THE RITCHIE CENTRE

2022 Student Research Projects
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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
- Inflammation
- Reproductive health and pregnancy
- Infant and child health
- Cancer
- Hormones and health

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

Our students
- Are exposed to university, institute and hospital research
- Attend national and international conferences
- Publish their research (there were 41 student first author publications in 2020)
- 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 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 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.
The Ritchie Centre

Location
Hudson Institute of Medical Research
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Centre Head
Professor Stuart Hooper

The Ritchie Centre is Australia’s premier clinical and research Centre for women, babies and children. The Ritchie Centre offers a unique setting where research advances can be rapidly applied for the benefit of women, seriously ill infants and children. This has led to rapid translation of its basic research into clinical trials and clinical practice.

The Ritchie Centre is strategically located within the Monash Medical Centre. Integration into the daily life of the hospital means that its researchers are able to develop research in response to the complications that present in the clinical setting and demonstrated the value of bringing together a critical mass of dedicated scientists and clinicians to undertake translational research.

The Centre’s mission to improve the health of women, infants and children through innovative research is achieved through its unique associations as the principal research Centre of the Monash University Department of Obstetrics and Gynaecology and the Department of Paediatrics, Monash Women’s Services, Monash Newborn and Melbourne Children’s Sleep Centre. It is also a major research partner of the Monash Children’s Hospital.

The Ritchie Centre has over 150 research staff and students, including fetal physiologists, sleep physiologists, immunologists, stem cell biologists, neonatologists, paediatricians, obstetricians, gynaecologists, and radiologists.

Research Groups Heads

Women’s Health
Prof Caroline Gargett

Fetal & Neonatal Health: Respiratory & Cardiovascular
A/Prof Graeme Polglase

Fetal & Neonatal Health: Brain Injury & Neurodevelopment
A/Prof Suzie Miller

Infant and Child Health
Prof Rosemary Horne

Cell Therapy & Regenerative Medicine
A/Prof Rebecca Lim
Women’s Health

Characterising novel targets for the treatment of endometriosis

Suitability: Honours, Masters
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Fiona Cousins, Prof Caroline Gargett
Email: fiona.cousins@hudson.org.au

Project Description: Endometriosis is a chronic disorder that has a major impact on quality of life. Despite its high prevalence, there is a lack of understanding of its pathogenesis, there is no cure, and current treatment options are limited to medicines with side effects or invasive surgery. We are aiming to develop new therapeutic strategies that focus on the immune system and not a woman’s menstrual cycle, like most current treatments. Interferons are a family of cytokines that have anti-pathogen and anti-tumour actions. They work by controlling cell growth, survival, migration and activation in immune cells that cause inflammation.

Interferon epsilon (IFNε) is a novel cytokine and immunomodulator that is constitutively expressed and only in the female reproductive tract (FRT) epithelium. IFNε exerts its protective effects in the FRT to prevent bacterial/viral infections and cancers. IFNε exerts a protective effect against the development of ovarian cancer in pre-clinical mouse models and can also reduce cancer metastases when given as a therapeutic in these mice. Given the similarities between ovarian cancer and endometriosis; increased cell growth and adaptation to an inflamed environment, we are interested to see whether IFNε may play a role in endometriosis pathogenesis and whether it can be used as a new therapeutic for the disease.

Keywords: endometriosis; immune system; immunomodulation; endometrium; women’s health

A novel non-invasive diagnostic for endometriosis/adenomyosis

Suitability: PhD/Honours/Masters
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leader: Prof Caroline Gargett, Dr Caitlin Filby
Email: caroline.gargett@hudson.org.au

Project description: Women with endometriosis and adenomyosis suffer for up to 10 years in pain before a diagnosis is made. This is in part due to lack of a non-invasive diagnostic test. Endometriosis affects 10% of girls and women and is characterised by lesions of endometrial tissue form throughout the pelvic cavity, causing pain, disease and infertility. Adenomyosis is a related condition where lesions form within the myometrial layer of the uterus. This project will build upon our novel findings that menstrual fluid may serve as a novel non-invasive diagnostic for endometriosis and adenomyosis. The project involves quantitation and functional characterisation of endometrial stem/progenitor cells and plasma proteins. Techniques include tissue culture, flow cytometry, ELISA, and immunofluorescence. Techniques employed can be tailored to suit the interests of the student. This project has international funding.

If no lab access can be granted because of COVID-19 lockdown measures, a systematic review of available studies will be carried out, and own data will be analysed

Keywords: Endometriosis, flow cytometry, stem cells, diagnostics
Women’s Health

Preparing endometrial mesenchymal stem cells for clinical application by defining molecular pathways using integrated sequencing technologies

**Suitability:** PhD  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project Leaders:** Prof Caroline Gargett, Dr Saedeh Darzi, Dr Caitlin Filby  
**Email:** caroline.gargett@hudson.org.au

**Project Description:** Pelvic organ prolapse (POP) is a debilitating condition affecting 1 in 4 women. It results from incomplete repair of pelvic tissues following vaginal birth which often progresses to POP years later. We are developing tissue engineering approaches using endometrial mesenchymal stem cells (eMSC) we discovered together with nanomaterials to treat and prevent POP. As we prepare our eMSC for clinical translation, we need to ensure the novel culture methods we have developed are safe. This project will use integrated ATAC-seq (Assay for Transposase-Accessible Chromatin using sequencing) and RNA-seq in serum-free culture media containing a unique small molecule inhibitor that keeps the eMSC in the undifferentiated state.

This project will reveal the changes in the transcriptional landscape and gene pathways involved in maintaining eMSC self-renewal, the reversibility of this culture method and any oncogene activation, generating safety and mechanistic data for applying to regulatory authorities for licencing our eMSC product for clinical use in treating and preventing POP. This project has NHMRC funding and will provide an opportunity to develop skills in molecular sequencing, analysing vast quantities of data and interact with bioinformatic collaborators at Warwick University, UK. Other techniques are primary cell isolation, eMSC purification and culture, flow cytometry, PCR, cell proliferation and apoptosis assays.

**Keywords:** endometrial mesenchymal stem cells; tissue engineering, pelvic organ prolapse; women’s health; RNAseq, ATACseq

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Nanostructured and 3D Bioprinted Cellular Surgical Constructs for Pelvic Organ Prolapse Treatment

**Suitability:** Honours/PhD  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project Leaders:** Dr Shayanti Mukherjee, Prof Caroline Gargett, Prof Jerome Werkmeister, A/Prof Anna Rosamilia  
**Email:** caroline.gargett@hudson.org.au

**Project Description:** Pelvic organ prolapse (POP) results from childbirth injury, affecting 25% of all women. It causes bladder, bowel and sexual dysfunction. POP is treated by surgery, frequently augmented by mesh, but failure and complication rates are high. We are investigating regenerative medicine approaches to improve treatment outcomes using cell-based therapy delivered in novel degradable biomaterials. To this end we have designed nanomeshes and 3D printed meshes which are boosted with therapeutic human endometrial mesenchymal stem cells (eMSC). There are 3 projects available to examine the effect of using these bioengineered constructs as surgical implants in animal models.

1. The first project looks at the foreign body response to implanted meshes in aged parous sheep
2. The second examines the effect of varying design aspects of 3D printing such as porosity, mesh fiber thickness etc. on the surgical performance of meshes.  
3. We are also examining the biomechanics of the tissues at the nanoscale using atomic force microscopy to understand the overall strength of the tissues after treatment.

This project is supported by NHMRC funding  

**Keywords:** 3D Printing, Nanofabrication, Cell culture, Flow cytometry, histological, immunofluorescence and confocal microscopy, biochemical and biomechanical analyses will be undertaken.
Women’s Health

Decoding the significance of endometriosis risk

**Suitability:** Honours/PhD/Masters  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project Leaders:** Prof Caroline Gargett, Dr Caitlin Filby  
**Email:** caroline.gargett@hudson.org.au

**Project description:**  
Endometriosis is a devastating chronic disease affecting 10% of girls and women, where cells of endometrial histology form lesions throughout the pelvic cavity, causing pain, disease and infertility. The causes are unknown, although genetic risk plays a role. Current treatments are often ineffective with side effects. Recent work by us and our collaborator Prof Grant Montgomery at UQ (Sapkota, 2017) indicate that endometrial stem/progenitor cells may cause lesion formation and this may be due to single nucleotide polymorphisms (SNPs) in over 14 regions of the genome that are associated with increased risk of endometriosis. This project aims to decode the biological significance of these SNPs in endometriosis by isolating stem/progenitor cell populations in women with endometriosis. The study will use tissue culture, fluorescent activated cell sorting, organoid culture and single cell RNA sequencing, mouse models. Techniques employed can be tailored to suit the interests of the student. This project has international funding.

*If no lab access can be granted because of COVID-19 lockdown measures, a systematic review of available studies will be carried out, and own data will be analysed.*

**Keywords:** Endometriosis, organoids, single cell sequencing, stem cells, genetics

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Endometrial mesenchymal stem/stromal cell strategies to modulate the immune system for treating inflammatory diseases

**Suitability:** Honours/PhD  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project Leaders:** Dr Shanti Gurung, Prof Caroline Gargett, Prof Jerome Werkmeister  
**Email:** shanti.gurung@hudson.org.au or caroline.gargett@hudson.org.au

**Project Description:** We discovered endometrial mesenchymal stem/stromal cells (eMSC) in the highly regenerative lining of the uterus. We have also developed a reproducible protocol using a small molecule regulator to manufacture large doses of safe culture-expanded eMSC whilst retaining their potency. With comprehensive RNA-sequencing analysis and functional and protein studies, we found that eMSC have angiogenic, antifibrotic and immunomodulatory properties. We also identified eMSC’s potential for intercellular communication via exosomes, nanoparticle vesicles containing proteins, RNA, miRNA, which are one of the most efficient cellular messengers. Graft Versus Host Disease (GvHD) is a serious life-threatening complication allogeneic (non-self) organ/tissue/cell transplantation. We are investigating the application of eMSC in modulating inflammation using in vitro and a mouse model of GvHD. This project will use co-culture of eMSC/ exosomes with immune cells and a mouse model of GvHD.

**Methods:** cell culture, primary human cell isolation (eMSC and immune cells), exosome isolation (ultracentrifugation) and characterisation using ExoView R100, Mass spectrometry proteomics, RNA/micro RNA sequencing, bioinformatics, flow cytometry, protein arrays, immunohistochemistry, mouse surgeries.

**Keywords:** endometrial mesenchymal stem cells, exosomes, bioinformatics, immunoregulation, GvHD, cell transplantation
Women’s Health

Endometrial organoids: novel tools for precision gynaecological medicine

**Suitability:** Honours/PhD/Masters  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project Leaders:** Prof Caroline Gargett, Dr Caitlin Filby  
**Email:** caroline.gargett@hudson.org.au

**Project description:**  
Organoids are miniature organs cultured in a dish that enable disease modelling and development of precision medicine. This project will utilize this exciting tool to generate organoids from human and mice to study endometrial stem cell biology and its role in the formation of endometriosis. Endometriosis is a disease affecting 10% of women, where by endometrial cells form lesions in pelvic cavity, causing pain, disease and infertility. This project will generate a new system for investigating the causes of endometriosis and a patient-derived biobank for disease phenotypic profiling, drug discovery and precision medicine. Techniques include tissue culture, organoids, fluorescence activated cell sorting, in vitro assays, immuno-fluorescence and mouse models. Techniques employed can be tailored to suit the interests of the student.

*If no lab access can be granted because of COVID-19 lockdown measures, a systematic review of available studies will be carried out, and own data will be analysed.*

**Keywords:** Endometriosis, flow cytometry, stem cells, diagnostics, organoids, precision medicine

Tissue clearing microscopy in endometrium and uterine fibroids

**Suitability:** Honours/Masters/PhD  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project Leaders:** Dr Thomas Tapmeier, Prof Caroline Gargett  
**Email:** thomas.tapmeier@monash.edu

**Project description:** Immunohistochemistry is an established method to identify cell types in Pathology. However, the sectioning of tissues means that the three-dimensional context is lost, and has to be reconstructed painstakingly from individual sections. New microscopy techniques such as tissue clearing microscopy (Susaki 2015) allow for the preparation of tissue blocks and imaging in three dimensions, thus delivering a comprehensive picture of the arrangement of cells of various type within the tissue. In addition, tissue architecture, often an important feature of pathophysiology, is preserved. However, the constituent parts of different tissues demand differential treatment before tissue clearing microscopy is possible. Fatty tissues for example are easily cleared by removing the lipid compartment of the tissue constituents, whereas collagen-rich tissues are proving challenging to clear so far. We have carried out initial experiments on imaging in uterine fibroids, collagen-rich benign tumours of the myometrium, and this project will optimise buffer conditions and identify cell types within the cleared tissue blocks by immunofluorescence staining.

**Methods:** tissue preparation, two photon microscopy, light sheet microscopy, immunostainings (immunofluorescence), image analysis.

**Keywords:** Imaging, tissue clearing microscopy, light sheet microscopy, immunofluorescence
Women’s Health

Exosome population concordance within sample species

Suitability: Honours/Masters/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Thomas Tapmeier, Dr Shanti Gurung, Prof Caroline Gargett
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Project description: Exosomes are small, nanosized vesicles produced by most cells and readily found in bodily fluids which carry surface markers and genetic material from their cell of origin (Colombo 2014). This makes exosomes an attractive candidate diagnostic and therapeutic tool, and they have recently seen increased attention as potential biomarkers for diseases such as obesity and diabetes, pre-eclampsia, and cancer.

Endometriosis is a disease affecting up to 10% of women of reproductive age and characterized by menstrual and non-menstrual pain, often aggravated during and after coitus. Additionally, up to half of women with endometriosis experience a degree of infertility, as well as mental health issues and fatigue (Zondervan 2018). No clinically relevant biomarker is available. We recently isolated exosomes from peritoneal fluid with a view to investigating these as potential biomarkers (Nazri 2020). Peritoneal fluid is not readily available as a sample, and peripheral or menstrual blood would be easier to obtain. However, it remains unclear how the exosome populations within different sample fluids relate, and whether there is an exchange between exosomes within the peritoneum and peripheral and menstrual blood.

This project will investigate exosomes in peritoneal fluid and peripheral and menstrual blood within the same patients in order to determine the potential of exosomes isolated from one or the other fluid as biomarkers. A mouse model of endometriosis will be set up to test our hypotheses in vivo.

Methods: Cell culture, exosome isolation, ultracentrifugation, nanosight tracking analysis, Exoview immunocapture analysis, immunoblotting, RNA extraction, proteomics, microarrays. For PhD candidates: mouse model of endometriosis.

Keywords: Exosomes, endometriosis, biomarkers.

Metformin for ovulation induction in women with polycystic ovarian syndrome

Suitability: Honours, BMedSc
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Rui Wang Prof Ben Mol
Email: rui.wang@monash.edu

Project description: Polycystic ovary syndrome is one of the most common conditions in women of reproductive age. Insulin resistance is common in PCOS, and can augment excess local ovarian androgen production, resulting in premature follicular atresia and anovulation. Therefore, metformin, an insulin-sensitising medication, has been proposed treating in ovulation induction. While metformin has been most widely studied in PCOS with a reassuring safety profile, its effectiveness in improving reproductive outcomes has been controversial for decades. Existing randomised controlled trials (RCTs) comparing metformin versus clomiphene have shown conflicting results. The conclusion of the latest Cochrane systematic review based on aggregate data was inconclusive due to high heterogeneity between these trials.

Given the heterogeneous nature of the study population as well as the variations in reporting, it is impossible to undertake reliable subgroup analysis to identify who benefits most from metformin or clomiphene. In addition, subgroup analysis based on aggregate data is prone to ecological bias. Individual participant data meta-analysis (IPDMA) has the potential to overcome the above-mentioned problems by standardising the inclusion/ exclusion criteria and harmonising the subgroup choice and statistical analysis (14). It has been considered the gold standard for evidence synthesis. The project is based upon our previous work with the International Ovulation Induction IPDMA Collaboration.

In this project, the candidate will perform an IPDMA, compare the effectiveness of metformin versus clomiphene via a personalized approach.

Keywords: polycystic ovary syndrome, infertility, ovulation induction, metformin, clomiphene, Individual participant data, meta-analysis.
**Women’s Health**

**Assessing the Beneficial Effects of Antioxidants**

**Suitability:** Honours/PhD  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project leaders:** Dr Sarah Marshall, Prof Euan Wallace  
**Email:** sarah.marshall@monash.edu

**Project description:** Early in pregnancy, the maternal vasculature undergoes dramatic adaptations to help support both the mother and the developing baby throughout pregnancy. However, failure of the maternal vasculature to fully adapt can result in the pregnancy disease known as pre-eclampsia (PE). PE affects approximately 1/20 pregnancies and is a leading cause of maternal and fetal morbidity and mortality worldwide. Unfortunately, disease severity often results in premature babies. Recently, it has become apparent how important the maternal vasculature is for disease development, making it a target to alleviate the clinical symptoms of PE and prolong pregnancy.

Cruciferous vegetables, such as broccoli, provide a variety of beneficial health effects. So far, evidence suggests that novel compounds found in green leafy vegetables may have beneficial affects throughout the body, including the vasculature. Therefore, this project aims to identify whether these extracts can promote systemic health and be potential novel treatments for women with pre-eclampsia. This project will specifically explore the placental and vascular effects.

**Key words:** pregnancy; pre-eclampsia; placenta; vascular dysfunction; wire myography; vascular reactivity

**Assessing survival and viability of human placental (trophoblast) cells**

**Suitability:** Honours  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project leader:** Dr Sarah Marshall  
**Email:** sarah.marshall@monash.edu

**Project description:** Preeclampsia is a pregnancy disorder characterised by hypertension with proteinuria, maternal organ dysfunction or fetal growth restriction. Each year preeclampsia is the cause of death in over 60,000 women and in more than 500,000 babies globally. The pathophysiological mechanisms underlying the disease are not entirely clear, however we do know that placental (trophoblast) cells are major contributors to this disorder. Therefore, the trophoblast cells of the placenta are very important research tools to help us better understand preeclampsia and to help us identify potential treatments for this disorder.

This project will involve the collection and culturing of trophoblast cells from the placenta of women undergoing elective caesarean. Then, survival and viability of these cells will be assessed after treatment with new compounds that could be future treatments for preeclampsia.

**Key words:** Pregnancy, preeclampsia, placenta, trophoblast, cell culture
Reducing stillbirth in Victoria

**Suitability:** Honours/Masters by Research

**Location:** Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton

**Project Leaders:** Dr Miranda Davies-Tuck, Dr Mary Ann Davey

**Email:** miranda.davies@hudson.org.au

**Project description:**

Every day six women in Australia have a stillborn baby. This number hasn’t changed very much over the past 20 years. We - the Department of Obstetrics and Gynaecology - together with Safer Care Victoria in the Department of Health and Human Services are key partners in a national effort to reduce stillbirth. We are leading investigators in the Australian Stillbirth Centre for Research Excellence (Stillbirth CRE), an NHMRC-funded initiative and I am Victoria’s representative on the Commonwealth government’s stillbirth action plan steering committee. There is an urgency to make stillbirth less common in Australia. We would love you to join us in achieving that.

There are a range of projects on offer - these include population-based and clinical epidemiology studies, evidence synthesis (e.g. systematic reviews and meta-analysis) and basic science laboratory studies using human tissue to explore the drivers for stillbirth and the impact of interventions to uncover new approaches to improve care for women for tomorrow.

**Keywords**

obstetrics, stillbirth, public health, big data, pregnancy, labour, women’s health, perinatal, mortality

Reducing preterm birth

**Suitability:** PhD/Masters/Honours

**Location:** Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton

**Project Leaders:** Dr Mary Ann Davey, Dr Kirsten Palmer

**Email:** mary-ann.davey@monash.edu

**Project description:**

Preterm birth remains a major cause of perinatal mortality and long-term morbidities. It remains one of the greatest medical challenges of our time. Reducing preterm birth a health priority. Led by the Department of Obstetrics and Gynaecology at Monash University, Victoria is a member of the Australian Preterm Birth Prevention Alliance. The goal of the Alliance is to reduce preterm across Australia. At Monash, we are leading the charge for Victoria. Come and join us. Be part of the most important movement in obstetrics in the country. In collaboration with Safer Care Victoria, there are a number of projects looking at the best way to reduce preterm birth. Our research is shaping how government supports and drives change in clinical care. The research is based at Monash Medical Centre and in Safer Care Victoria, Department of Health in the city (Lonsdale Street).

**Keywords:** preterm, premature, perinatal, birth, pregnancy, labour, fetus, newborn, baby, paediatrics, obstetrics, NICU
Women’s Health

Usefulness of clinical research in Obstetrics & Gynaecology

Suitability: PhD
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leaders: Prof Ben Mol
Email: ben.mol@monash.edu

Project description:
Blue-sky research cannot be easily judged on the basis of practical impact, but clinical research is different and should be useful. It should make a difference for health and disease outcomes or should be undertaken with that as a realistic prospect. Ioannides showed that many studies, even in the major general medical journals, do not satisfy these features, and very few studies satisfy most or all of them. Most clinical research therefore fails to be useful not because of its findings but because of its design.

In this project, we will assess the usefulness of clinical research in Women’s health. We will study the problem base, context placement, information gain, pragmatism, patient centeredness, value for money, feasibility, and transparency of papers published in high ranked journals. This information could fuel an altered approach which could easily produce more clinical research that is useful, at the same or even at a massively reduced cost.


Keywords
Obstetrics, Gynaecology, Women's Health

Quality and integrity of randomized controlled trials: systematic review of a sample of studies

Suitability: BMedSc
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leaders: Prof Ben Mol, Dr Wentao Li
Email: ben.mol@monash.edu

Project description:
Randomized controlled trials (RCTs) provide the most reliable information to guide clinical practice. We regrettably came across a number of RCTs concerning important clinical topics published in top rank journals having critical issues with respect to randomization, analysis, reporting, and feasibility. In the view of the rapidly growing number of RCTs and a high proportion of RCTs yielding positive findings, it is critical to ensure the quality and data integrity of RCTs. However, little attempts have been made to systematically evaluate the quality of published RCTs.

Research aims: We aim to systematically review the quality and data integrity of a sample of RCTs published in top journals of Obstetrics and Gynaecology in the last five years.

Keywords
Randomised controlled trials, systematic review, data integrity, quality assessment
Women's Health

Reporting of non-inferiority trials in reproductive medicine

Suitability: Honours, BMedSc
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Rui Wang Prof Ben Mol
Email: rui.wang@monash.edu

Project description:
A non-inferiority trial aims to evaluate whether a new treatment is not worse than a standard treatment by more than an acceptable amount, while the new treatment has other advantages, such as greater availability, less expensive, less invasive and/or fewer side effects. Non-inferiority trials require more care on the design, analyse and report. Poor conduct and reporting could be associated with misleading conclusions, resulting in research waste and misguidance of clinical practice. In reproductive medicine, non-inferiority trials are frequently used to assess new treatment strategies. In this project, the candidate will systematically search and critically appraise the reporting of published non-inferiority trials in reproductive medicine.

Keywords
reproductive medicine, clinical trials, non-inferiority, new treatment, systematic review, treatment assessment

Individual methods for induction of labour

Suitability: PhD, Honours, BMedSc, Masters
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Wentao Li, Prof Ben Mol
Email: wentao.li@monash.edu

Project description:
About 1 in 3 pregnant women have an induction of labour (IOL). However, 1 in 5 IOLs fail to result in vaginal birth and different methods for IOL may carry different risks for mothers and their babies. Identifying optimal methods of IOL has strong implications for the well-being of women and babies. Existing evidence is inconclusive in establishing optimal methods for IOL. To date, there is no consensus on which IOL methods are most effective and safe, and in which, resulting in wide practice variation that exposes some women and babies to less effective and/or riskier IOL methods. A one-solution-fits-all approach has been applied in previous studies on IOL. There is a lack of consideration for the variability of women’s individual characteristics and it was generally assumed that any method for IOL works in the same way for all women, which is unlikely. Little attention has been paid to personalised medicine that customises options of IOL methods to patient subgroups.

Study aim: To generate personalised evidence for women with different characteristics, which will be translated into tools to aid in IOL decisions by tailoring to individual circumstances. Methods and techniques Individual participant data (IPD) meta-analysis and network meta-analysis using IPD. Why us? We are an internationally recognised clinical research team in obstetrics and gynaecology with impactful outputs that change and define the modern practice. Students who work with us apply cutting-edge methods to address important questions and have the opportunities to interact and collaborate with eminent researchers in this field around the world. Experts in epidemiology and statistics offer critical methodological support to research projects in our team. Why this project? This is a large-scale clinical research project that involves multiple comparisons. Students could lead parts of the project. The infrastructure of the project is well-established including the IPD international collaboration, statistical expertise, and administrative support. This research may improve the well-being of millions of women and babies around the world each year. Previous students who worked on this topic, being first authors, have successfully published original papers in leading journals. Join us to perform research that changes the world.

Keywords
clinical research; obstetrics; meta-analysis; evidence-based practice; induction of labour; personalised medicine; precision medicine; individual participant data; randomised controlled trial
Women’s Health

PhD in Clinical Epidemiology in women’s health

Suitability: PhD
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leaders: Prof Ben Mol, Dr Wentao Li
Email: ben.mol@monash.edu

Project Description:
The overall PhD program will focus on addressing undetermined evidence for clinical practice in women’s health. This aim will be achieved through clinical research on major questions with appropriate design and robust methodology. The candidate will identify knowledge gaps and opportunities to promote evidence that guides practice. These gaps will be identified through comprehensive reviews of the quality and credibility of current clinical research on major topics. These gaps will be addressed through the application of new research with state-of-the-art methodology, informed by stakeholder engagement.

Keywords
clinical epidemiology, evidence-based clinical practice, quality review of clinical research, public health

Towards evidence-based clinical management in reproductive health

Suitability: PhD, Masters by Research
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leaders: Prof Ben Mol, Dr Wentao Li
Email: ben.mol@monash.edu

Project Description:
One in six couples at reproductive age suffer from infertility. Optimising clinical managements for couples with infertility based on high-quality evidence is critical in improving reproductive health outcomes for these couples. The overall PhD program will focus on addressing undetermined evidence for clinical practice in reproductive health. This aim will be achieved through large-scale evidence synthesis projects on major questions with state-of-the-art next-generation evidence synthesis methodology, including network meta-analysis and individual participant data meta-analysis. The candidate will identify knowledge gaps and opportunities to promote evidence that guides practice. These gaps will be identified through comprehensive reviews of the quality and credibility of current clinical research on major topics. These gaps will be addressed through the application of new research with state-of-the-art methodology, informed by stakeholder engagement.

Keywords
Evidence-based medicine, reproductive health, reproductive medicine, meta-analysis, infertility, evidence synthesis, epidemiology
Fetal & Neonatal Health: Respiratory and Cardiovascular

Transition to Life After Birth

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Stuart Hooper, Dr Kelly Crossley, Dr Erin McGillick
Email: Kelly.crossley@hudson.org.au

Project Description: The transition to life after birth is one of the greatest physiological challenges that humans face. At birth, the airways are cleared of liquid, to allow the entry of air, which increases pulmonary blood flow and closes vascular shunts that pass the lungs during fetal life. Most infants smoothly make this transition, but many don't which can be life threatening and cause life-long problems.

The aim of this project is to study the changes that occur at birth and to identify factors that both facilitate and impede these changes to reduce the risks that newborn infants face.

Imaging the Entry of Air into The Lungs at Birth

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Stuart Hooper, Dr Erin McGillick
Email: erin.mcgillick@hudson.org.au

Project Description: The transition to air-breathing at birth is dependent upon airway liquid clearance which allows gas exchange to commence. This occurs smoothly in most infants, but preterm infants have difficulty in clearing their lungs of liquid. Using a synchrotron, we can image the entry of air into the lungs at birth and the simultaneous changes in blood flow to the lungs. The aim of this project is to identify factors that promote air entry into the lungs and the increase in pulmonary blood flow at birth to improve the transition to newborn life.

Preventing Lung Disease in Very Premature Babies

Suitability: Honours, PhD, BMedSc(Hons)
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: A/Prof Megan Wallace and Prof Stuart Hooper
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Phone: 03 8572 2812 (A/Prof Wallace)

Project description: Very premature babies are born with immature lungs, so they often need respiratory support. However, this can injure their lungs and lead to abnormal lung development called bronchopulmonary dysplasia (BPD). There are no treatments to prevent or reverse BPD, because the mechanisms leading from injury to abnormal lung development are not known. We have recently identified several factors that are activated by injury and that may lead to BPD suggesting they could be future therapeutic targets to prevent BPD. This project will involve studies using molecular techniques to manipulate these factors in premature rabbits.

Keywords
Preterm birth, lung development, bronchopulmonary dysplasia, respiratory support
Fetal & Neonatal Health: Respiratory and Cardiovascular

**Improving breathing of preterm newborns exposed to inflammation during pregnancy**

**Suitability:** Honours/PhD  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project Leaders:** A/Prof Graeme Polglase, Dr Vanesa Stojanovska  
**Email:** graeme.polglase@monash.edu and vanesa.stojanovska@hudson.org.au  
**Phone:** 03 8572 2822 (A/Prof Polglase) 03 8572 2797 (Dr Stojanovska)

**Project Description:** Preterm babies exposed to inflammation during pregnancy have a high incidence of breathing difficulties and brain injury, which often lead to cerebral palsy. Many of these babies will require invasive respiratory support at birth, and whilst this is life-saving, it can exacerbate the already ongoing inflammation, and worsen brain injury.

Our current research focuses on how intrauterine infection and inflammation (chorioamnionitis) affects the neural control of respiration, and whether anti-inflammatory treatments can protect these nerves and improve fetal and neonatal breathing. This project involves work with small and large animal models, fetal/neonatal physiology, protein and molecular techniques, histology, immunohistochemistry and microscopy.

**Improving the transition at birth in asphyxiated infants**

**Suitability:** Honours/PhD  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project Leaders:** A/Prof Graeme Polglase, Prof Stuart Hooper  
**Email:** graeme.polglase@monash.edu  
**Phone:** 03 8572 2822 (A/Prof Polglase)

**Project Description:** Approximately 9000 newborns die in developing countries every day because of asphyxia – 30-50% die on their birthday. Approximately 13% of infants that require resuscitation at birth actually have access to the appropriate facilities to receive this life-saving intervention. There is therefore a critical need to develop simple and translatable strategies that improve the transition at birth for asphyxiated infants.

Our current research is focused on improving the transition at birth for asphyxiated preterm and term infants. This involves investigating the utility of delayed cord clamping, cord milking and improving resuscitation strategies including chest compressions delivery, with the ultimate aim of identifying strategies directly translatable to the developing world, which significantly reduces death and disability in this population. The experiments include whole-animal physiology, molecular biology and immunohistochemistry.
Fetal & Neonatal Health: Respiratory and Cardiovascular

Reducing the risk of pulmonary hypertension in infants with a congenital diaphragmatic hernia

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Kelly Crossley, Prof Stuart Hooper, Dr Beth Allison
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Project Description: This project focuses on congenital diaphragmatic hernia (CDH), a birth defect characterised by a failed closure of the diaphragm, creating a continuity between the thoracic and abdominal cavities. As a result, there is displacement of abdominal organs into the chest and this limits the space for the lungs to develop in the fetus. This leads to small lungs with abnormal airways and vessels, a condition called lung hypoplasia.

Whilst in utero, lung hypoplasia is not a problem as the fetus receives oxygen via the placenta, but immediately after birth is potentially lethal. It often results in respiratory insufficiency requiring respiratory support with invasive mechanical ventilation and is complicated by persistent pulmonary hypertension of the newborn (PPHN). The latter is caused by a smaller cross-sectional area of the lung vasculature combined with raised vascular tone due to increased muscularisation of the vessels. Overall, postnatal mortality of CDH is high (30-40%) and is significantly worse when complicated with severe PPHN (up to 56%).

There is an urgent need to mitigate the effects of PPHN and improve outcomes for infants born with CDH. We believe that by optimising the transition period immediately after birth we could significantly reduce the risk of pulmonary hypertension. We propose further pre-clinical studies that will answer fundamental questions about the management of the transition period for these challenging infants.

Evaluating the outcomes of undergraduate medical and biomedical student research

Suitability: Honours, BMedSc(Hons)
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: A/Prof Megan Wallace and A/Prof Tim Cole
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Phone: 03 8572 2812 (A/Prof Wallace)

Project Description: Undertaking a research Honours degree is widely considered to develop conceptual, strategic and critical thinking skills, analytical, presentation and communication skills, to result in published journal articles and to provide a competitive career advantage. Despite this widely held belief, there is very little definitive data to support these assumptions. A long-term outcomes survey of Honours students and supervisors will capture this information for the first time.

Aim 1. Evaluate the student learning experience and determine whether it has translated into: ongoing utilisation of critical thinking and research skills, ongoing involvement in research and attainment of higher career positions and salaries, by Monash medical and biomedical science graduates, 2, 5 and 10 years after graduating with Honours compared to Course and year-level matched graduates who did not undertake a research Honours.

Aim 2. Determine the research outputs (publications, presentations, changes to policy or practice etc) of Monash medical and biomedical science graduates 2, 5 and 10 years after graduating with BMesSc (Hons) or BMS(Hons) compared to Course and year-level matched graduates who did not undertake a research Honours year.
Fetal & Neonatal Health: Respiratory and Cardiovascular

NICU emergencies: frequency, risk factors, causes and potential treatments

Suitability: Honours/PhD/BMedSci
Location: The Ritchie Centre, Department of Paediatrics, Monash Medical Centre, Clayton
Project Leaders: Dr Doug Blank, Dr Calum Roberts
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Project Description: There is no appropriate algorithm for neonatal emergencies that occur in the neonatal intensive care unit (NICU). NeoResus, and other neonatal resuscitation guidelines, cover management at birth, as the newborn initiates breathing air. However, this is only relevant for the first minutes after birth and there is little data and guidance of what are the common emergencies in the NICU and how we should respond. The paediatric advanced lifesaving algorithms are not likely relevant to the hospitalised neonate, either.

We propose a prospective observational study and documentation of all emergency events in the NICU and special care nursery at Monash-Clayton. We will video record all buzzer events and examine the video and data from the patient’s monitor. We will review the causes, responses, and solutions to the emergency. The first goal of the project is to characterise when, who, and what are the nature of the emergencies. Subsequently, we aim to develop and test protocols to address NICU emergencies.

The Baby Directed Umbilical Cord cutting physiology study: a randomised controlled trial (Baby-DUCC)

Suitability: Honours/BMedSci
Location: The Ritchie Centre, Department of Paediatrics, Monash Medical Centre, Clayton
Project Leaders: Dr Doug Blank, Dr Calum Roberts Prof Stuart Hooper, Prof Peter Davis (External)
Email: doug.blank@hudson.org.au, calum.roberts@monash.edu

Project description:
Over 5% percent of all infants born worldwide will need help breathing after birth, including up to 12% of infants born under emergency conditions in Victoria. Currently, resuscitation guidelines state if an infant is not breathing after birth, the umbilical cord should cut so that the infant can be moved to a resuscitation platform where the clinician breathes for the infant by pushing air and oxygen into the newborn’s lung (positive pressure ventilation or PPV). Studies show that clinicians need 2 minutes to provide effective PPV. During that delay, the compromised infant is not receiving oxygen and the infant’s heart rate typically falls to a dangerously low rate.

We hypothesise that the compromised infant who needs help after birth will benefit from remaining connected to their mother and their placenta via the umbilical cord while a clinician is helping the infant breathe. Maintaining the connection with the mother and the placenta through the umbilical cord provides the non-breathing infant fresh oxygen and good blood flow from the placenta while the infant is struggling to breath.

We believe that improved oxygen levels and a normal heart rate in the first minutes of life may decrease the risk of death and significant brain damage in the newborn who isn’t breathing well. Birth asphyxia, or failure to initiate and sustain spontaneous breathing at birth, claims the lives of more than 800,000 infants every year, most of these infants die in resource limited countries. In large interventional studies, implementation of simple resuscitation techniques, dropped the rates of death from birth asphyxia by over 40%.

Ventilation prior to umbilical cord clamping, or Baby-Directed Umbilical Cord Clamping (Baby-DUCC) may offer the next step in reducing the rates of death from birth asphyxia even further. The purpose of our trial is to prove that Baby-DUCC provides a physiological advantage over the current standard of care. We are seeking a high-motivated student to help run the trial, including recruit and consent eligible patients, attend births to ensure adherence to the trial protocol and collect data, and analyse and present the data. We also will mentor our student to generate a novel "side-study" using data collected in the Baby-DUCC RCT.

We will support our student from development of the side-study idea through the manuscript submission process until successful publication. In the media: https://www.smh.com.au/national/baby-s-first-breath-could-wait-a-minute-if-study-strikes-right-cord-20180524-p4zha9.html

Keywords
Neonatal resuscitation, delayed cord clamping, randomised controlled trial, neonatal emergency, obstetric emergency, respiratory support
Fetal & Neonatal Health: Respiratory and Cardiovascular

Can we assess the need for resuscitation based on general appearance of the newborn?

Suitability: Honours/PhD/BMedSci
Location: The Ritchie Centre, Department of Paediatrics, Monash Medical Centre, Clayton
Project Leaders: Dr Doug Blank, Dr Calum Roberts
Email: doug.blank@hudson.org.au, calum.roberts@monash.edu

Background: Over 5% of all babies born worldwide need help breathing at birth. Failing to establish breathing after birth, claims the lives of more than 800,000 babies every year, accounting for 25% of neonatal deaths. After birth, the newborn must rapidly transition from having a liquid-filled lung and being dependent on the placenta for oxygen to an aerated lung that can successfully exchanges respiratory gases. Over 90% of very preterm infants (VPTIs, born at <32 weeks’ gestational age) require assistance breathing at birth despite 90% of these infants breathing spontaneously within 1 minute. However, this breathing effort is not maintained and one-third of VPTIs are intubated for mechanical ventilation in the delivery room, which increases the risk of death, chronic lung disease and long-term neurodevelopmental impairment. A better understanding of lung aeration and interventions that enhance spontaneous breathing efforts of VPTIs at birth will improve outcomes.

Project Description: Is the initial assessment of premature baby accurate, specifically tone? This is an observational study using videos of very premature infants from the “Nasal versus facemask CPAP for initial respiratory support in very term infants, an RCT,” (ANZTRN1260001086954, http://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=380186&isReview=true) to test tone as a signal for respiratory effort and spontaneous breathing. Facemask CPAP has a high risk of failure in the delivery room because the technique is difficult and pressure to the newborn’s face may cause apnoea, vocal cord closure, and bradycardia.

The vast majority of very preterm infants (born at <32 weeks gestational age) will need help breathing after birth, but will breath spontaneously, which was not previously appreciated until recent publications. We hypothesise that nasal CPAP may be superior to facemask CPAP to maintain adequate respiratory effort because nasal CPAP can be applied as quickly and easily as facemask CPAP, but does not require the same dexterity to avoid mask leak or excessive pressure to the infant’s face.

Current neonatal resuscitation guidelines include complex algorithms that compensate for failure of facemask CPAP by providing PPV at potentially injurious inflation pressures, exposure to toxic levels of oxygen, and performing emergent intubations in difficult conditions on unstable newborns followed by mechanical ventilation. If our study hypothesis is proven correct, we anticipate changes to neonatal resuscitation guidelines and improved outcomes for babies born at <32 weeks because of less exposure to PPV, hyperoxia, emergent intubation, and mechanical ventilation during neonatal resuscitation.

We will create a focused 30 second, blinded clip of the baby immediately after being placed on the resuscitation table. Blinded assessors rate the baby’s tone as 0, 1, or 2. Three groups of preterm infants are created and outcomes are measured: initial HR, initial SpO2, need for PPV, maximum oxygen, maximum PIP, DR intubation, surfactant, etc.

Prospective students will also help recruit and enrol patients in the RCT and be exposed to neonatal intensive care, joining rounds and teaching sessions as appropriate.

Keywords: neonatal resuscitation, apnoea, respiratory drive, positive pressure ventilation (PPV), continuous positive airway pressure (CPAP), video review
Fetal & Neonatal Health: Brain Injury and Neurodevelopment

Using heart rate variability to predict clinical disease in preterm babies

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: A/Prof Flora Wong, Prof Rosemary Horne, Dr Stephanie Yiallourou
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Project Description: The early clinical signs of diseases in the preterm baby in the neonatal intensive care unit (NICU) are often very subtle and difficult to detect. However, once the infection or disease is developed, the preterm baby often deteriorates and becomes sick very rapidly. We aim to develop a new method using heart rate variability (HRV) to detect early clinical diseases. HRV is a measure of the beat-to-beat variation in time between each heartbeat. This variation is controlled by an important part of the nervous system called the autonomic nervous system (ANS). Our project will assess HRV as a non-invasive way to identify changes in the clinical condition of the preterm baby. We have recently acquired a clinical research software known as ICM+, developed at Cambridge University. The ICM+ software offers data collection and real-time analysis, facilitating personalised medicine. ICM+ can be connected to our bedside monitors in the NICU and perform continuous analyses of the HRV in real-time, on multiple babies simultaneously.

We propose that continuous HRV can be used to assess well-being of the preterm babies in NICU, detect early infections and predict bleeding in the brain.

RESEARCH PLAN: In preterm babies born at ≤28 weeks of gestation, the ECG recording from the NICU cot side monitor will be continuously analysed for HRV in the first 4 weeks of life, using the ICM+ software. Clinical records of the babies will be examined to determine periods of when the baby was clinically stable and when the baby suffered from infection and/or developed bleeding in the brain.

Keywords: Prematurity, heart rate variability, infection, brain injury

Ganaxolone: A New Treatment for Neonatal Seizures

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research: Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Tamara Yawno, Prof Suzie Miller, Dr Michael Fahey
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Phone: 03 8572 2796 (Prof Miller)

Project Description: Seizures in neonates are relatively common; they are powerful predictors of long-term cognitive and developmental impairment. There is also a significant concern about current anti-seizure therapies, which can cause brain injury as they have the potential to be neurotoxic. We will investigate the effects of the synthetic GABAA agonist ganaxolone, or phenobarbitone given at the onset of seizure in term fetal sheep caused by hypoxia ischemia. This project will utilise our established fetal sheep model, with state-of-the-art monitoring equipment to investigate brain activity and brain histopathology.

Keywords: ganaxolone, neonatal seizures, brain injury, new born, brain activity.
Fetal & Neonatal Health: Brain Injury and Neurodevelopment

Improving functional deficits associated with fetal growth restriction

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Suzie Miller, Dr Emily Camm, Dr Amy Sutherland
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Phone: 03 8572 2796 (Prof Miller)

Project Description: Fetal growth restriction (FGR) is a serious, but common pregnancy complication, describing the infant that is born very small due to failure to achieve normal growth. FGR is present in up to 9% of pregnancies in Australia, and is strongly associated with complications after birth, including brain injury that underlies the motor deficits associated with cerebral palsy or, more subtle but no less significant cognitive dysfunctions. There are currently no antenatal or postnatal treatments that can improve outcomes for FGR infants, but this is an area of strong research interest. For obvious reasons we cannot test interventions or treatments in human pregnancies or infants, and therefore animal models of FGR are required to examine whether neuroprotective treatments are safe, feasible, and can significantly improve functional outcomes.

In the current study we will examine treatment strategies to improve the structure and function of the FGR lamb brain. A number of different neuroprotective strategies are of interest that could potentially be applied either during pregnancy (antenatally) or after birth (postnatally) that aim to optimise brain development.

Treatments of interest include anti-oxidants, anti-inflammatory compounds, and cord blood stem cells. We will apply complimentary assessments of brain structure and function to test the efficacy of our neuroprotective treatments of interest.

Keywords: brain development, neuroprotection, fetal growth restriction, FGR, IUGR

Developing 3D brain organoids to model perinatal brain injury

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Courtney McDonald, A/Prof Michael Fahey
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Phone: 03 8572 2799 (Dr McDonald)

Project description: We are developing 3-dimensional human brain organoids using induced pluripotent stem cells (iPSCs). We can model the effect of neuroinflammation in our brain organoids, thereby creating an in vitro model of perinatal brain injury. We will use this in vitro 3D model to test the mechanism of action of umbilical cord blood and mesenchymal stem cells, specifically assessing the paracrine and direct effects and determine the optimum stem cell type for reducing neuroinflammation. This project will involve extensive cell culturing with both iPSCs and perinatal stem cells, multicolour flow cytometry and molecular analysis using PCR and protein assays.
Fetal & Neonatal Health: Brain Injury and Neurodevelopment

The effect of maternal obesity on placental morphology and function

Suitability: Honours/PhD  
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
Project Leaders: Dr Emily Camm, Prof Suzie Miller  
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Phone: 03 8572 2820 (Dr Camm)  

Project Description: Obesity is one of today’s most blatantly visible – yet most neglected – public health issues. In Australia, overweight and obesity impacts 63% of Australian adults and 30% of children and adolescents, and is the fastest-growing cause of chronic disease. Currently, over 50% of women are entering pregnancy either overweight or obese. Alongside pregnancy complications, such as gestational diabetes mellitus (GDM) and pre-eclampsia, increasing evidence implicates maternal obesity as a major determinant of health during both childhood and later adult life with an increased risk of future obesity, cardiometabolic disease, and poor neurodevelopmental outcomes. These inter-generational effects of obese pregnancy have profound public health implications and highlight the urgency of establishing the mechanisms involved. As the interface between the mother and fetus, the placenta may be an important mechanistic link between maternal obesity and offspring outcomes. It provides oxygen, nutrients, hormones and growth factors essential for intrauterine growth and development. Mitochondria produce the energy for these processes in the form of adenosine triphosphate (ATP) by oxidative phosphorylation (OXPHOS). To date, little is known about the actual OXPHOS capacity of the placenta in obese women, or its association with child health.

This project will examine the effect of maternal prepregnancy obesity on placental morphology and mitochondrial function. This project will utilise human placenta collected from term caesarean-section deliveries.

Keywords: Obesity, placenta, mitochondria

Optimising a model of preterm brain injury in the neonatal rat

Suitability: Honours/PhD  
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
Project Leaders: Dr Courtney McDonald, Dr Tayla Penny  
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Phone: 03 8572 2799 (Dr McDonald)  

Project Description: Babies that are born preterm are at risk of experiencing injury to the white matter of the brain, and as such developing neurodevelopmental disorders such as cerebral palsy. Cerebral palsy is the most common childhood motor disability and is associated with both motor and cognitive deficits. This project aims to develop and optimise a small animal model of preterm brain injury using neonatal rat pups. The effectiveness of this model can be tested by utilising a suite of behavioural tests previously determined by our group, as well as through analysis of brain tissue using immunohistochemistry, flow cytometry and PCR. This model will also be used to test potential therapies for preterm brain injury, including umbilical cord blood (UCB) stem cell therapies. This project will involve small animal work including long-term monitoring and behavioural testing. You will also learn techniques involving immunohistochemistry, histology, microscopy and molecular analysis.
Fetal & Neonatal Health:
Brain Injury and
Neurodevelopment

Neural stem cell therapy for preterm brain injury

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Courtney McDonald, Prof Suzie Miller, A/Prof Michael Fahey
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Phone: 03 8572 2799

Project description: Neural stem cells (NSCs) offer great promise as a neuroprotective therapy against a range of neurological conditions, like cerebral palsy. NSC therapy has been shown in small animal models to reduce brain injury. However, NSCs have never been tested in a large animal model of preterm brain injury. In this project we will assess whether NSC transplanted directly into the preterm brain can engraft and regenerate damaged brain tissue.

For this project we will use our in-utero sheep model of umbilical cord occlusion to induce preterm brain injury and test early and late treatment with NSCs to determine the optimal time of NSC therapy. As part of this project, you will learn large animal surgery, fetal monitoring, brain immunohistochemistry, protein analysis and cell culture techniques.

Is Neural stem cell therapy safe and feasible in a neonate?

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Courtney McDonald, Prof Suzie Miller, A/Prof Michael Fahey
Email: courtney.mcdonald@monash.edu
Phone: 03 8572 2799 (Dr McDonald)

Project description: Neural stem cells (NSCs) offer great promise as a neuroprotective therapy against a range of neurological conditions, like cerebral palsy. NSCs are currently being investigated in clinical trials for adult neurological conditions and these studies have shown that for NSCs to be effective they need to be injected directly to the brain and immune suppression must also be administered. These procedures carry increased risk and the detrimental effect these procedures may have on the neonate are currently unknown.

This project is aimed to test the long-term safety and feasibility of transplanting high doses of NSCs into the neonatal brain and co-administering immunosuppression. These experiments will be performed in lambs and we will perform neurodevelopmental follow-up until 3 months of age to determine the safety of these procedures.

As part of this project, you will learn large animal surgery, neonatal sheep monitoring, behavioural testing, brain immunohistochemistry and cell culture techniques.
Infant and Child Health

Cell therapies for neonatal conditions

Suitability: Honours/BMedSc
Location: Monash Health Translation Precinct (Monash Medical Centre)
Project Leaders: Dr Atul Malhotra, Dr Courtney McDonald, Prof Suzie Miller
Email: atul.malhotra@monash.edu

Project Description
Opportunities exist to join a world leading team in translational cell therapy research. Projects offered include lab work in cell characterisation, profiling, expansion and related studies. There are also opportunities to be involved in either or both clinical and pre-clinical neonatal cell therapy translational work.

Keywords
stem cells, neonatal, brain, lung

Are Sleep Spindles Associated with Neurocognitive Deficits in Children with Sleep Disordered Breathing?

Suitability: Honours/PhD/Masters
Location: Department of Paediatrics, Level 5 Monash Children’s Hospital
Project Leaders: Prof Rosemary Horne
Email: rosemary.horne@monash.edu
Phone: 8572 2827

Project Description:
A particular phenomenon of the electroencephalography (EEG) wave form is the sleep spindle, believed to function as mechanism through which long-term changes are made in the neocortex and as a mechanism for maintaining sleep. Sleep spindles have also been associated with different aspects of cognitive performance in healthy children.

Sleep disordered breathing (SDB), is a very common condition in children, and has been associated with neurocognitive deficits. To date, it is not known whether the poor neurocognition in children with SDB is related to a loss of sleep spindles. This study will investigate sleep spindles in children with SDB and determine if there is an association between sleep spindle numbers and neurocognitive deficits. The student will be involved in conducting sleep studies (polysomnography) and analysis of electroencephalography data.

Evaluation of innovative digital monitoring devices in neonates

Suitability: Honours/BMedSc
Location: Monash Health Translation Precinct (Monash Medical Centre)
Project Leaders: Dr Atul Malhotra, Dr Faezeh Marzbanrad
Email: atul.malhotra@monash.edu

Project description:
Opportunities exist to join a world leading team in translational cell therapy research. Projects offered include lab work in cell characterisation, profiling, expansion and related studies. There are also opportunities to be involved in either or both clinical and pre-clinical neonatal cell therapy translational work.

Keywords
stem cells, neonatal, brain, lung
Infant and Child Health

Long-term consequences of respiratory instability on neurodevelopmental and cardiovascular outcomes in preterm infants

Suitability: Honours/PhD/Masters
Location: Department of Paediatrics, Level 5 Monash Children’s Hospital
Project Leaders: Prof Rosemary Horne, A/Prof Flora Wong
Email: rosemary.horne@monash.edu
Phone: 8572 2827

Project description:
In Australia about 26,873 infants are born preterm each year. Despite an increase in survival, developmental morbidity has not improved, with more than half of surviving infants born < 28 weeks of gestation growing up with significant neurodevelopmental impairment. Even infants born moderately or late preterm (> 32 weeks of gestation) are at double the risk for neurodevelopmental disability at 2 years of age compared to term born peers, with impairments being mainly in the cognitive domain. With the rising rate of preterm birth world-wide, focus on hitherto unrecognised and untreated central apnoea and periodic breathing will determine if this common problem contributes to adverse outcomes.

This study will answer important clinical questions: How do the falls in cerebral oxygenation associated with these immature breathing patterns affect neurodevelopmental outcomes? Which infants should be screened? Which infants may need treatment? Such a study would make a significant contribution to improving outcomes and reducing the long-term consequences of preterm birth.

Keywords
preterm infants, developmental outcomes, apnoea, sleep

Bad sleep is bad for your cardiovascular health

Suitability: Honours/PhD/Masters
Location: Department of Paediatrics, Level 5 Monash Children’s Hospital
Project Leaders: Prof Rosemary Horne, Dr Lisa Walter
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Phone: 8572 2827

Project description:
The research of my group focuses on sleep in infants and children. This is of the utmost importance to the health of every baby and child. Sleep is the primary activity of the brain during early development. By the age of 2 years a child has spent a total of 13 months sleeping! Between 2 and 5 years of age children spend equal amounts of time asleep as awake. A common cause of sleep disruption in childhood is partial or complete upper airway obstruction, termed sleep disordered breathing, with the hallmark feature being snoring. The repetitive airway obstruction leads to intermittent periods of hypoxia, with perhaps even more damaging rapid re-oxygenation after release of the obstruction, which is known to lead to brain injury. Repetitive events also cause surges in blood pressure, which leads to hypertension. In this project we will examine the effects of sleep disordered breathing on vascular stiffness. Vascular stiffness reflects the compliance of the large conductance vessels and is an important contributor to increased cardiac stress and a risk factor for adverse cardiovascular events. It is a non-invasive method of assessing vascular dysfunction.

Students will be involved in analysing the physiological data collected during overnight clinical sleep studies and will have the opportunity to participate in these in the brand-new Melbourne Children’s Sleep Centre, Monash Children’s Hospital to understand how the data are collected.

Keywords
Sleep, Children, Obstructive Sleep Apnoea
**Infant and Child Health**

**The effects of preterm birth on the development and consequences of obstructive sleep apnoea in childhood**

**Suitability:** Honours/PhD/Masters  
**Location:** Department of Paediatrics, Level 5 Monash Children’s Hospital  
**Project Leaders:** Prof Rosemary Horne, Dr Lisa Walter  
**Email:** rosemary.horne@monash.edu  
**Phone:** 8572 2827

**Project description:**
Children born preterm are 3-5 times more likely to be diagnosed with obstructive sleep apnoea (OSA) than those born at term. We have previously shown in children born at term that OSA has significant effects on the cardiovascular system with increased blood pressure and impaired autonomic control of heart rate. In our studies of infants born preterm we have shown that they have impaired control of blood pressure and heart rate which continues for at least the first 6 months after term equivalent age, but to date we have not carried out longitudinal studies into childhood.

In this study we will analyse overnight polysomnographic studies of children referred to the Melbourne Children’s Sleep Centre to identify if the severity and consequences of OSA are exacerbated in those children who were born preterm. Specifically we will look at nocturnal dipping (the fall in heart rate and blood pressure when you go to sleep) and cardiovascular responses to respiratory events. OSA is associated with adverse cardiovascular outcomes in adults including hypertension which is thought to be due to the repeated surges in blood pressure at respiratory event termination. Premature birth also increases the risk of adverse cardiovascular outcomes in adults. Identifying if these risks are present in children will support early detection and treatment of OSA in children born preterm and will improve their long-term cardiovascular health.

**Keywords**  
sleep, premature birth, obstructive sleep apnoea

**Understanding ventilatory control in children with Prader Willi Syndrome**

**Suitability:** Honours/PhD/Masters  
**Location:** Department of Paediatrics, Level 5 Monash Children’s Hospital  
**Project Leaders:** Prof Rosemary Horne  
**Email:** rosemary.horne@monash.edu, bradley.edwards@monash.edu  
**Phone:** 8572 2827

**Project description:**
Individuals with Prader Willi Syndrome (PWS) have impairments in ventilatory control and are predisposed toward sleep disordered breathing due to a combination of characteristic craniofacial features, obesity, hypotonia, and hypothalamic dysfunction. In order to understand the underlying causes of ventilatory control instabilities, we typically measure the sensitivity of the negative feedback loop controlling breathing (i.e. loop gain). Interestingly, we have recently completed studies showing increased ventilatory instability (which is often termed a system with a high loop gain) in children with a high number of central apnoea’s.

However, it is not known if children with PWS have similarly high loop gain or whether the recurrent central apnoea’s seen in this condition are a manifestation of depressed ventilatory drive (low loop gain). Understanding this mechanism will allow tailored treatment of central sleep apnoea in children with PWS. Students will learn how to analyse sleep studies in children with PWS to determine loop gain. They will be involved in data analysis, statistical analysis and preparing the study for publication. Students will also be able to interact with postgraduate research students, attend weekly research meetings and be involved in an active paediatric research group.

**Keywords:** sleep, children, paediatrics, control of breathing
Infant and Child Health

Cerebral oxygenation in preterm babies in the neonatal intensive care unit

Suitability: Honours/BMedSc(Hons)/Joint PhD/Exchange Program
Location: Department of Paediatrics, Level 5
Monash Children’s Hospital
Project Leaders: A/Prof Flora Wong
Email: flora.wong@monash.edu, rosemary.horne@monash.edu
Phone: 03 85723655

Project description:
Preterm infants are at high risk of brain injury, mainly due to low blood flow and oxygenation in the brain. With this project we aim to assess the impact of various physiological and environmental factors on brain oxygenation level in the very preterm infants undergoing intensive care. The various factors to be investigated include blood pressure fluctuations, cardiac output, apnoea’s, oxygen desaturations, ventilation changes and blood sampling procedures. We will use Near Infrared Spectroscopy to measure cerebral oxygenation non-invasively by the cot side of preterm infants, and correlate the changes with the various factors being investigated.

The project will provide important knowledge on the effects of common physiological events, and interventional therapies on brain oxygen levels in these very small infants. The information may provide the basis on which brain protection strategies can then devised. Large amount of data has been collected on infants studied whilst receiving care in the Neonatal Intensive Care Unit at Monash Medical Centre (MMC). Cerebral oxygenation is measured at the cot side using Near Infrared Spectroscopy (NIRS) and expressed as tissue oxygenation index (TOI, %).

The infants are studied weekly, for 2-3 hours at each study. During the study, the infant spends half of the time sleeping prone (on the belly) and half of the time sleeping supine (on the back). Effects of physiological changes and clinical events will be correlated with changes in TOI in the preterm infants. We are currently analysing the effects of apnoea’s and periodic breathing on the brain oxygenation in these preterm infants, and how these change during different sleeping positions.

Keywords
Preterm brain, brain oxygenation, infant sleep, periodic breathing, apnoea
Infection, Inflammation and Immunity

**Targeting IL-1β for prevention of inflammation-induced brain injury in premature infants**

**Suitability:** Honours/PhD  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research, Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project Leaders:** Dr. Robert Galinsky, Prof Rod Hunt  
**Email:** robert.galinsky@hudson.org.au, rod.hunt@monash.edu

**Project Description:** Inflammation-induced brain injury remains one of the main causes of disability after premature birth. There is no effective treatment. The pro-inflammatory cytokine interleukin-1β (IL-1β) has been implicated in inflammation-induced brain injury through activation of cerebral microglia (the brain’s resident immune cell) however it remains unclear whether this association is causal.

This project is aimed at understanding the role of IL-1β in inflammation-induced preterm brain injury and evaluating whether an FDA approved IL-1 receptor antagonist can improve outcomes.


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**Developing new anti-cytokine therapies for preventing brain injury in the preterm infant**

**Suitability:** Honours/PhD  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research, Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project Leaders:** Dr. Robert Galinsky, Prof Rod Hunt  
**Email:** robert.galinsky@hudson.org.au, rod.hunt@monash.edu

**Project Description:** Inflammation-induced brain injury remains one of the main causes of lifelong disability after birth. There is no effective treatment. Elevated levels of inflammatory proteins (cytokines) are strongly associated with brain inflammation and impaired neurodevelopment in the womb and after preterm birth. Developing therapeutic interventions to target these proteins could provide a new approach for reducing the incidence and severity of disability after preterm birth.

This project aims to improve our understanding of how cytokines disturb healthy brain development and develop new anti-cytokine therapies for inflammation-induced brain injury.

Infection, Inflammation and Immunity

An anti-inflammatory approach to preterm neuroprotection

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research, Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr. Robert Galinsky, A/Prof Claudia Nold, Prof Marcel Nold
Email: robert.galinsky@hudson.org.au, marcel.nold@monash.edu, claudia.nold@hudson.org.au

Project description: Chronic inflammation after preterm birth is strongly associated with impaired brain development and life-long disability. There is no effective therapy to prevent inflammation-induced impairments in brain developmental after preterm birth. We will assess how effectively two innovative anti-inflammatory mediators, interleukin 1 receptor antagonist (IL-1Ra) and IL-37, protect against inflammation induced impairments in brain development in newborn mice (neurologically similar to preterm infants at ~30 weeks of gestation) exposed to chronic inflammation. We will quantify whether increased levels of IL-1Ra or IL-37 improve brain development, as reflected in biochemical and cellular markers of inflammation, white matter development and neuronal maturation on days 3 and 28 of life.

Research techniques: Various aspects of work with mice, workup of tissues for various downstream applications, flow cytometry, histology, immunohistochemistry, protein detection by ELISA

Closing the gaps – paediatric reference intervals of pro-inflammatory and anti-inflammatory cytokines

Suitability: Honours/BMedSci/PhD
Location: Hudson Institute of Medical Research, Level 1, 27-31 Wright St, Clayton
Project Leaders: Prof Marcel Nold, A/Prof Claudia Nold, Dr Ina Rudloff
Email: marcel.nold@monash.edu, claudia.nold@hudson.org.au

Project description: Cytokines have attracted substantial attention as diagnostic biomarkers for infectious and inflammatory diseases in recent years. However, understanding of maturation of the immune system and normal ranges for various patient age brackets in health and disease have not been established. Cytokines play an important role in maintaining homeostasis on the one hand, and a wide range of childhood diseases on the other hand. Their potential as diagnostic and prognostic biomarkers that may guide treatment in infectious, autoimmune, allergic, and haematological diseases is beginning to be recognised. Studies have suggested that cytokine production is influenced by age; however, larger datasets on cytokine profiles for healthy neonates, infants and children are lacking.

The aim of this study is to investigate cytokine concentrations in healthy infants and children, and to explore conditions that influence cytokine production in the paediatric age group. For Honours, this project will involve the following approaches and techniques: - Obtaining and working up samples in collaboration with the Department of Paediatrics and Pathology - Clinical data entry in an electronic database - Elisa or multiplex protein quantification assays to measure serum/plasma markers in infants and children. For candidates interested in a PhD, the study’s scope is easily expandable to investigate further age groups and diseases.

Keywords: cytokines, inflammation, reference ranges, paediatric, children, infants
Infection, Inflammation and Immunity

Exploring a New Frontier: The Immune and Coagulation Systems of the Premature Infant and their Relevance for the Risk of the Major Diseases of Prematurity

Suitability: Honours/BMedSci/PhD
Location: Hudson Institute of Medical Research, Level 1, 27-31 Wright St, Clayton
Project Leaders: Prof Marcel Nold, A/Prof Claudia Nold, Dr Ina Rudloff
Email: marcel.nold@monash.edu, claudia.nold@hudson.org.au

Project Description: The immune and coagulation systems of preterm infants are largely unknown, a problematic blank page for clinicians, a true frontier for researchers. The dearth of information on preterm immunity and coagulation is explained by our inability until recent times to extract large amounts of information from the 0.5 ml samples available from the tiny patients, remembering they have as little as 35 ml of blood. Our laboratory is conducting an exciting study on blood taken from extremely premature infants at 5 time points, thus allowing for a unique longitudinal view of plasmatic and cellular immunity as well as coagulation.

To explore these systems in depth, we use cutting edge methods such as protein arrays and multi-colour flow cytometry, which students will learn. Access to the babies’ clinical data we enable us to perform correlation analyses to probe the relevance of our findings to the major diseases of prematurity such as bronchopulmonary dysplasia, intracranial haemorrhage and necrotising enterocolitis. These insights may identify biomarkers and/or new therapeutic targets, which are direly needed as several of these diseases are life-threatening and currently untreatable.

Direct clinical relevance: high Hands-on learning opportunities: Multi-colour flow cytometry, protein arrays, cell culture of primary human blood cells.

Keywords
preterm infants, inflammation, lung, gut, bronchopulmonary dysplasia (BPD), necrotising enterocolitis (NEC), interleukin, histology, flow cytometry, immunohistochemistry

Novel Anti-inflammatory cytokines and cell therapies for the treatment of inflammatory bowel disease

Suitability: Honours/BMedSci/PhD
Location: Hudson Institute of Medical Research, Level 1, 27-31 Wright St, Clayton
Project Leaders: Dr Rimma Goldberg, A/Prof Claudia Nold, Prof Marcel Nold, Prof Colby Zap
Email: rimma.goldberg@monash.edu

Project Description: Inflammatory bowel disease is a chronic immune mediated disorder affecting the intestine with no known cure. The pathogenesis of this disease results from immune dysregulation and an imbalance between pro inflammatory cells and cytokines. IL37 is a novel anti-inflammatory cytokine which is reduced in the circulation of patients with autoimmune diseases, including inflammatory bowel disease. Human peripheral blood mononuclear cells are capable of producing IL37, and in particular the T cell subset. Aberrant helper T cell responses play a key role in the pathogenesis of IBD.

Thus it is of paramount importance to understand the triggers for pro and anti-inflammatory cytokine production by T cell subsets of patients with inflammatory bowel disease.

This project will first look at characterising IL37 production in different cell subsets in the blood and lamina propria of patients with inflammatory bowel disease. Concurrently, patient data on disease activity, medication use and response will be collected. Disease activity and response to currently available medications will be correlated with IL37 production to assess whether this cytokine plays a role not only in pathogenesis of disease, but also response to immunomodulating medications. Regulatory T cells (Tregs) are responsible for dampening down aberrant inflammation and control autoimmune disease. Tregs are dysfunctional in inflammatory bowel disease.

The second part of this project will look at defining the ability of Trig to respond to and produce IL37 as a means of developing a highly novel cell-based therapy.

Keywords: preclinical study, inflammatory bowel disease, inflammation, immunology, interleukins, regulatory t cell, cell therapy
Infection, Inflammation and Immunity

Novel Anti-inflammatory Approaches for Currently Untreatable Diseases of the Preterm Baby: human specimen analysis and animal models of bronchopulmonary dysplasia and necrotising enterocolitis

Suitability: Honours/BMedSci/PhD
Location: Hudson Institute of Medical Research, Level 1, 27-31 Wright St, Clayton
Project Leaders: A/Prof Claudia Nold, Dr Ina Rudloff, Dr Nadia Deen
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Project Description:
The severe chronic lung disease bronchopulmonary dysplasia (BPD) causes considerable suffering for premature infants and their families and contributes substantially to health care costs. Necrotising enterocolitis (NEC) is a disease of the premature gut that is poorly understood and carries a high mortality. No effective therapy is known for either devastating disease. In view of the importance of inflammation for BPD and NEC, we will assess how effectively innovative anti-inflammatory treatments protect against BPD and NEC. In newborn mice with a BPD-like lung disease, we will quantify if treatments protect against the development of lung pathology as reflected in biochemical and cellular markers of inflammation and loss of alveolocapillarisation and vascularisation on day 3 and 28 of life. In a newborn mouse model of NEC, involving formula feeding for 3 days and brief exposure to cold and hypoxia, we will assess the protective properties of immunotherapies by histology and flow cytometry and by analysis of selected biochemical markers. In human specimen we will assess the underlying mechanism of disease.

Direct clinical relevance: high. Hands-on learning opportunities: Various aspects of work with mice, workup of tissues for various downstream applications, flow cytometry, histology, immunohistochemistry, protein detection by ELISA. Established collaboration with the Monash Health department of Paediatric Surgery to collect human specimen including blood, intestinal and stool samples.

Keywords: preterm infants, inflammation, lung, gut, bronchopulmonary dysplasia (BPD), necrotising enterocolitis (NEC), interleukin, histology, flow cytometry, immunohistochemistry

Baby Microbiome: Investigating the Human Neonatal Lung and Gut Microbiome and its impact on Health Outcome

Suitability: Honours/BMedSci/PhD
Location: Hudson Institute of Medical Research, Level 1, 27-31 Wright St, Clayton
Project Leaders: A/Prof Claudia Nold, Dr Ina Rudloff, Prof Marcel Nold
Email: claudia.nold@monash.edu, ina.rudloff@hudson.org.au, marcel.nold@hudson.org.au

Project Description: The neonatal microbiome, in healthy full-term infants and in preterm infants presents with a highly dynamic nature. As such, the microbiome is extremely susceptible to external influences that can dramatically affect the short- and long-term health of the infant. In this project we set out to investigate the underlying mechanisms how the intestinal and pulmonary microbiome influences the neonatal immune system and thereby impacts disease outcome.

In collaboration with Monash Children’s we collect clinical data and samples from term and preterm infants. This project gives you the opportunity to closely work with clinical collaborators and also have the opportunity to gain experience in a diverse set of molecular techniques

Keywords: microbiome, immunology, intestine, lung
Cell therapy and regenerative medicine

Isolation and Expansion of Umbilical Cord Blood Stem Cells for Regenerative Medicine

Suitability: Honours/PhD/BMedSc/Masters
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Graham Jenkin, Dr Courtney McDonald, Dr Tayla Penny
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Phone: 0419534101 (Prof Jenkin)

Project Description: Umbilical cord blood (UCB) is one of the richest sources of "young" haematopoietic stem cells. Currently, more than 3000 UCB stem cell transplants are performed each year. However, these are mostly restricted to children, as UCB samples usually do not contain sufficient stem cells to treat adults. The umbilical cord and cord blood also contains multiple potentially efficacious cell types for a range of diseases. Hence, this research project aims to develop and refine methods for expanding the number of stem cells obtained from human UCB and umbilical cord under laboratory conditions and translation of this research to the clinic.

This stem cell research could help save lives of people suffering from blood disorders, cancers and auto-immune diseases. The experiments will include cell culture and gene analysis/molecular biology techniques and transplantation of UCB stem cells to determine their efficacy.

Novel derivation and gene editing of human haematopoietic stem cells and differentiation to immune cell types

Not available 2021/2

Suitability: Honours/PhD/Masters/BMedSc
Location: The Ritchie Centre / Cartherics, Hudson Institute of Medical Research; Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Richard Boyd, Prof Graham Jenkin, Dr Roland Shu, Dr Nicholas Boyd
Email: graham.jenkin@monash.edu
Phone: 03 8572 2801 (Prof Jenkin)

Project Description: Human hematopoietic stem cells (HSCs) will be isolated from umbilical cord blood and expanded in large numbers for clinical therapies. This project will use novel cutting edge technology to edit the genetic profile of HSCs to enable their universal transplantation across histocompatibility barriers and their differentiation into strategically sculptured cancer fighting immune cells. Multiple samples of human umbilical cord blood are being banked by large private and public banks but are only being used sparingly for treatment of patients receiving chemotherapy for restoration of their bone marrow blood cell populations in a number of cancers. The more widespread use of banked cord blood samples is hampered by the need to partially match the HLA type to the transplant recipient.

This project will involve testing the concept of gene editing the major histocompatibility antigens (type I HLA-A, HLA-B and type II HLA-DR). This would essentially create universal compatibility at the major HLA loci. HLA-C, which exists as two types HLA-C1 and C2, is more easily matched to recipients and the presence of HLA-C prevents destruction of HLA-A and HLA-B null (KO) cell types by Natural Killer (NK) cells, so would not need to be edited out for such cells to act as universal donor cells. In addition, cord blood HSCs can be differentiated into T cells, NK cells, macrophages and other cells of the immune system. The PhD would involve the gene editing of cord blood HSCs and their differentiation, via their transformation into iPSCs, into functional immune cells for assessment of their ability to kill target cancer cells. Their immune compatibility will be tested in vitro and in vivo models.

Keywords
Haematopoietic Stem Cells, CAR-T, Immunotherapy, Stem Cells, Clinical Translation, Cartherics Commercial Clinical Translation Projects, Regenerative Medicine
Cell therapy and regenerative medicine

The development of macrophages from iPSC (iMacs) for novel cancer immunotherapy

Suitability: PhD/Honours
Location: The Ritchie Centre / Cartherics, Hudson Institute of Medical Research; Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Graham Jenkin
Co-supervisors: Prof Alan Trounson, Dr Frederico Calhabeu, Prof Richard Boyd
Email: graham.jenkin@monash.edu

Background
Immunotherapy as a discipline has provided a potentially revolutionary approach to combatting cancer. While CAR technologies have provided unheralded advances in blood cancer treatment, they are currently mono-directional targeting one cancer marker. They also fail to engage the advantages of the patient's "polyvalent" immune system. In this regard, the first line of defence of the immune system centres around more functionally "primitive" but ultimately critical macrophage lineage cells. Macrophages represent a major, underutilized, potential pillar in cancer immunotherapy. Macrophages themselves are heterogeneous with two main functionally distinct subsets: M1 (pro-inflammatory) and M2 (anti-inflammatory). M1 are clearly the most important for attacking cancer and are the focus of this project.

However, macrophages have a very short half-life but can be produced effectively and efficiently from haemopoietic stem (HSC) cells. Very recently two groups have addressed the problem of the short half-life of macrophages by using iPSC technology. iPSCs have effectively limitless capacity for self-renewal. If they can be successfully differentiated into macrophages this could overcome the major shortfall of their life span. Although macrophages have long been impervious to genetic manipulation, researchers have recently discovered a new type of viral vector that allows them to engineer the cells to retain and bolster their cancer-attacking abilities when injected into solid tumours in mice.

This project takes its lead from the Cartherics platform which uses iPSCs derived from homzygous haplotype donors, to minimise MHC mismatch and immune rejection.

Aims of project:
1. To develop the technology for inducing macrophages from iPSC (iMacs).
2. To preferentially induce M1 macrophages by varying the differentiating conditions to block the M2 pathway or promote the M1 pathway.
3. To characterise these cells phenotypically and functionally (pro- versus anti – inflammatory cytokines; CD surface expression).
4. To endow these cells with a cancer specific CAR such as a TAG-72 CAR.
5. To develop stable TAG-72 Car-expressing iPSC clones.
6. To genetically engineer the iPSC to enhance iMac function and longevity.
7. To show that engineered iMac/CAR-iMac/ gene KO iMac possess essential properties of PBMC-derived macrophages, such as homing capacity and cytotoxicity activity (phagocytosis). iPSC-derived macrophages capacity to eliminate human ovarian cancer will be assessed both in vitro and in vivo. An in vivo bioluminescence imaging method will be used to evaluate the capacity of iMacs to kill human ovarian cancer in NSG mice.
8. To explore the additive benefits of iMacs followed by, or coupled with, iNK or iT cells for cancer killing capacity in NSG mice.

Supervision: Main supervisor: Professor Alan Trounson; Co-Supervisors: Dr Frederico Calhabeu, Professor Richard Boyd


Keywords
Immunotherapy, Cancer Therapy, iPSCs, Chimeric Antigen Receptor Technology, Ovarian Cancer
Cell therapy and regenerative medicine

Optimising the function of anti-cancer killer T cells: the role of endogenous TCR in CAR-T function and overcoming exhaustion to supercharge CAR-T cells

Not available 2021/2

Suitability: Honours/PhD/Masters
Location: The Ritchie Centre / Cartherics, Hudson Institute of Medical Research; Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Richard Boyd, Prof Graham Jenkin, Co-supervisor: Dr Vera Evtimov
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Project description: Chimeric Antigen Receptor T cells are providing extraordinary results in the clinic, particularly for haematological malignancies. As exciting and tantalising as this immunotherapy revolution is, there are still major hurdles to be overcome in optimising their clinical utility. This project will apply the rules that govern normal endogenous T cell function to CAR-T cells, to help their functional impact across a range of cancers and to increase their longevity after transplantation. Recent studies have shown that T cell exhaustion significantly impacts the ability for chimeric antigen receptor (CAR-) T cells to remain potent killers.

Overall, this project will aim to characterise how T cell receptor (TCR) mediated activation and ultimately modulation of T cell exhaustion will enhance CAR-T potency in vitro and in vivo. Preclinical studies conducted by Cartherics to date have demonstrated that T cell hyper-activation leads to the potent, indiscriminate elimination of target cells induced by both CAR-T and non-transduced T cells. Through real-time cell monitoring we have identified a collection of culture conditions which have the ability to augment CAR-T function in vitro. Importantly, manipulation of exogenous growth factors and cytokines significantly enhances target cell elimination to the detriment of target-antigen specificity.

This project would use these findings as a springboard to further explore activation/exhaustion and how we could manipulate these elements to generate CAR-T cells that can reduce tumour burden AND persist indefinitely to ultimately improve the efficacy of CAR-T treatment.

Keywords
CAR-T, Immunotherapy, Stem Cells, Clinical Translation, Cartherics Commercial Clinical Translation Projects, Regenerative Medicine

Genetically engineered human MSCs as supporting inducers of in vitro T-cell production

Not available 2021/2

Suitability: PhD/Honours/Masters/BMedSc
Location: The Ritchie Centre / Cartherics, Hudson Institute of Medical Research; Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Richard Boyd, Prof Alan Trounson, Prof Graham Jenkin, Co-supervisors Dr Roland Shu, Dr Nicholas Boyd
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Project description: Genetically modified chimeric antigen receptor T cells (CAR-T cells) represent a new revolution in anti-cancer immunotherapy. A major problem, however, is that the treatment currently relies on using the cancer patients own blood but they invariably have too few T cells available for genetic enhancement. Furthermore, prior treatment with chemotherapy substantially reduces their function. This study aims to develop a new approach to generating CAR-T cells from stem cells. T cells derived in vitro from both hematopoietic stem/progenitor cells (HSCs) and induced human pluripotent stem cells (iPSCs) offer great potential advantages in generating a self-renewing source of T cells that can be readily genetically modified for immunotherapy.

The project aims to generate a genetically modified human stromal cell line from human Mesenchymal Stem Cells (MSC), for supporting the T cell in vitro differentiation. In the thymus, complex interactions between stromal cells, cell-surface ligands, cytokines, chemokines, and extracellular matrix create a microenvironment that guides T-lymphocyte differentiation from bone-marrow-derived progenitors. The OP9-DL culture system permits the generation of HSC-derived T cells in vitro, serving both as a means to facilitate the study of T-cell differentiation, as well as the potential to produce large numbers of cells for adoptive transfer. OP9-DL1 cells provide Notch signalling, which is a crucial mediator of T-cell development. The mouse bone marrow (BM)-derived stromal cell line, called OP9, is engineered to overexpress the Notch ligand, Delta-like ligand 1 (Dll-1), hence the line is termed OP9-DL1.

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Cell therapy and regenerative medicine

Elimination of cancer stem cells using chimeric antigen receptor T cells. Not available 2021/2

Suitability: PhD/Honours/BMedSc
Location: The Ritchie Centre / Cartherics, Hudson Institute of Medical Research; Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Richard Boyd, Prof Alan Trounson, Prof Graham Jenkin, Co-supervisor: Dr Vera Evtimov
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Project description: Disease relapse in CAR-T therapies of solid tumours suggests that current treatments lack the ability to eliminate the small subset of cells known as cancer initiating cells or cancer stem cells (CSCs). We propose to use the sophisticated specificity of immunotherapy to target surface membrane antigens present on the CSC, negating the current need for the cancer cell to be proliferating for killing efficacy of CAR-T therapies.

This project will aim to phenotypically and functionally characterise CSCs from multiple cancer indications including ovarian, gastric and cutaneous T cell lymphoma and demonstrate the ability of CAR-T cells to effectively eliminate these cells in vitro and in vivo. At the conclusion of this project, you will have successfully characterised the CSC subpopulation in select cancer indications and demonstrated that CAR-Ts are able to completely eliminate these cells both in vitro and in vivo.

Keywords
Cancer Therapy, CAR-T Therapies, T-cell generation, Clinical Translation, Immunotherapy, Cancer Stem Cells, Cartherics


Suitability: PhD/Masters
Location: The Ritchie Centre / Cartherics, Hudson Institute of Medical Research; Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Richard Boyd, Prof Graham Jenkin, Co-supervisors: Dr Roland Shu, Dr Vera Evtimov, Dr Nicholas Boyd
Email: graham.jenkin@monash.edu
Phone: 0419534101 (Prof Jenkin)

Project description: Cellular immunotherapy with chimeric antigen receptors (CARs) have provided unprecedented results in treatment of liquid cancers. However, inherently, these treatments face major challenges to reach mass adoption. Furthermore, autologous CAR-T treatments can require ~2 months to manufacture (often time patients don’t have) and produce variable (often insufficient) cell numbers as a result of poor immune systems hampered by chemotherapy. An on-demand, highly defined, universal product, which is compatible with multiple patients is required to unlock cellular immunotherapy therapy for the public. The answer lies in the utilisation of stem cells. Cartherics is focused on developing a scalable, clinically applicable manufacture system to differentiate induced pluripotent stem cells (iPSC) to CAR+ cytotoxic cells: T-cells and Natural killer (NK) cells.

To enhance the potency and longevity of NK immune-therapeutics, this PhD will investigate a new alternative to inserting an entire synthetic CAR signalling system into the NK cells. Via CRISPR/Cas9 gene-editing, the terminal binding domain of NK surface receptors will be replaced with single chain variable fragments (scFV) that work as targets for cancer cells. Upon binding, all the natural activation and killing mechanisms related to that NK surface receptor will be engaged, giving the NK cell the potential to alleviate short-falls of CAR-triggered cytotoxicity and enhance the effect of tumour specific NK cell killing.

The project will involve CRISPR-Cas9 and scFv-R gene editing of iPS cells and, upon successful conversion to mature NK cells characterised via flow cytometry, the in vitro and in vivo activity of iPSC derived scFv-R-NKs will be compared with PBMC scFv-R NKs in vitro and in vivo in animal models.
Contact our supervisors

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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.

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