HUDSON
INSTITUTE OF MEDICAL RESEARCH

CENTRE FOR REPRODUCTIVE HEALTH

2021 Student Research Projects

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

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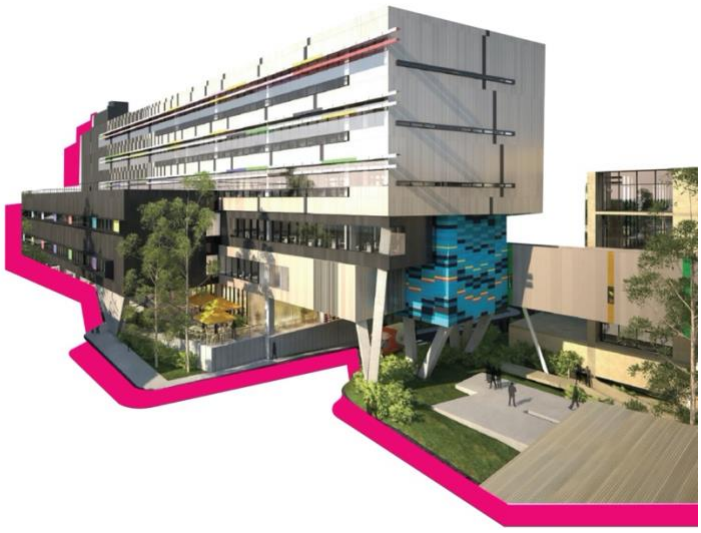

The Translational Research Facility is connected via a link bridge to Monash Health. The facility provides a crucial link between our scientific discoveries and medical treatments, housing nine world-leading technology platforms and an eight-bed, 21-chair Clinical Trials Centre that support the transition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

Welcome to Hudson Institute

Hudson Institute specialises in discoveries in four areas of medical need

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

Our 448 scientists and students focus on laboratory discovery science, plus translational research – taking discoveries to patients and industry for real-world impact.

296 STAFF

152 STUDENTS

50 RESEARCH GROUPS

283 RESEARCH PUBLICATIONS

Students at a glance 2019

58 POSTGRADUATE AND HONOURS STUDENTS COMPLETED

152 STUDENTS
113 PHD
4 MASTERS
35 HONOURS

28 STUDENTS WITH MEDICAL TRAINING

We educate and train more than 150 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 (there were 43 student first author publications in 2019)
- Are mentored by leading supervisors and their teams
- Regularly win prestigious prizes and awards
- Take part in regular networking and learning and development programs.

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 infant and child health, reproductive health and pregnancy, inflammation, and cancer.

Our Institute is home to 448 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 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 rapidly 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

Functional RNAomics
Dr Minna-Liisa Anko

Germline Stem Cell Biology
Dr 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: PhD/Doctorate, Masters by Research, Honours

Project leader: Prof Kate Loveland

e: kate.loveland@hudson.org.au

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: An importin protein that mediates growth factor signaling and pathway crosstalk: Its roles in spermatogenesis

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. We are investigating an importin protein, IPO5 (also named importin 5), a nucleocytoplasmic transport factor which selectively binds and carries cytoplasmic cargo proteins into the nucleus. It can control signaling by Transforming Growth Factor-beta superfamily proteins (for example, Bone Morphogenetic Proteins {BMPs} and activins) as well as Wnts. Our published work has demonstrated that IPO5 synthesis is highly regulated during spermatogenesis, both in fetal life and in adulthood, and we have an ongoing research effort to identify what its cargo and functions are during spermatogenesis. Our research primarily uses cell lines and mouse tissues. Approaches include biochemical characterisation of binding partners at different stages of spermatogenesis, and cell culture to reveal how IPO5 regulates signaling crosstalk during spermatogenesis. Knockdown of specific pathway components (siRNA) or signalling pathways (application of selective inhibitors) is followed by measurements of pathway activity using direct reporters of transcriptional activation (eg. luciferase activity), analysis of downstream target gene activity, and evaluation of cellular functions (migration, adhesion, proliferation, survival, differentiation).

Keywords: Cell signaling, spermatogenesis, nucleocytoplasmic transport, cell differentiation

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 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: 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 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: PhD/Doctorate, Masters by Research, Honours

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

Molecular Biology of Reproduction

Research Group: Germ Cell Development and Epigenetics

Project: Pharmaceutical impacts on germline epigenetics and offspring health and development

Suitability: PhD/Doctorate

Project leader: A/Prof Patrick Western

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Project description: Germ cells are specialised cells found in the developing testes and ovaries that form sperm in males, or oocytes (eggs) in females. Sperm and oocytes transmit the parent's genetic and epigenetic information to the offspring. Epigenetic modifications to the chromatin (DNA plus the proteins that package it) provide a long-term "directory" or "memory" of which genes should be switched on or off in each cell, and thereby underpin cell identity and organ function. Conversely, disrupted epigenetic states occur in diseases including cancer, metabolic and behavioural disorders. Importantly, epigenetic modifications are reversible in normal cells, allowing gene activity to be changed when necessary. This occurs most extensively in developing germ cells in which epigenetic information is re-set to equip the oocyte with the appropriate epigenetic information for directing embryonic and post-natal development in the offspring. Significantly, epigenetic programming is susceptible to alteration by environmental influences such as chemicals, diet and drugs. Altered epigenetic states can be transmitted to the next generation and affect health and development in the offspring. Such changes contribute to the developmental origins of health and disease (DOHaD) in a parent's offspring. The Germ Cell Development and Epigenetics group aims to improve understanding of epigenetics in the germ cells and the effects of epigenetic change on the offspring. Specifically, we use gene mutations and drugs to disrupt epigenetic modifier function in mouse germ cells to determine: (i) the function of specific epigenetic modifiers in germ cell development, and (ii) the ability of germ cells with altered epigenetic states to direct development in the parent's offspring. Therapeutic drugs that target epigenetic mechanisms are used to treat an increasing number of diseases, including cancer and neurological conditions such as epilepsy. However, whether these drugs alter germ line epigenetics and potentially the inheritance of epigenetic information remains largely unknown. Using in-vivo drug dosage in mice and a model in which drug treatment is known to affect brain development and behaviour, this project will examine whether a specific epigenetic modifying drug impacts directly on neural stem cell development in utero, and whether the drug has impacts on epigenetic programming in sperm and oocytes that affect neural development in offspring. Outcomes for germ cell development and epigenetics will be measured by profiling genome-wide transcriptional and epigenetic outcomes in neural stem cells and in germ cells. The project will use an established model to determine how a pharmaceutical that inhibits an essential epigenetic modifying mechanism alters the patterning of epigenetic information in the germline and how this impacts on health and developmental outcomes in offspring. Understanding these processes is

essential to understand how epigenetic information in the parent affects development in offspring.

Keywords: Epigenetics, reproduction, germ cells, inheritance, pharmaceuticals

Research Group: Functional RNAomics

Project: Discovering the role of miRNA processing in cancer

Suitability: PhD/Doctorate, Masters by Research, Honours, Short projects

Project leader: Dr Minna-Liisa Anko

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Project description: Previous studies suggest that overexpression of an RNA binding protein called SRSF3 is required for cancer cell growth and survival, however the underlying molecular mechanisms remain unclear. We have discovered a novel gene expression signature that in associated with SRSF3 expression both in normal highly proliferating cells such as embryonic stem cells and cancer cells. We have mechanistically shown that SRSR3 directly regulates the production of defined set of small noncoding RNAs, microRNAs, that are central for this so-called 'Oncomir-1 gene expression signature'. This project investigates how SRSF3 and potentially together other RNA binding proteins regulate the production of oncogenic miRNAs, with the focus on colorectal cancer.

Keywords: RNA binding protein, cancer, oncogene, gene expression, Australian Regenerative Medicine Institute

Project: No nonsense-regulated RNA degradation as a novel way to control gene expression

Suitability: PhD/Doctorate, Masters by Research, Honours, Short projects

Project leader: Dr Minna-Liisa Anko

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Project description: Nonsense mediated mRNA decay is a means to remove faulty transcripts that could have detrimental consequences for cells. We have found that cells also use this mechanism to regulate gene expression. This project will investigate this novel way to control gene expression by regulated RNA degradation. The focus will be the role of regulated RNA degradation in stem cells.

Keywords: RNA degradation, gene expression, RNA binding proteins

Project: RNA biology of blood cell production – how platelets get their RNA

Suitability: PhD/Doctorate, Masters by research, Honours, Short projects

Project leader: Dr Minna-Liisa Anko

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Project description: Platelets are an essential component of the haemostatic system and low platelets counts are harmful. 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. The aim is to understand why blood cells such as megakaryocytes are vulnerable to alterations in RNA processing and how we can harness the RNA processing machinery to treat haematological disorders.

Keywords: RNA processing, gene expression, blood cell, platelet

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: Dr 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: Biomarkers of endometriosis

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

Project leader: Dr Tracey Edgell

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Project description: This project will examine serum and saliva for endometriosis biomarkers that diagnose and stratify for disease severity and related infertility. The project will profile glycosylation changes to the proteins produced by the endometrium lining of the uterus, to identify the unique disease associated glycoforms. The project will utilise lectins and agglutinins as tools to examine both human endometrial tissue and secretions using histochemical and western blot techniques. Complimenting this will be an affinity-proteomic study in collaboration with Baker IDI to identify individual protein glycosylation changes for subsequent validation in an antibody-based assay of patient samples.

Keywords: Endometriosis, diagnostic, biomarkers, glycosylation

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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