HUDSON
INSTITUTE OF MEDICAL RESEARCH

CENTRE FOR REPRODUCTIVE HEALTH

2020 Student Research Projects

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

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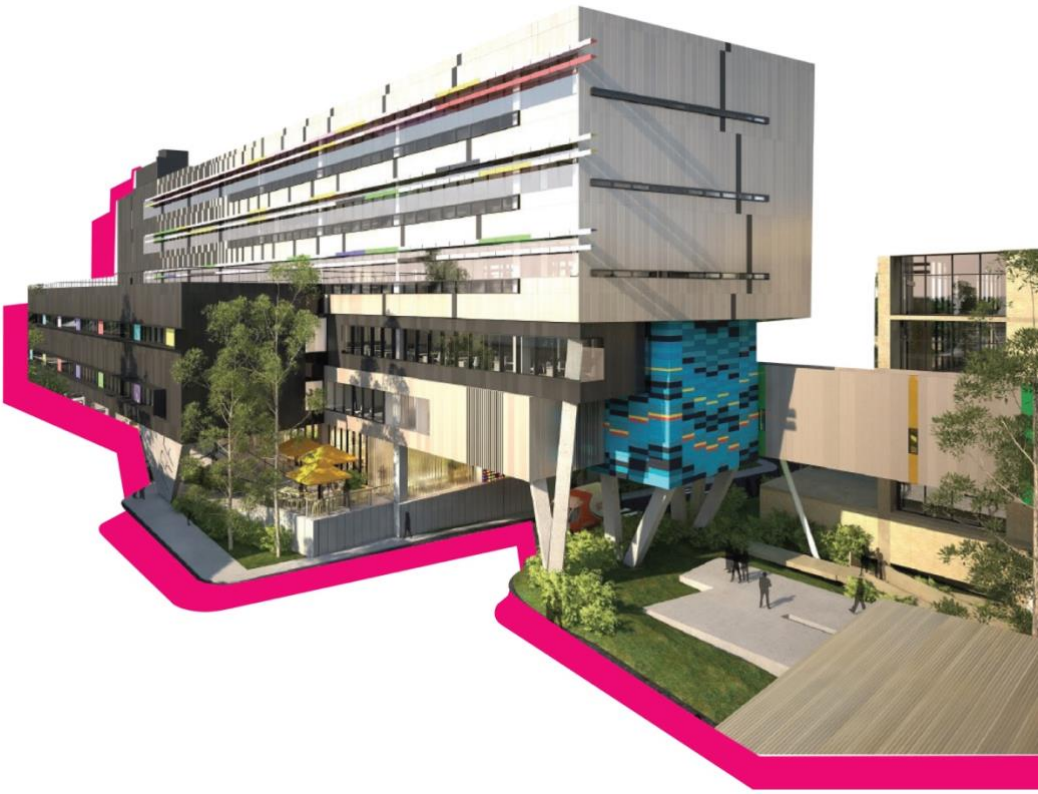

The Translational Research Facility is connected via a link bridge to Monash Health, and provides a crucial link between our scientific discoveries and medical treatments. The facility houses nine world-leading technology platforms and an eight-bed, 21-chair Clinical Trials Centre supporting the transition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

Welcome to Hudson Institute

Hudson Institute specialises in discoveries in four areas of medical need

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

Our impact is on precision medicine, stem cell therapies, women's health, hormone disorders, fertility, infection, chronic disease and child development.

Our 475 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 2018

We educate and train nearly 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 (74 student first author publications in 2018)
- 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 have the opportunity 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 Translational 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.

Centre for Reproductive Health

Location: Centre for Reproductive Health, Hudson Institute of Medical Research, Monash Medical Centre, Clayton

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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 Groups Heads

Testis Development and Germ Cell Biology
Professor Kate Loveland

Implantation and Placental Development
Professor Guiying Nie

RNA Biology in Health and Disease
Dr Minni Anko

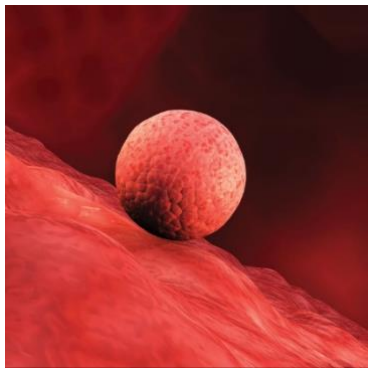
Ovarian Biology
Professor Jock Findlay

Endometrial Remodelling
Professor Lois Salamonsen

Endocrinology and Immunophysiology
Professor Mark Hedger

Male Fertility Regulation
Dr Peter Stanton

Germ Cell Development and Epigenetics
Associate Professor Patrick Western



Uterine and Placental Biology

Research Group: Endometrial Remodelling

Project: Menses, mood and the munchies: examining and modulating gut and brain function during menstruation

Suitability: PhD/Doctorate, Honours

Project leaders: Dr Jemma Evans, Co-Supervisor

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Project description: Millions of women of reproductive age experience a variety of menstrual-associated disorders including excessive period pain (dysmenorrhoea) and heavy menstrual bleeding (menorrhagia). These complications are associated with a normal physiological process, but have a significant impact on normal functioning and quality of life. Superimposed on these menstrual disorders are a cluster of menstrual associated symptoms. Among these, gastrointestinal (GI) upsets and mood disorders (PMS) can be considered as further impacting on quality of life. The number of women affected by these complications is difficult to estimate, however, a recent report (Bernstein, 2014) indicated that women who have emotional symptoms (depression/anxiety) pre- or during menses are more likely to have gastrointestinal upsets and painful periods, highlighting a possible link between these complications. Additionally, there is a reported role for the gut microbiome in hormonal cycling (Neuman, 2015) and brain function (Kennedy, 2016). However, the link between periods, gut function and mood has not been explored and it is unknown whether these can be altered via dietary manipulation. Women are becoming resistant to a reliance on pharmacological interventions to control menstrual associated symptoms. As a result, there is increased interest in the impact of lifestyle alterations on heath. Dietary intervention is a promising area whereby the gut microbiome may be manipulated and therefore health outcomes may be modulated.

Aims:

1) Characterise changes in the gut microbial profile during different phases of the menstrual cycle; determine whether changes in microbial composition are associated with the physiological and psychological symptoms experienced by women with dysmenorrhoea and PMS.

2) Determine the effect of prebiotic-associated alterations in the gut microbiota on the severity of menstrual-associated pain, gastrointestinal symptoms, dietary changes, sleep quality and mood. Research plan: 20 women of reproductive age will be recruited who present with menstrual pain, GI symptoms and PMS. These women will be tracked for 3 cycles with pain, digestion (GI) and mood symptoms recorded throughout each menstrual cycle, and food intake recorded via Easy Diet Diary (mobile phone application). Validated questionnaires will be used where possible (eg. GSRS: Gastrointestinal Symptom Rating Scale, DASS-21: Depression, Anxiety & Stress Scale – 21 questions, Pittsburgh Sleep Quality Questionnaire) in conjunction with a mobile phone menstrual cycle tracking application (Clue). In the first menstrual cycle immediately after women are recruited, stool samples will be collected for microbial analysis during proliferative, secretory and menstrual phase. After tracking for a further 2 cycles to determine each individual woman's cyclic baseline in terms of gastrointestinal function, mood and pain (particularly during menstruation) women will be randomised to:

- Control group: fully digestible starch (maltodextrin; 20g/day), or
- Prebiotic group: resistant starch (20g/day)

Each woman will continue to record GI symptoms, mood and pain as indicated above for a further 3 menstrual cycles. During the final cycle (cycle 6) the faecal microbiome will again be assessed during the proliferative, secretory and menstrual phases. Statistical analysis will be undertaken to determine whether prebiotics altered the gut microbiota, and in concert with this altered pain intensity, mood, dietary intake, sleep quality and gastrointestinal symptoms. Predicted outcomes: We hypothesise that dietary prebiotic supplementation will modulate the gut microbiome, improve menstrual-associated mood disorders and reduce menstrual pain and gastrointestinal symptoms. This work will provide a proof of concept to improve menstrual-associated quality of life for millions of women through dietary prebiotic intervention. Skills acquired by student: collection of survey data from research participants, quantitative statistical analysis, working with gut microbiota data, interpretation of dietary analysis data (Foodworks), scientific writing.

Keywords: Women's health, menstruation, gastrointestinal symptoms, prebiotic, resistant starch, mood, sleep, nutrition, diet, pain, gut microbiome, gut microbiota, menstrual disorders, PMS, emotional well-being

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

Project: Impact of extracellular matrix turnover products on female fertility

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

Project leader: Dr Tracey Edgell

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Project description: Our work investigates endometrial aspects of female infertility. A central theme of our work is to understand the mechanisms of infertility in order to provide better diagnostic and therapeutic options for women seeking to start a family. The endometrium is formed within a network of extracellular matrix composed of proteins such as fibrin and collagen. Our laboratory has identified a variety of protease activities within the uterus which will contribute to the turnover of this matrix essential to the continual growth and remodelling of the endometrium during the menstrual cycle and pregnancy. This project will identify fragments of matrix proteins within the uterine environment and examine them for vasoactivity, angiogeneic potential and cellular invasion effects within the context of human reproduction. Further identification of fragments with diagnostic or prognostic potential in predicting adverse pregnancy events will be investigated.

Keywords: Endometrium, reproduction, pregnancy, IVF, extracellular matrix, protease, enzymatic digestion

Research Group: Implantation and Placental Development

Project: Blood vessel endothelial aging and pregnancy disease preeclampsia

Suitability: PhD/Doctorate, Masters by Research, Honours

Project leader: Prof Guiying Nie

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

Project leader: Prof Guiying Nie

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Project description: Preeclampsia is a life-threatening disorder of pregnancy that is 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 disorder associated with renal failure, seizures and stroke. Currently the only effect “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, pregnancy complications

Project: Uterine surface remodelling for embryo implantation and IVF success

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

Project leader: Prof Guiying Nie

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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, IVF, fertility, infertility, pregnancy

Ovarian Biology

Research Group: RNA Biology in Health and Disease

Project: Discovering the role of miRNA processing in cancer

Suitability: PhD/Doctorate, 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’.

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, Australian Regenerative Medicine Institute

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

Suitability: PhD/Doctorate, 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, Australian Regenerative Medicine Institute

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

Suitability: PhD/Doctorate, Honours, Short Projects

Project leader: Dr Minna-Liisa Anko

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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: Stem cell, RNA binding protein, pluripotency, Australian Regenerative Medicine Institute

Male Reproductive Biology

Research Group: Testis Development and Germ Cell Biology

Project: Immune cell regulation of male fertility and testicular cancer progression

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

Project leader: Prof Kate Loveland

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Project description: This work will examine the vital roles of immune cells in supporting testis development, maintenance of spermatogonia required for adult fertility, and exacerbation of the pathology associated with germ cell tumours that form in young men. These experiments will examine what factors are produced by testicular immune cells to identify that they are required for normal testis development and fertility. In addition, inflammatory cells are common in established testicular tumours, and we have begun to define the key immune cells present in human testicular cancers in collaboration with colleagues at the Justus-Liebig University in Giessen, Germany and at the University of Copenhagen in Denmark. With colleagues at the Burnet Institute in Melbourne we will employ our established model using human immune cell preparations from peripheral blood in co-culture with a human testicular cancer (seminoma) cell line. Analysis of key signaling pathway components (e.g. cytokines, growth factors, their receptors and downstream targets) will be performed using RNA and protein analysis methodologies, while regulation of their functionality will be undertaken using selective pathway inhibitors and siRNAs targeting specific signaling machinery. Archival and fresh samples from patients with testicular cancer will be evaluated to ascertain the cell-specific roles of key signaling pathways. This will allow us to map how tumour and immune cells interact so we can decipher the crosstalk between immune cells and human germ cell tumours, and develop strategies to limit the spread of this disease that profoundly affects the reproductive health of young men.

Keywords: Male fertility, infertility, testis cancer, immunology, cancer, cell signaling, tumour microenvironment

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

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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. 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: Male Fertility Regulation

Project: How does activin regulate adult testis function?

Suitability: PhD/Doctorate, Honours

Project leader: Dr Peter Stanton

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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

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. New therapeutic drugs that target epigenetic mechanisms are being used to

treat an increasing number of diseases, including cancer and neurological conditions. Whether these drugs alter germ line epigenetics and potentially the inheritance of epigenetic information remains unknown. This project will examine how epigenetic modifying drugs impact on oocyte development and the patterning of epigenetic information in the germ line. Using organ culture and in-vivo drug dosage in mice we will challenge developing germ cells with specific epigenetic modifying drugs. Outcomes for germ cell development and epigenetics will be measured using immunofluorescence, qRTPCR and flow cytometry. This project will determine whether pharmaceuticals that inhibit epigenetic modifying enzymes alter 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 the offspring.

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

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 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/

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