE FOR REPRODUCTIVE HEALTH

2023 Student Research Projects

MHTP Monash Health Translation Precinct | MONASH University | HUDSON INSTITUTE OF MEDICAL RESEARCH | Monash Health

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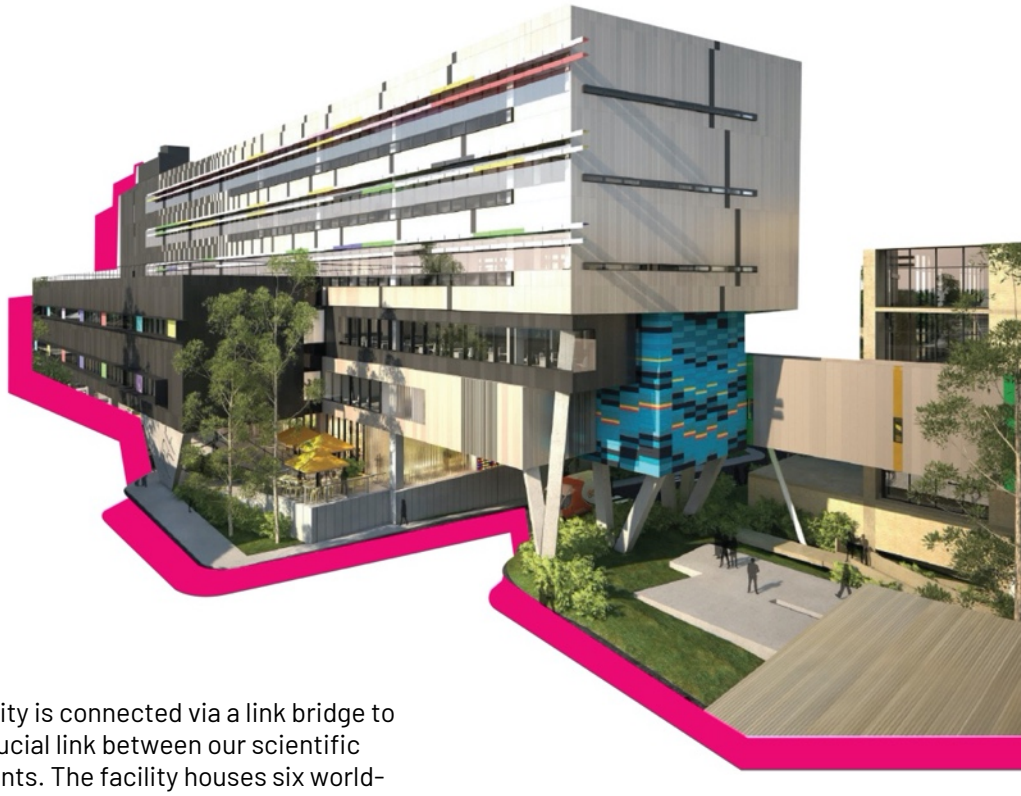

The Translational Research Facility is connected via a link bridge to Monash Health and provides a crucial link between our scientific discoveries and medical treatments. The facility houses six world-leading technology platforms and an eight-bed, 21-chair Clinical Trials Centre that support the transition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

Welcome to Hudson Institute

Hudson Institute specialises in discoveries in five areas of medical need

- **Inflammation**
- **Reproductive health and pregnancy**
- **Infant and child health**
- **Cancer**
- **Hormones and health**

Our 443 scientists and students focus on laboratory discovery science and translational research – taking discoveries to patients and industry for real-world impact.

267 STAFF

176 STUDENTS

45 RESEARCH GROUPS

257 RESEARCH PUBLICATIONS

Students at a glance 2021

68 POSTGRADUATE AND HONOURS STUDENTS COMPLETED

176 STUDENTS 125 PhD 1 MASTERS 50 HONOURS

26 STUDENTS WITH MEDICAL TRAINING

We educate and train more than 170 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

- Are exposed to university, institute, and hospital research
- Attend national and international conferences
- Publish their research in high impact journals
- Are mentored by leading supervisors and their teams
- Win prestigious prizes and awards
- Join regular networking and learning and development programs, including the off-site Institute student retreat
- Learn a range of dynamic and transferable skills for careers in the biomedical and clinical research sectors including commercialisation

All work and no play ...

Our students can join in a range of student networking and social events organised by Hudson Institute Student Society (HISS), including being part of the management committee.

Our precinct

Hudson Institute is a leading Australian medical research institute recognised internationally for discovery science and translational research into inflammation, reproductive health and pregnancy, infant and child health, cancer, hormones and health.

Our Institute is home to 443 world-class scientists, who push the boundaries of scientific knowledge to answer complex questions about human disease, including prevention and treatment.

We are a founding member of the Monash Health Translation Precinct (MHTP) with partners Monash Health and Monash University. Our close ties with clinicians and industry enable us to translate our discoveries into new preventative approaches, therapies and devices for patients.

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

Working alongside clinicians in Melbourne hospitals for more than 50 years, our scientists pioneered IVF and stem cell discoveries and are now leading developments in cell therapies, paediatric cancer and the human microbiome. Our worldwide scientific and medical collaborations provide a foundation for transformative healthcare programs across the globe.

Centre for Reproductive Health

Location

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Centre Head

Professor Kate Loveland

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

Research Group Heads

Testis Development and Germ Cell Biology
Professor Kate Loveland

Endocrinology and Immunophysiology
Professor Mark Hedger

Germ Cell Development and Epigenetics
Associate Professor Patrick Western

Germline Stem Cell Biology
A/Prof Robin Hobbs

Endometrial Remodelling
Dr Tracey Edgell

Male Reproductive Health

Research Group: Testis Development and Germ Cell Biology

Project: Regulation of the germline and fetal organ growth by environmental cues

Suitability: Masters by Research, Honours

Project leader: Prof Kate Loveland

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Project description: The cells that form into sperm and eggs in adults play a unique and fundamental role in human health and well-being, because they transmit the parent's genes to the next generation. In addition to transmitting DNA, gametes also carry the 'epigenome', chromatin modifications that determine which genes are switched on and off. However, when sperm and egg precursors form during pregnancy, the fetus may be exposed to profound changes in the maternal environment brought on by pre-eclampsia, medications and infection. To understand how fetal exposure to maternal stressors affects the epigenome of sperm and egg precursors and impacts on growth of organs in the fetus, projects will use materials from animal models and human clinical samples. Culture experiments will be conducted using placentas to identify genes that are targets of maternal stress in this organ, and to evaluate their downstream impacts on cellular functions.

Keywords: Cellular stress, infertility, fetal growth, epigenetics

Project: How do interactions between TGFbeta superfamily signalling and endocrine disruptor chemicals influence male fertility

Suitability: Masters by Research, Honours

Project leader: Prof Kate Loveland

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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 with the same target genes and processes affected by endocrine disrupting chemicals to influence testis development. To understand the relevance of this for male fertility and how disruptions can lead to male infertility, we undertake cellular and biochemical analyses using animal models and primary organ cultures of testes (in which the cellular communication processes are intact), as well as cell lines and isolated cells. Thus we will directly interrogate how crosstalk arising from exposure to these two factors affects whether the testis develops normally or not.

Keywords: Male infertility, cell signalling, development, TGFbeta superfamily biology, endocrine disruptor chemicals

Research Group: Endocrinology and Immunophysiology

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

Suitability: PhD/Doctorate, Masters by Research, Honours

Project leader: Prof Mark Hedger

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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 is a cytokine that 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. Futhermore, the unique immune-privileged environment in the testis favours persistent viral infections. Many viruses, including Covid19, can infect the testis. We are using the Zika virus as a model to study what factors increase the susceptibility of the testis to viruses. We are investigating if a novel anti-viral protein Interferon epsilon can be used against viruses in the testes.

Keywords: Inflammation, men's health, infertility, testis, epididymis, immunoregulation, infection, interferons, bacteria, viruses, autoimmunity

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

Suitability: PhD/Doctorate, Masters by Research, Honours

Project leader: Prof Mark Hedger

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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 can also involve studies of the role of activin in controlling inflammation, infection and immunity in the male tract.

Keywords: Inflammation, men's health, fertility, chronic pain, epididymis, immunity, infection, immune privilege, autoimmunity

Project: Uncovering the novel phenotype of macrophages in the testis

Suitability: PhD/Doctorate, Masters by Research, Honours

Project leader: Prof Mark Hedger

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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.

Keywords: Inflammation, men's health, fertility, testis, immunoregulation, macrophages

Molecular Biology of Reproduction

Research Group: Germ Cell Development and Epigenetics

Project: Defining the epigenetic origins of maternally inherited disease

Suitability: PhD/Doctorate, Honours

Project leader: A/Prof Patrick Western

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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 epigenetic programming in oocytes, and (ii) how EED-mediated programming in oocytes affects development and postnatal health in offspring. (iii) how altered fetal and placental development in offspring affects the mother's physiology. This research will involve application of genome-wide sequencing, immunofluorescence and confocal imaging and a range of molecular and cell biological approaches. 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: Potential impacts of epigenomic drugs on female fertility and reproductive health

Suitability: PhD/Doctorate, Masters by research, Honours

Project leader: A/Prof Patrick Western

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Project description: Epigenetics provides an interface between the environment and DNA function through the ability of epigenetic modifications to regulate gene expression. Environmental disruption of epigenetic programming is considered to underlie developmental origins of disease, a process by which early changes in development lead to life-long health consequences. 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 specialised function. Changes to this long-term memory are thought to underlie developmental origins of disease, but the epigenetic mechanisms involved are poorly understood. Epigenetic modifiers have been widely studied in some somatic tissues, but their roles in regulating ovarian folliculogenesis, female fertility and female endocrine state are poorly understood. The follicle encompasses the functional unit of the ovary and regulates endocrine homeostasis, leading to multiple influences, including on infertility, ovarian function and endocrine state. Impacts on ovarian function can compromise female reproductive health, including long term physiological impacts on fertility and endocrine state and consequences including increased incidence of bone, metabolic, heart and cardiovascular disease EED and EZH2 are essential components of the highly conserved epigenetic modifier, Polycomb Repressive Complex 2. PRC2 is also dysregulated in cancer, and drugs have been developed to target PRC2. However, these drugs act systemically, and their potential impacts on the ovary remain unknown. Recent work in our laboratory demonstrates that PRC2 plays essential roles in ovarian development. However, the role of PRC2 in regulating development of these organs and the consequences of epigenetically dysregulating function of PRC2 as a potential off-target impact of clinical treatment remain unknown, raising the possibility that measures that preserve fertility options and/ovarian function may be beneficial to patients.

This project will use drugs that inhibit PRC2 function to treat ovarian tissue in culture to determine the potential for these drugs to have off-target impacts on folliculogenesis and/or ovarian function. A range of state of the art technologies, including immunofluorescence, advanced imaging, genome-wide sequencing, morphological and physiological, will be used to determine the impacts of PRC2 inhibiting drugs on ovarian cultures. The data obtained will reveal how epigenetic mechanisms regulate the ovarian function, providing insight into the epigenetic regulation of the ovary and processes regulating endocrine physiology. The project will address a critical knowledge gap in endocrinology and reproductive health by defining novel epigenetic processes that underpin ovarian function, aspects of which may be altered by lifestyle factors such as diet and drugs. Specifically, as PRC2 is commonly dysregulated in cancer (including ovarian cancer) and drugs targeting PRC2 have been developed for treatment, this work will also provide essential preclinical insights into the possible impacts of specific cancer therapies on endocrine state and whether patients should undergo fertility preservation.

Keywords: Ovary, epigenetics, endocrinology, fertility, cancer

Research Group: Germline Stem Cell Biology

Project: Preservation and regeneration of male fertility by germline stem cells

Suitability: PhD/Doctorate, Masters by Research, Honours

Project leader: A/Prof Robin Hobbs

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Project description: Maintenance of fertility in men is dependent on a population of germline stem cells (known as spermatogonial stem cells or SSCs) within the testis that continually produce maturing germ cells for production of sperm. Male infertility is surprisingly common and disrupted formation or function of SSCs is potentially involved in a large number of these cases. Importantly, germline cells are highly sensitive to many cancer therapies including chemotherapeutic drugs and cancer patients can be at a high risk of permanent infertility. Therapy-resistant SSCs can restore sperm production in individuals but cellular pathways mediating the regenerative response of SSCs following testis damage remain poorly understood. This project aims to study and dissect cellular pathways and mechanisms regulating the SSC regenerative response using mouse models of chemotherapy-induced infertility. The project will involve SSC culture, molecular biology, biochemistry and genomics techniques. Development of therapies capable of promoting SSC regenerative capabilities may ultimately help in the reversal of infertility caused by cancer treatment.

Keywords: Stem cells, fertility, regeneration

Uterine Biology

Research Group: Endometrial Remodelling

Project: Endometrial proliferative phase as a determinant of embryo implantation

Suitability: PhD/Doctorate, Masters by Research, Honours, BMedSc(Hons), Short projects

Project leader: Dr Tracey Edgell

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Project description: Our laboratory has identified biomarkers associated with endometrial receptivity and consequent IVF failure and success. Utilising protein based techniques we are seeking to improve current knowledge of how endometrial receptivity develops with the aim of future therapy development to overcome infertility without resort to expensive IVF procedures.

This project theme builds on our earlier studies to identify changes to the cytokine/chemokine and proteome of the endometrium during the proliferative phase which are associated with subsequent implantation failure. This project examines the identified proliferative phase factors for their influence on known biomarkers of endometrial receptivity developed in the later secretory phase of the menstrual cycle. This project will further refine and use our developed 3D human cell model of endometrial gland formation in addition to other protein analysis techniques e.g. western blotting, Luminex, ELISA.

Keywords: Endometrium, proliferative phase, embryo implantation, infertility, pregnancy

Contact our supervisors

Students are encouraged to contact 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 that 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 Hudson Institute's website, or the project supervisor can help you enrol.

w: hudson.org.au/students/courses-available/

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