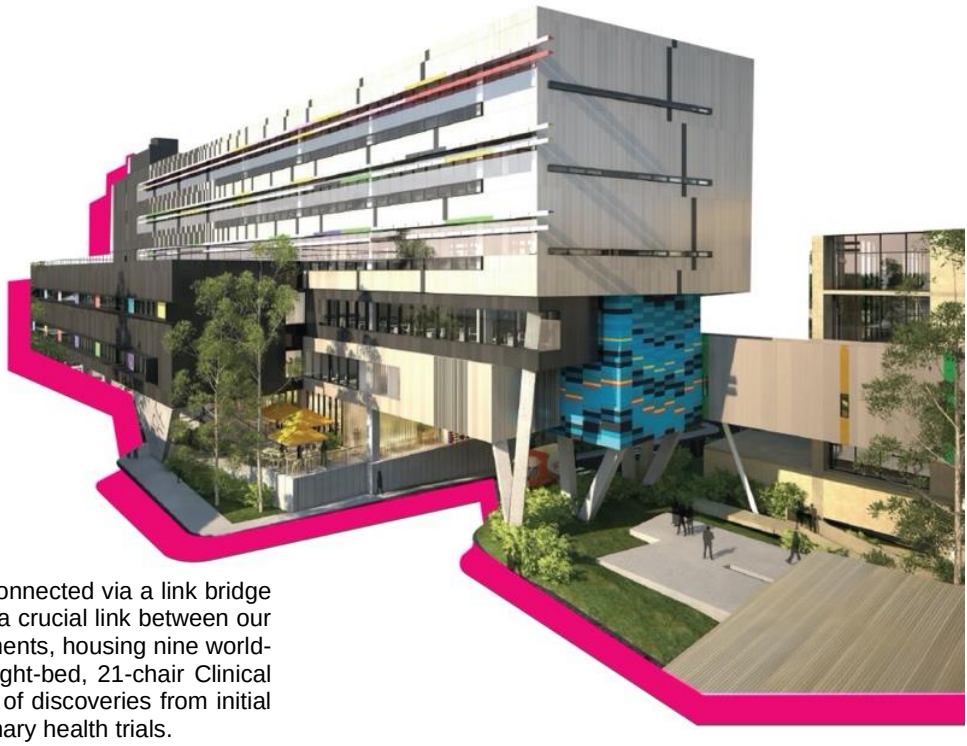
HUDSON
INSTITUTE OF MEDICAL RESEARCH

CENTRE FOR ENDOCRINOLOGY AND METABOLISM

2021 Student Research Projects

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

Contents



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 research discoveries have translational impact in:

- **Precision medicine**
- **Stem cell therapies**
- **Newborn health**
- **Rare diseases**
- **Hormone disorders**
- **Fertility**
- **Women's health**
- **Infection**
- **Chronic disease**

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 in 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

- Gain exposure 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
- Have opportunities to participate in 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.

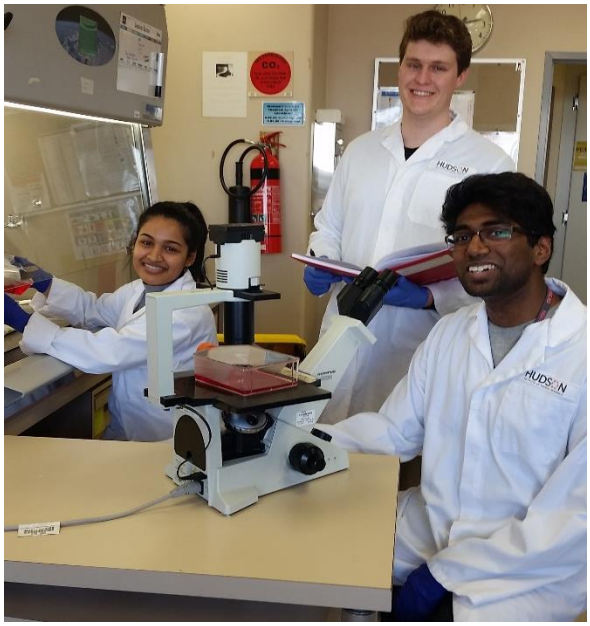
Our Institute is home to 448 world-class scientists, who push the boundaries of scientific knowledge to answer complex questions about human disease, including prevention and treatment.

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.

About the Centre for Endocrinology and Metabolism



Location:

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w: hudson.org.au/research-centre/centre-for-endocrinology-and-metabolism/

Centre Head:

Professor Peter Fuller AM

About the Centre:

The complex endocrine system impacts all aspects of health and disease. As the pre-eminent centre for endocrinology research originating from Prince Henry's Institute, laboratories in the Centre for Endocrinology and Metabolism at Hudson Institute of Medical Research undertake basic and clinical research.

The Centre's goal is to improve the understanding of the role of hormones in human biology and disease to tackle key health challenges facing Australian and global communities, including reproductive health, bone health and cancer metastasis, cardiovascular disease, hypertension and endocrine cancers. Clinical translation of these findings to improve diagnosis, therapeutic intervention and prevention of disease remains a key focus for the Centre.

Research Groups and Leaders

Cancer Drug Discovery
Head: Associate Professor Colin Clyne

Clinical Andrology
Head: Professor Robert McLachlan AM

Hormone Cancer Therapeutics
Head: Dr Simon Chu

Metabolic Bone Research
Head: Associate Professor Frances Milat

Sex Development
Head: Professor Vincent Harley

Steroid Receptor Biology
Head: Professor Peter Fuller AM

Cancer

Research Group: Cancer Drug Discovery

Nuclear receptor pharmacology

Suitability: Honours, Masters by Research, PhD

Project leader: Associate Professor Colin Clyne

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Project description: Anti-estrogen therapies, while very successful in the treatment of many breast cancers, are not effective for patients whose tumours do not express the estrogen receptor. Many patients who do respond to these drugs eventually become resistant to their effects. We are identifying alternative molecules related to the estrogen receptor (nuclear receptors) that could be exploited as novel breast cancer therapeutics. We have shown that one such receptor, LRH-1, induces cell proliferation, invasion and cancer stem cell-like phenotypes, making it an attractive target for cancer therapy development. We also recently demonstrated that LRH-1 interacts strongly with the estrogen biosynthetic pathway. To verify our findings and aid understanding of the role of LRH-1 in both the normal breast and breast cancer, we have developed a transgenic mouse model in which expression of human LRH-1 is directed specifically to the mammary gland. We have also shown that LRH-1 activity can be inhibited by peptides that block its interactions with co-regulator proteins, and are also currently using *in silico* and structural approaches to design small drug-like molecules that act in the same manner. Projects are available using both the animal model and *in vitro* pharmacology approaches.

Keywords: breast cancer, cancer, estrogen, nuclear receptors

Understanding resistance to breast cancer therapies

Suitability: Honours, Masters by Research, PhD

Project leader: Associate Professor Colin Clyne

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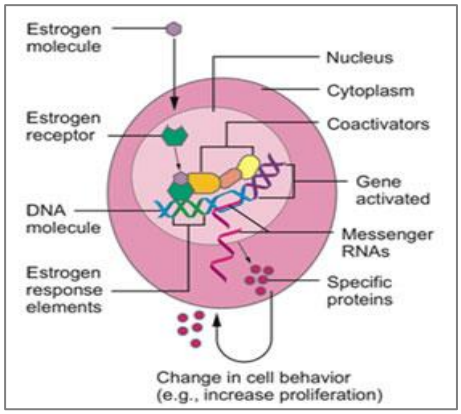
Project description: Most breast cancer patients have tumours that require the female sex hormone estrogen to grow and develop. Blocking this action of estrogen (using drugs like tamoxifen) is a commonly used and effective therapy. However, many patients develop resistance to these drugs, leading to disease recurrence with poor prognosis. Understanding how therapeutic resistance occurs is therefore critical for the development of more effective therapies. We have identified a novel protein (of unknown function) that becomes activated in breast cancers that have developed resistance to tamoxifen. We have shown that this protein amplifies the effects of estrogen, making breast cancer cells more responsive to the hormone, and increasing their ability to divide and spread. This effect may make cells less responsive to tamoxifen, thereby contributing to the development of resistance. This project aims to:

- understand how this protein modulates estrogen action at the molecular level; and
- determine its potential as a marker to identify patients who may not respond well to tamoxifen.

Keywords: breast cancer, cancer, endocrinology, estrogen, nuclear receptors



Research Group: Hormone Cancer Therapeutics

Molecular pathogenesis of granulosa cell tumours of the ovary

Suitability: Honours, Masters by Research, PhD

Project leaders: Dr Simon Chu; Professor Peter Fuller

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Project description: Granulosa cell tumours (GCT) of the ovary are endocrine tumours that both make and respond to hormones. We have recently confirmed a key mutation in the *FOXL2* gene in >90% of adult GCT. We have also found that 40% of GCT contain a mutation in the telomerase gene. Our group seeks to understand the molecular events that lead to the development of advanced and/or aggressive tumours for which there is an 80% mortality. Current studies seek to establish the

genomic landscape of these tumours using whole exome sequencing with transcriptomic analyses and microRNA analyses. Other studies explore the role of genes that we have identified as being overexpressed in advanced disease, including the telomerase gene, with a view to developing novel therapeutic strategies.

Keywords: cancer, ovarian cancer, granulosa cell tumour, therapeutics, signalling pathways, transcription factors, nuclear receptors, estrogen

Role of XIAP in endocrine cancer (ovarian and thyroid)

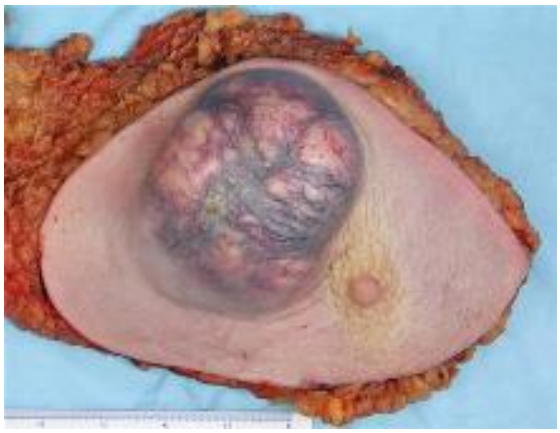
Suitability: Honours, Masters by Research, PhD

Project leaders: Dr Simon Chu; Professor Peter Fuller; Dr Michael Mond

e: simon.chu@hudson.org.au

Project description: The X-linked inhibitor of apoptosis (XIAP) is a member of a family of endogenous caspase inhibitors that act as antiapoptotic factors. XIAP is the most potent caspase inhibitor, blocking both intrinsic and extrinsic apoptotic signals through direct caspase binding. Due to its prominent ability to control cell death and its elevated expression in human cancers, XIAP has become an attractive therapeutic target for novel anti-cancer treatment. Small-molecule inhibitors are in various stages of development, from preclinical to phase II clinical trials. XIAP has an important role in both ovarian cancer and thyroid cancer. This project will explore the efficacy of inhibiting XIAP in combination with targeting a key nuclear receptor in both cancers using unique *in vitro* systems with innovative technology and novel therapeutic compounds, with the ultimate goal of providing an essential pre-clinical, proof-of-concept approach for translation to the clinic.

Keywords: cancer, ovarian cancer, thyroid cancer, granulosa cell tumour, therapeutics, signalling pathways, transcription factors, nuclear receptors, estrogen, XIAP, apoptosis



Elucidating novel functions of MAGMAS signalling in ovarian cancer progression and chemoresistance

Suitability: Honours, Masters by Research, PhD

Project leaders: Dr Simon Chu; Professor Nuzhat Ahmed; Professor George Kannourakis

e: simon.chu@hudson.org.au

Project description: Ovarian cancer is asymptomatic and there are no sensitive and specific markers to detect it at an early stage. Seventy-five percent of the women (more than 900 Australian women per year) diagnosed with stage III/IV disease have a five-year survival rate of less than 30%. The development of recurrent peritoneal metastases after standard chemotherapy treatment is a major clinical issue in the management of ovarian cancer patients. Hence, there is an urgent need to identify molecules that can be manipulated in conjunction with chemotherapy treatment to provide better outcomes for ovarian cancer patients. Mitochondria are key organelles in many metabolic and biosynthetic pathways, and the adaptation of cancer cells towards mitochondrial function is crucial during neoplastic transformation. Genes encoding mitochondrial proteins have shown encouraging results as potential therapeutic targets for cancer. Our laboratory has recently identified novel expression of mitochondria-associated granulocyte macrophage colony-stimulating factor signalling molecule (MAGMAS) in ovarian tumours. MAGMAS, also referred to as PAM16, was previously described as a mitochondria-associated protein, involved in pre-protein import into mitochondria and essential for cell growth and development. The protein also has an important role in controlling oxidative damage. Hence, the expression of MAGMAS, which is significantly elevated in advanced-stage ovarian tumours compared to benign ovarian tumours, warrants further investigation. This study is based on the hypothesis that MAGMAS, through its inherent ability to regulate cell growth and oxidative stress, is directly responsible for driving ovarian tumourigenesis at the primary tumour site, within the ascites fluid, and subsequent ongoing disease progression in ovarian cancer patients after chemotherapy treatment. This study therefore aims to investigate the role of MAGMAS in ovarian cancer progression, metastasis and chemoresistance-associated recurrence.

Keywords: cancer, ovarian cancer, mitochondria, mitochondria-associated granulocyte macrophage colony stimulating factor, molecular biology, CRISPR, xenografts

Endocrinology and Metabolism

Research Group: Metabolic Bone Research

Osteoporosis and metabolic bone disorders

Suitability: BMedSci, PhD

Project leader: Associate Professor Frances Milat

e: fran.milat@hudson.org.au

Project description: We are currently involved in a variety of projects aimed at improving health outcomes in patients with metabolic bone disorders and osteoporosis. These projects include the optimisation of bone health in adults with neurological disability, understanding osteoporosis in haemoglobinopathies, the evaluation and management of bone disorders in chronic kidney disease and the management of bone health in premature ovarian insufficiency. Projects are available in all of these areas.

Research Group: Steroid Receptor Biology

Evaluating the prevalence of primary aldosteronism in patients with stroke and/or atrial fibrillation

Suitability: Masters by Research, PhD

Project leaders: Dr Jun Yang; Dr Ben Clissold

e: jun.yang@hudson.org.au

Project description: Primary aldosteronism (PA) is the most common, and a potentially curable, cause of hypertension, estimated to affect 5-10% of all hypertensive patients. It leads to greater cardiovascular injury than hypertension alone. In particular, PA confers a 3-4 fold increase in the risk of stroke and atrial fibrillation compared to essential hypertension in blood pressure-matched patients. However, PA screening is not actively recommended in stroke/atrial fibrillation (AF) management guidelines. Given the potential health impact of diagnosing a potentially curable form of hypertension, and reducing the risk of stroke and AF, we seek to evaluate the prevalence of PA in patients presenting to Monash Health with either acute stroke or transient ischemic attack. This project has the potential to change management guidelines for hypertension in stroke patients and optimise the timely diagnosis of PA.

Keywords: primary aldosteronism, stroke, TIA, hypertension, endocrine hypertension, aldosterone

Exploring endocrine hypertension in Indigenous populations

Suitability: Masters by Research, PhD

Project leader: Dr Jun Yang

e: jun.yang@hudson.org.au

Project description: Aboriginal patients experience a disproportionate burden of cardiovascular disease, with hypertension being a key modifiable risk factor. The prevalence of primary aldosteronism, as the most common and potentially curable secondary cause of hypertension in non-Indigenous populations, has never been explored in Indigenous populations. We will engage with Indigenous communities in Victoria to gauge their attitude towards hypertension diagnosis and treatment, and seek their input in exploring primary aldosteronism in their communities.

Keywords: primary aldosteronism, hypertension, endocrine hypertension, Aboriginal patients, Indigenous health

Evaluating the cost-effectiveness of screening for PA in all versus subgroups of hypertensive patients

Suitability: BMedSci, Masters by Research, PhD

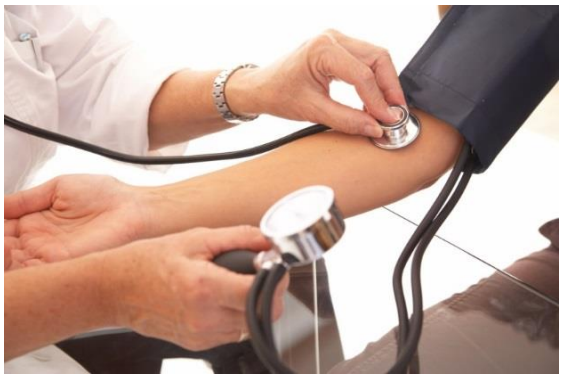
Project leaders: Dr Jun Yang; Associate Professor Gang Chen

e: jun.yang@hudson.org.au

Project description: Primary aldosteronism (PA) is the most common, and a potentially curable, cause of hypertension, estimated to affect 5-10% of all hypertensive patients. It leads to greater cardiovascular injury than hypertension alone. Studies have demonstrated the cost-effectiveness of screening patients with resistant hypertension for PA, but there are no economic modelling studies of screening newly diagnosed hypertensive patients. An early diagnosis is likely to be less complicated for a patient than long-standing disease, and offer greater benefit in reducing cardiovascular risk. However, without a formal cost analysis, hypertension screening guidelines will remain locked in the

past to the detriment of our community. This project will use the cost-utility analysis (CUA) approach to estimate the incremental costs and effectiveness of using aldosterone-renin ratio (ARR) to screen for PA in primary care versus no screening. The within-trial analysis will be extrapolated using a Markov model, consisting of health outcomes following screening procedures versus no screening, to capture the long-term cost. The quality of life and direct medical costs will be collected from a current trial. The estimates of the effect on long-term health outcomes, quality of life and costs (such as cost savings of cardiovascular events averted) will be made from a comprehensive literature review. Sensitivity analysis will be performed to evaluate the cost-effectiveness of ARR screening in all versus subgroups of hypertensive patients. The outcomes will directly influence policy.

Keywords: primary aldosteronism, cost-effectiveness, hypertension, endocrine hypertension, aldosterone, health economics



Identification of novel transcriptomic markers of PA

Suitability: Honours, BMedSci, Masters by Research, PhD

Project leaders: Dr Jun Yang; Dr Morag Young

e: jun.yang@hudson.org.au

Project description: Whilst dichotomous thresholds are currently used to diagnose primary aldosteronism (PA), emerging data supports the concept of a continuum of aldosterone excess. A longitudinal cohort study showed that higher aldosterone in the setting of a suppressed renin level (392 of 850 normotensive patients) was significantly associated with the development of hypertension. A robust cellular marker of aldosterone excess that correlates strongly with clinical outcomes following mineralocorticoid receptor (MR) antagonist treatment or adrenalectomy will complement the aldosterone-renin ratio (ARR) and confirmatory tests in the diagnostic algorithm for PA. As peripheral blood monocytes highly express the MR, they represent an accessible MR-responsive tissue to study aldosterone-induced changes in gene transcription. A number of genes identified by previous students will be characterised *in vitro* using RT-PCR and cell culture to confirm a change in their expression in response to MR activation or antagonism. These may then be validated in larger patient cohorts as robust biomarkers of aldosterone excess and inappropriate MR activation.

Keywords: primary aldosteronism, biomarker, hypertension, endocrine hypertension, aldosterone

Establishment of a national primary aldosteronism registry to enable comprehensive data collection

Suitability: Masters by Research

Project leader: Dr Jun Yang

e: jun.yang@hudson.org.au

Project description: Clinical registries play an important role in measuring healthcare delivery, supporting quality improvement and evaluating clinical outcomes, particularly in the long-term. There are no primary aldosteronism (PA) registries in Australia. This is in contrast to other countries which lead the research in PA, including China (CONPASS PA Study Group - 3 publications in leading endocrine journals in 2018), Japan (JPAS - 6), Taiwan (TAIPAI - 8) and Germany (German Conn's Registry - 10). Based on our existing REDCap database, we will develop a multicentre registry to systematically collect comorbidities, diagnostic parameters and long-term outcomes of patients with PA, both in and outside of clinical trials.

Keywords: primary aldosteronism, registry, hypertension, endocrine hypertension, aldosterone

Structure-function relationships of the mineralocorticoid receptor

Suitability: Honours, Masters by Research, PhD

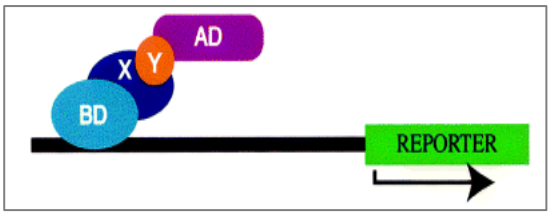
Project leader: Professor Peter Fuller

e: peter.fuller@hudson.org.au

Project description: The mineralocorticoid receptor (MR) is an important therapeutic target in cardiovascular disease. We have identified interactions of the receptor that differ between the physiological hormones, aldosterone, cortisol and progesterone. We also have access to novel therapeutic agents in development. Understanding these interactions and their structural basis will lead to the development of new therapeutic agents. The studies involve the use of yeast 2-hybrid

screens, transactivation assays, structural analysis, mutation detection, comparative biology and a series of unique transgenic mouse models in which the MR has been either mutated or removed (knocked-out). This work is also associated with our clinical program.

Keywords: aldosterone, mineralocorticoid, receptor, adrenal



Genetic Diseases

Research Group: Sex Development

Characterisation of novel gonadal targets of *Sox9*

Suitability: Honours, Masters by Research, PhD

Project leader: Professor Vincent Harley

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Project description: For the majority of disorders of sex development (DSD) cases, the underlying genetic aetiology is unknown. In males, *Sox9* is a critical 'hub' gene involved in sexual development. We hypothesise that *Sox9*'s downstream targets are also essential for gonadal development and mutated in DSD patients. By extensive data mining of gonadal microarrays, RNAseq, and *Sox9* ChIPseq, we have identified genes directly regulated by *Sox9*. These candidate genes are up-regulated in XY mouse testis compared to XX ovaries during development and down-regulated in sex-reversed XY ovaries ablated for *Sox9*. We will perform detailed expression profiling in XX and XY embryonic gonads of wild-type mice during the critical sex determination period E11.5-E13.5, postnatally and at adult stages. We will also perform *Sox9* ChIPseq on gonads and promoter/enhancer analyses, and screen DSD patients towards validation.

Keywords: sex determination, *Sox9*, disorders of sex development, molecular genetics, sex differences

FGF signalling and sex reversal

Suitability: Honours, Masters by Research, PhD

Project leader: Professor Vincent Harley

e: vincent.harley@hudson.org.au

Project description: We have identified the first *FGFR2* mutations in XY female sex-reversed disorders of sex development (DSD) patients. One case, a heterozygous *FGFR2c*-C342S mutation in a patient with both 46,XY gonadal dysgenesis and Crouzon syndrome, is unusual since gonadal defects have not yet been reported in Crouzon patients. We will use our 'knockin' *Fgfr2c*C342Y and 'knockout' *Fgfr2c*-/- mouse models to understand the role of *FGFR2* in testis determination and disease, and to identify *FGFR2*-regulated genes and signalling pathways which might be defective in DSD patients. Analyses of male and female markers will be carried out, as well as markers of FGF signalling. Training includes basic cell and molecular biology as well as embryonic microdissection, whole mount/section *in situ* hybridisation and immunofluorescence.

Keywords: *FGFR2*, sex determination, sex reversal, disorders of sex development, mouse models

ATR-X syndrome and gonadal development

Suitability: Honours, Masters by Research, PhD

Project leader: Professor Vincent Harley

e: vincent.harley@hudson.org.au

Project description: The ATR-X syndrome, an X-linked recessive developmental disorder affecting males, belongs to a growing list of disorders of sex development (DSD) which affect 1% of all newborns. Clinical features include mental retardation, alpha-thalassemia and skeletal and genital abnormalities. The focus of our work is to investigate the role of *ATRX* in gonadal development.

Keywords: sex determination, ATRX syndrome, human genetics, disorders of sex development

Identifying the genes responsible for disorders of sex development (DSD)

Suitability: Honours, PhD

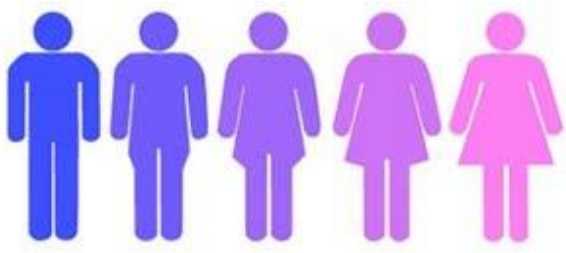
Project leader: Professor Vincent Harley

e: vincent.harley@hudson.org.au

Project description: Disorders of sex development (DSDs), formerly known as intersex, are congenital conditions where gonadal or anatomical sex is atypical. DSDs encompass a wide range of abnormalities, including hypospadias (abnormal urinary opening in males), gonadal dysgenesis (underdeveloped or imperfectly formed gonads) and ambiguous genitalia, and sex reversal (i.e. XX males and XY females). Our aim is to identify genes causing DSDs, and the molecular mechanisms underlying testis and ovary formation in the mammalian embryo. This proposal will provide new insights into the molecular control of testis development, and

thus offer the potential to improve diagnosis and clinical management of DSDs. Approaches include human genetics, as well as molecular, cell and developmental biology. See: Ono M. and Harley V. (2013) Disorders of sex development: new genes, new concepts. *Nature Reviews Endocrinology* 9:79-91; visit the website for the NHMRC Program on DSDs: http://dsdgenetics.org/.

Keywords: sex determination, genes, human genetics, disorders of sex development



The biological basis of gender identity

Suitability: Honours, PhD

Project leader: Professor Vincent Harley

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Project description: Gender identity is the gender with which a person identifies. Studies suggest that gender identity is affected by genetic, prenatal hormonal or postnatal social determinants. We are investigating the role of genes in patients with gender identity disorders. This project involves undertaking genetic association studies in the world's largest cohort of male-to-female transsexuals. It focuses upon genes involved in sex hormone synthesis and signalling.

Keywords: gender identity, gene associations, sex hormones

SRY: A risk factor for Parkinson's disease in males

Suitability: Honours, Masters by Research, PhD

Project leader: Professor Vincent Harley

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Project description: Parkinson's disease (PD) is a debilitating neurodegenerative disorder, triggered by the death of dopamine neurons in the brain region known as the substantia nigra. Whilst the mechanisms underlying dopamine cell loss in PD are unclear, it is clear that males are more susceptible to PD than females. We have identified that the male sex-determining gene *SRY* directs a novel genetic mechanism of dopamine cell death in males. Understanding when and how *SRY* increases the vulnerability of male dopamine neurons to injury will help to explain why males are more susceptible to PD and to identify *SRY* as a novel target for neuroprotective therapy in male PD patients.

Keywords: Parkinson's disease, brain differences, sex differences, *SRY*

How are male and female brains different?

Suitability: Honours, PhD

Project leader: Professor Vincent Harley

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Project description: Male and female brains differ in anatomy, chemistry and behaviour. The prevailing dogma that estrogen is the key factor involved in brain sex differentiation was challenged by our discovery of a direct role in the brain for the Y chromosome gene, *SRY*, in the control of voluntary movement, only in males. This project seeks to identify the target genes that the SRY transcription factor controls in the brain. Approaches include cell and molecular biology techniques (RNAseq, ChIPseq) and rodent dissection of the substantia nigra.

Keywords: SRY, brain differences, sex differences

Reproduction and Development

Research Group: Hormone Cancer Therapeutics

Role of XIAP in normal ovarian folliculogenesis

Suitability: Honours, Masters by Research, PhD

Project leaders: Dr Simon Chu; Professor Peter Fuller; Professor John Silke

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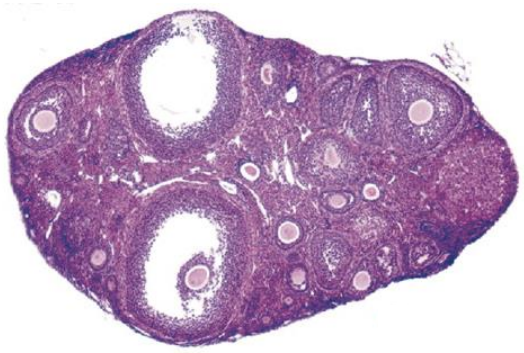


Project description: The X-linked inhibitor of apoptosis (XIAP) is a member of the inhibitor of apoptosis (IAP) superfamily, which are endogenous caspase inhibitors that act as anti-apoptotic factors. The expression pattern of XIAP in the ovary suggests it is a critical regulator of follicular atresia. Using single and double IAP knockout mice, this project aims to understand the role of XIAP in normal folliculogenesis. This study will involve histological analyses of ovaries at different stages of development and gene expression studies to characterise the ovarian phenotype. We expect these studies will yield novel data regarding ovarian function.

Keywords: ovary, folliculogenesis, ovarian function, apoptosis, XIAP

Research Group: Steroid Receptor Biology

Mineralocorticoid receptor regulation of gene expression in reproductive tissue

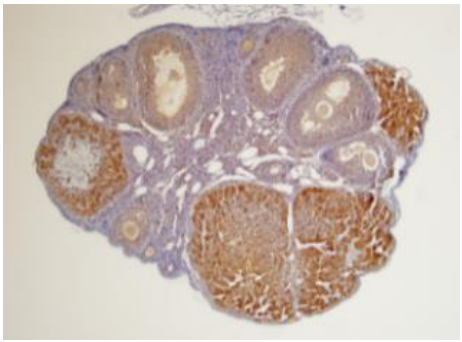
Suitability: Honours, Masters by Research, PhD

Project leader: Professor Peter Fuller

e: peter.fuller@hudson.org.au

Project description: The mineralocorticoid receptor (MR) is best known for its involvement in the regulation of salt and water balance. However, non-classical tissues have been identified as expressing MR, giving rise to the hypothesis that the MR also plays a regulatory role in these tissues. We have identified a number of genes that are directly regulated by the MR and are seeking to understand their mechanism of regulation in mammary and ovarian tissue *in vitro* and *in vivo*. The role of this receptor in breast and breast cancer is emerging as a potentially important story given that MR involvement appears to be linked to differentiation and apoptosis during mammary tissue development. We have created a tissue-specific knockout mouse to investigate the impact of MR loss on mammary and ovarian tissue development and function. In granulosa cell and breast cancer cell lines, we will manipulate the MR to evaluate the signalling mechanisms involved. Insights gained from these studies may lead to the development of new therapeutic agents for breast cancer treatment and infertility.

Keywords: mineralocorticoid, mammary tissue, knockout



Contact our supervisors

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

STEP 1: Find a project you are interested in from this book or at hudson.org.au/research-centre/centre-for-endocrinology-and-metabolism/

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

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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