HUDSON
INSTITUTE OF MEDICAL RESEARCH

THE RITCHIE CENTRE

2020 Student Research Projects

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

Contents

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

Welcome to Hudson Institute

Hudson Institute specialises in discoveries in four areas of medical need

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

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

Our 475 scientists and students focus on laboratory discovery science, plus translational research – taking discoveries to patients and industry for real world impact.

Students at a glance 2018

We educate and train nearly 180 students through our academic affiliation with Monash University. Our postgraduate training is predominantly through the School of Clinical Sciences at Monash Health, part of the Faculty of Medicine, Nursing and Health Sciences at Monash University.

Our students

- Get exposure to university, institute and hospital research
- Attend national and international conferences
- Publish their research (74 student first author publications in 2018)
- Are mentored by leading supervisors and their teams
- Regularly win prestigious prizes and awards
- Have continuous opportunities for networking, learning and development

All work and no play …

Hudson Institute is not all about work. Our students have the opportunity to join in a range of student networking and social events organised by the Hudson Institute Student Society (HISS).

Our precinct

Hudson Institute is a partner in the Monash Health Translation Precinct (MHTP), a major medical and scientific research hub at Monash Medical Centre in Clayton.

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

With our precinct partners, Monash University and Monash Health, our site brings together world-leading scientists, clinicians and educators to collaborate on innovative discoveries that advance human health.

Our Translational Research Facility (TRF) is connected to Monash Health via a walkway and provides a crucial link between our scientific discoveries and medical treatments.

The facility houses laboratories alongside nine state of the art technology platforms and an eight-bed, 21-chair Clinical Trials Centre supporting the transition of discoveries from initial Phase I testing to Phase IV primary health trials.

The Ritchie Centre

The Ritchie Centre Hudson Institute of Medical Research, Monash Medical Centre, Clayton

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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 Suize Miller

Infant and Child Health
Prof Rosemary Horne

Infection, Inflammation & Immunity
A/Prof Tim Moss & Prof Jim Buttery

Cell Therapy & Regenerative Medicine
A/Prof Rebecca Lim

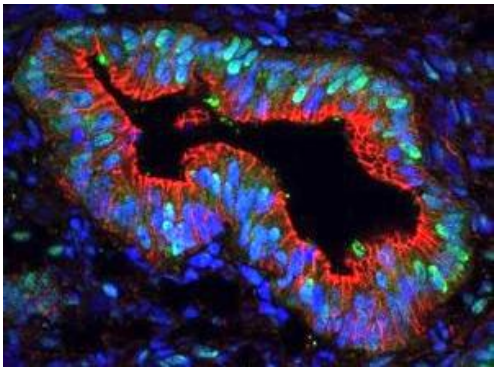
Women's Health

Testing the in vivo regenerative potential of putative stem cell populations from the endometrium

Suitability: Honours
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: The endometrium is the lining of the uterus and contains adult stem cells that are thought to be responsible for its ability to rapidly regenerate during each menstrual cycle. Finding markers to identify endometrial stem cells is an important area of research. We are investigating candidate endometrial stem cells using cells surface markers in human tissue, and transgenic reporters in mice. The ultimate test of stem cell potential is whether these cells can form endometrium. To answer this question, we will assess the ability of putative endometrial stem cells from mouse and human to produce endometrium when transplanted into a mouse.

Keywords: endometrium, epithelial stem/progenitor cells; human; mouse; xenograft



Characterising the niche of endometrial stem/progenitor cells in endometriosis

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

Project Description: We discovered 2 types of adult stem cells in human endometrium – epithelial progenitor and mesenchymal stem cell (eMSC) - likely responsible for its regeneration each month during the menstrual cycle. We also identified specific surface markers of the epithelial progenitor (N-cadherin) and eMSC: SUSD2. Epithelial progenitors are found in the bases of the glands adjacent to the myometrium (uterine muscle) and eMSC have a perivascular location. Another set of markers CD146 and PDGFR-β showed that the eMSC were pericytes, located adjacent to the endothelial cells. In a sheep model, we found that CD271+ eMSC were also perivascular, located in the adventitia of larger vessels rather than pericytes. N-cadherin+ and SUSD2+ cells are shed during menstruation and are found in greater numbers in the pelvic cavity of some women with endometriosis compared to normal, likely contributing to its pathogenesis.

This project will undertake a detailed analysis of human and macaque endometrium, and in endometriosis and adenymyosis lesions using sophisticated confocal microscopy to determine the precise locations of endometrial epithelial progenitors, eMSC and their niche cells. Colocalisation with other functionally important markers (SSEA-1, Notch-1, Lgr5, Vwf, aSMA) and estrogen and progesterone receptors from normal, endometriosis and adenomyosis women will also be examined. This project will generate beautiful images showing precisely where epithelial progenitors and eMSC reside in endometrial tissue and in endometriosis lesions, providing insight into the role of endometrial stem/progenitor cells in endometriosis.

Keywords: endometrium, epithelial progenitor cells, mesenchymal stem cells; endometriosis; adenomyosis blood vessels; confocal microscopy

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 Leader: Prof Caroline Gargett, Dr Saeedeh Darzi, Dr Caitlin Filby
Email: *caroline.gargett@hudson.org.au*

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 nanobiomaterials 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 provides an opportunity to develop skills in molecular sequencing, analysing vast quantities of data and interact with bioinformatician 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

Nano-biomaterials to deliver a novel cell-based therapy for Treating and Preventing Pelvic Organ Prolapse using a Novel Ovine Preclinical Animal Model

Suitability: **Honours/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 Shayanti Mukherjee, 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 a regenerative medicine approaches to improve treatment outcomes using cell-based therapy delivered in novel degradable biomimetic nano-biomaterials. There are 2 pre-clinical projects available to examine the effect of using human endometrial mesenchymal stem cells (eMSC) labeled with a lentivirus vector to treat or prevent POP.

One project examines the effect of eMSC surgically delivered in novel nanobiomaterials in sheep with POP (detected by a novel fibre optic device) and the second examines the effect of eMSC in a self-assembling hydrogel injected into the vaginal wall of sheep following Bakri balloon induced injury (simulating birth injury). Cell culture, Flow cytometry, histological, immunofluorescence and confocal microscopy, biochemical and biomechanical analyses will be undertaken. This project is supported by NHMRC funding.
Flow cytometry, histological, immunohistochemistry, biochemical and biomechanical analyses will be undertaken.

Keywords:
endometrial mesenchymal stem cells; tissue engineering, pelvic organ prolapse; women's health; preclinical animal models, nano-biomaterials

Women's Health

Organoids from human and mouse endometrial epithelial stem/progenitor cells populations to evaluate endometriosis risk genes

Suitability: **Honours/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 Caitlin Filby, Dr Fiona Cousins
Email: *caroline.gargett@hudson.org.au*

Project description:
The endometrium is the lining of the uterus and contains adult stem cells we hypothesise are responsible for its ability to rapidly regenerate a centimetre of mucosal tissue during each menstrual cycle. We have identified the first marker identify rare endometrial epithelial progenitor cells in human endometrium.

We have also identified potential epithelial progenitors in the endometrium of transgenic telomerase reporter mice Organoids are mini versions of an organ produced in vitro from stem cell populations self-organizing in 3D culture and this technology was named by The Scientist magazine as one of the biggest scientific advancements of 2013.

The aim of this project is to develop organoids from
• human endometrial epithelial progenitor cells using our specific marker, N-cadherin
• mouse endometrial epithelial progenitors from the telomerase reporter mouse and to investigate the biology of these cells and test their function in vitro and in vivo.
The ultimate test of an adult stem cell potential is whether these cells can form endometrium. To answer this question, we will assess the ability of organoids generated from endometrial stem cells from human and/or mouse to produce endometrium when transplanted into a mouse.
This project will provide a greater understanding of how adult stem cells generate endometrium in normal development, during the menstrual cycle and in disorders of endometrial regeneration such as endometriosis.

Keywords:
organoids; endometrium, epithelial stem/progenitor cells; human; mouse; xenograft

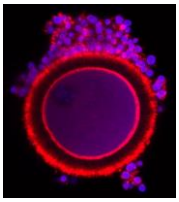
Temporal and spatial relationships between endometrial stem/progenitor cells and biological effectors of genetic risk from women with endometriosis: revealing the biological significance of endometriosis risk

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*

Endometriosis is a devastating chronic disease affecting 10% of girls and women, where cells of endometrial histology form lesions throughout the pelvic cavity and in rare cases at distant sites. Genetic and environmental factors influence risk of endometriosis, which is thought to arise from endometrial stem/progenitor cells. Recent work by our collaborator Prof Grant Montgomery at UQ (Sapkota, 2017) has unveiled single nucleotide polymorphisms (SNPs) in over 14 regions of the genome that are associated with increased risk of endometriosis. However, as these SNPs mostly occur in non-coding regions of the genome, how they confer increased risk of endometriosis is unknown. We are in the process of identifying effectors of these SNPs and these hits will be validated using immunofluorescence on endometrial tissues, organoids and patient derived xenografts.

This project aims to determine biological significance of these SNPs in endometriosis by isolating stem/progenitor cell populations in women with endometriosis with a low genetic risk score compared to those with a high genetic risk score and determining their expression and co-localisation using immunofluorescence and confocal microscopy. This project is suited to PhD, Honours or Masters students wanting to begin mid-2021 or 2022.

Keywords
endometriosis, endometrial stem cells, genetic risk factors,



Women's Health

Survival, progesterone resistance and angiogenesis of endometrial stem/progenitor cells from women with endometriosis: unravelling the biological 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*

Endometriosis is a devastating chronic disease affecting 10% of girls and women, where cells of endometrial histology form lesions throughout the pelvic cavity and in rare cases at distant sites. Genetic and environmental factors influence risk of endometriosis, which is thought to arise from endometrial stem/progenitor cells. Recent work by our collaborator Prof Grant Montgomery at UQ (Sapkota, 2017) has unveiled single nucleotide polymorphisms (SNPs) in over 14 regions of the genome that are associated with increased risk of endometriosis. However, as these SNPs mostly occur in non-coding regions of the genome, how they confer increased risk of endometriosis is unknown.

This project aims to determine biological significance of these SNPs in endometriosis by isolating stem/progenitor cell populations in women with endometriosis with a low genetic risk score compared to those with a high genetic risk score and determining their 1. gene expression profile after co-culture with stromal cells (using single cell RNAseq) 2. response to progesterone in vitro (using endometrial organoids) 3. angiogenesis response in vitro (using endometrial organoids) This project has international funding and provides an opportunity to develop skills in a number of techniques including fluorescent activated cell sorting (FACS), organoids, in vitro culture, stem cell biology, immunofluorescence. This project is most suited to a PhD student, and at later stages of the project there will be opportunities for Honours or Masters students.

Keywords
endometriosis, endometrial stem cells, gyneaecology, genetic risk, single cell sequencing, angiogenesis, progesterone resistance

Gene expression signatures of endometrial stem/progenitor cells from women with endometriosis: decoding the significance of endometriosis risk

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 Caitlin Filby,
Email: *caroline.gargett@hudson.org.au*

Endometriosis is a devastating chronic disease affecting 10% of girls and women, where cells of endometrial histology form lesions throughout the pelvic cavity and in rare cases at distant sites. Genetic and environmental factors influence risk of endometriosis, which is thought to arise from endometrial stem/progenitor cells. Recent work by our collaborator Prof Grant Montgomery at UQ (Sapkota, 2017) has unveiled single nucleotide polymorphisms (SNPs) in over 14 regions of the genome that are associated with increased risk of endometriosis. However, as these SNPs mostly occur in non-coding regions of the genome, how they confer increased risk of endometriosis is unknown.

This project aims to decode the biological significance of these SNPs in endometriosis by isolating stem/progenitor cell populations in women with endometriosis with a low genetic risk score compared to those with a high genetic risk score and determining their 1. gene expression profile (using single cell RNAseq) 2. organoid-forming capacity and cellular proliferation in vitro (using endometrial organoids) 3. lesion-forming capacity in vivo (using patient-derived xenografts) This project has international funding and provides an opportunity to develop skills in a number of techniques including fluorescent activated cell sorting (FACS), organoids, in vitro culture, RNAseq, bioinformatics, stem cell biology, mouse models, immunofluorescence. This project is most suited to a PhD students, and at later stages of the project there will be opportunities for Honours or Masters students.

Keywords
endometriosis, endometrial stem cells, genetic risk, organoids, gene expression, animal model

Women's Health

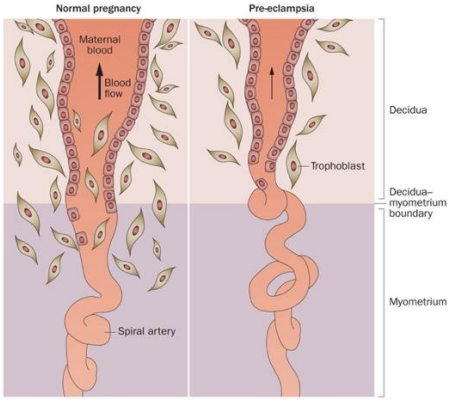
Assessing the Beneficial effects of Cruciferous Vegetable Extracts on the Vasculature

Suitability: Honours
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project leaders: Professor Euan Wallace, Dr Sarah Marshall
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 foetal 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 and brussel sprouts, provide a variety of beneficial health effects. So far, evidence suggests that novel compounds found in green leafy vegetables may have beneficial effects on the vasculature. Therefore, this project aims to identify whether these extracts can promote vascular health and be potential novel treatments for women with pre-eclampsia.

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



Reducing term stillbirth in South Asian born women

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Miranda Davies-Tuck, Dr. Mary-Ann Davey, Prof. Euan Wallace, A/Prof. Ryan Hodges
Email: miranda.davies@hudson.org.au

Project Description:
Despite decreases in the rates of both neonatal death and SIDS, the rate of stillbirth has remained largely unchanged in Australia for well over a decade. One group of women who have a much higher rate of stillbirth than other women giving birth in Australia are south Asian born women. These women – mainly Indian, Sri Lankan, Pakistani women – have a stillbirth rate twice that of both white Australian women and Chinese-born Australian women. We have shown that this difference appears to be due to accelerated placental ageing in south Asian women such that South Asian women have shorter pregnancies. Most maternity hospitals offer induction of labour or fetal surveillance for women whose pregnancy extends beyond 41 weeks. In mid-2017 we changed our protocol at Monash Health to offer surveillance or induction of labour for South Asian women at 39 weeks. We have a number individual projects aiming to assess the impact of the new guidelines at Monash Health.

Women's Health

Improving Induction of Labour

Suitability: **Honours**
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leader: Prof Euan Wallace
Email: *euan.wallace@monash.edu*

Description
This project seeks to develop a new care standard for the induction of labour in Victorian hospitals. There are a variety of methods of inducing labour, mostly related to the readiness of the cervix. In women where the cervix is not favourable, cervical priming is required before formal induction of labour. Historically this has been achieved with vaginal prostaglandins (e.g. Prostin gel or Cervadil). More recently, it has been shown that mechanical ripening, with a balloon catheter, is just as effective and may be safer. It is not known whether Victorian obstetricians have changed practice in response to this new knowledge.

This project will involve assessing induction of labour practices at all Victorian maternity hospitals, exploring opportunities for system improvement and better value-based healthcare. The project will be undertaken in collaboration with Safer Care Victoria and the Department of Health and Human Services, and with Health Purchasing Victoria. The project is ideally suited to an Honours program such as BMedSci or a Health Administration honours.

Keywords
obstetrics, induction of labour, health purchasing, Safer Care Victoria,

Working with Safer Care Victoria and Victorian Department of Health and Human Services

Suitability: **PhD/Masters by Research**
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leader: Prof Euan Wallace
Email: *euan.wallace@monash.edu*

Description
Safer Care Victoria is the state's lead agency for quality and safety improvement in healthcare. It is responsible for leading improvement in quality and safety in Victoria's hospitals and for oversight of quality and safety. There are abundant opportunities for research projects (Honours, Masters, PhD) in collaboration with Safer Care Victoria [SCV] (and other teams within the Department of Health more broadly). SCV has 11 Clinical Networks: Maternal and Newborn; Paediatric; Emergency Care; Critical Care (ICU); Cardiac; Renal; Palliative Care; Care of Older People; Infectious Diseases; Mental Health; Stroke. Each Network leads a program of research to inform future practice improvement. There are opportunities for research within each and all of the networks.

The majority of projects will involve large datasets, addressing whole of population health problems. Some may be more targeted to specific or emerging health issues. Projects suit all disciplines: medical students, medical graduates, nursing and midwifery students and graduates, allied health practitioners including paramedics. There are a limited number of BMedSci places available each year (maximum 4). Interest may be directed to SCV or lead Monash supervisor in first instance. Opportunities for undertaking a PhD should be first discussed with lead Monash supervisor prior to approaching SCV.

Keywords
healthcare, safety, quality, maternity, newborn, obstetrics, gynaecology, stroke, heart, cardiac, infectious diseases, surgery, palliative care, voluntary assisted dying, geriatrics, mental health, psychiatry, ICU, emergency care, kidney, renal

Women's Health

Exploring the role of VR in pain relief post laparoscopy

Suitability: **BMedSci (Honours)**
Location: Department of Obstetrics & Gynaecology, Monash Medical Centre, Moorabbin Hospital
Project Leader: Prof Beverley Vollenhoven, Dr Vinayak Smith
Email: beverley.vollenhoven@monash.edu, vinayak.smith@monash.edu

Background
Laparoscopy is a commonly performed gynaecological procedure. The studies surrounding post-operative pain in these women are sparse and conflicting. They however suggest the frequency of post-operative pain to be between 35 – 65%. The primary mechanisms of pain are theorised to be related to diaphragmatic irritation and peritoneal inflammation and stretching.

Virtual reality (VR) is a technological medium that is used to create simulated scenarios in which users are immersed and able to interact with the virtual environment (VE) through multisensorial stimulation[7]. There has been a recent interest in assessing its utility to provide analgesia in various field of medicine. As it stands, VR has demonstrated clinical efficacy in pain reduction whilst being well tolerated by patients as well. Importantly, a recent controlled trial by Tashijan et al. demonstrated a 24% drop in pain scores in patients utilising VR for acute pain post operatively.

Given the potential of VR to facilitate analgesia, the question of whether it can make post laparoscopy pain less painful and reduce opiate dependence does arise. This prompted us to design a pilot study to evaluate the efficacy of VR in this context. It is hoped that this can be used as a platform to design a larger sized controlled study should the results appear promising.

Aims
The aims and objectives of the following study is to function as a proof of concept study for examining the effect of VR on:

- Pain scores post laparoscopy
- Physiological parameters post laparoscopy
- Analgesia requirements post laparoscopy
- Same day discharge rates post laparoscopy
- Side effects generated and acceptability in participants
- Patients feedback of the device

Women's choices about twin birth

Suitability: **PhD/Masters by Research**
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leaders: Prof Euan Wallace, Dr Mary Ann Davey
Email: *euan.wallace@monash.edu*

Project description: The use of caesarean section for twin pregnancies in Australia has tripled over the past 20 years. Today, the majority of twins are born by caesarean section. There is no evidence that this has improved pregnancy outcomes. What remains unknown is why women are "choosing" caesarean section. Indeed, whether they are choosing or whether they are being advised by the practitioners looking after them. In this study, the student will undertake semi-structured interviews of women with a twin pregnancy giving birth at Monash Health. The interviews will explore autonomy, choice, decision reasoning, and influences underlying women's plans for their twin birth. The information will be used to develop decision tools for women and to inform public policy.

Improving Indigenous Perinatal Mortality

Suitability: **Honours**
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leader: Prof Euan Wallace
Email: *euan.wallace@monash.edu*

Description
This project seeks to better target healthcare improvement interventions to reduce perinatal mortality (stillbirth and neonatal death) in the indigenous (Koori) population in Victoria. Perinatal mortality rates among indigenous babies have been significantly higher than non-indigenous babies. In 2016, for the first time in Victoria, rates were similar due to a lower stillbirth rate but a higher neonatal mortality rate. The reasons for the lower stillbirth rate are unknown. In this project the student will work with the research team at Safer Care Victoria (and the Consultative Council for Obstetric and Paediatric Mortality and Morbidity) to understand the key differences in stillbirth and neonatal mortality rates between Koori and non-indigenous babies. Using these differences, including trends over time, the project seeks to derive recommendations for future care.
Keywords
stillbirth, neonatal death, perinatal mortality, Koori, indigenous, aboriginal, Safer Care Victoria

Fetal & Neonatal Health: Respiratory and Cardiovascular

Transition to Life After Birth

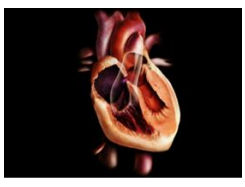
Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Stuart Hooper, Dr Kelly Crossley,
A/Prof Graeme Polglase, Dr Erin McGillick
Email: *stuart.hooper@monash.edu*
Phone: 03 8572 2871 (Dr Crossley)

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 by-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 Marcus Kitchen (Physics)
Email: *stuart.hooper@monash.edu*
Phone: 03 8572 2871 (Dr Crossley)

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 in premature animals.



What is the impact of common and novel blood pressure therapies on brain injury in growth restricted newborns?

Suitability: Honours
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Beth Allison, A/Prof Suzie Miller, A/Prof Graeme Polglase
Email: *beth.allison@hudson.org.au*
Phone: 03 8572 2488 (Dr Allison)

Project Description: Cardiovascular disease is one of the leading killers in the developed world. It is well accepted that growth restricted offspring have an increased susceptibility of cardiovascular disease as they age. Growth restricted infants require significant medical intervention following birth, and despite being essential for the newborns survival, can lead to brain injury. This project will aim to determine the relative brain injury following 4 hours of ventilation with either a common or novel blood pressure therapy. In this project we will be using an array of techniques including real-time PCR, histology, immunohistochemistry and image analysis.

Can we treat growth restricted fetuses in utero to improve cardiovascular function 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: Dr Beth Allison
Email: beth.allison@hudson.org.au
Phone: 03 8572 2488 (Dr Allison)

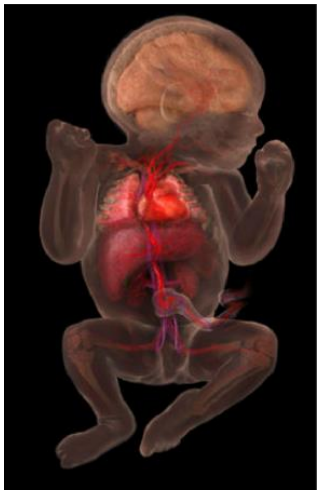
Project Description: Intrauterine growth restriction complicates 8% of pregnancies and increases risk for preterm birth and adverse brain development. Although there is no cure, we know that the nitric oxide pathway is involved in the increased risk of long term disease in growth restricted offspring. This project will investigate the ability of novel drugs treat growth restriction and improve cardiovascular outcomes for growth restricted newborns and adults. This project will be undertaken in rats and use techniques such as in vitro wire myography and histology to characterise cardiovascular function.

Fetal & Neonatal Health: Respiratory and Cardiovascular

Preventing Lung Disease in Very Premature Babies

Suitability: PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: A/Prof Megan Wallace, Prof Stuart Hooper
Email: *megan.wallace@monash.edu*
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.



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.

Fetal & Neonatal Health: Respiratory and Cardiovascular

Evaluating the outcomes of undergraduate medical and biomedical student research

Suitability: Honours
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
Email: *megan.wallace@monash.edu*
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 BMedSc(Hons) or BMS(Hons) compared to Course and year-level matched graduates who did not undertake a research Honours year.

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: Brain Injury and Neurodevelopment

Using heart rate variability to predict brain injury 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
Email: *flora.wong@monash.edu*
Phone: 03 85723655 (A/Prof Wong)

Project Description: The early signs of brain injury in preterm babies are often subtle and difficult to detect. However, once the brain injury is developed, there is no cure. This project aims to develop a new predictive method using heart rate variability (HRV) for early brain injury in preterm babies. The heart rates of all babies in the neonatal unit are monitored routinely using bedside ECG. We will use a research software known as ICM+, to perform continuous analyses of HRV on the ECG. We will validate the use of HRV for predicting brain injury identified on cranial ultrasound in preterm babies.

Coupling Between Brain Activity and Brain Blood Flow in The Immature Brain

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: A/Prof Flora Wong, A/Prof David Walker
Email: *flora.wong@monash.edu*
Phone: 03 8572 3655 (A/Prof Wong)

Project Description: Increase in brain activity is normally matched by an increase in brain blood flow to meet the metabolic demand. This is known as Neurovascular coupling, which is an important function in adults. However, little is known about neurovascular coupling in newborn babies. We aim to examine neurovascular coupling in the immature brain. In newborn lambs, we will measure changes in brain activity and brain blood flow. We will perform the studies in the Australian Synchrotron for state-of-the-art imaging of the brain blood vessels. We will also assess how different drugs used on sick human babies would affect the immature brain.

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, A/Prof Suzie Miller, Dr Michael Fahey
Email: *tamara.yawno@hudson.org.au, suzie.miller@monash.edu, michael.fahey@monash.edu*
Phone: 03 8572 2796 (A/Prof Miller)

Project Description: Seizures in neonates are quite 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 $GABA^A$ 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.

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: A/Prof Suzie Miller, Dr Amy Sutherland
Email: *suzie.miller@monash.edu*
Phone: 03 8572 2796 (A/Prof Miller)

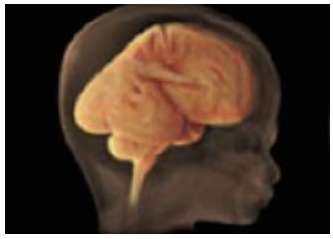
Project Description: Fetal growth restriction (FGR) is a serious, but common pregnancy complication, describing the infant that is born very small due to failure to achieve normal growth. FGR is present in up to 9% of pregnancies in Australia, and is strongly associated with complications after birth, 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

Protecting the Brain from Injury at Preterm Delivery

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 Kelly Crossley
Email : *graeme.polglase@monash.edu*, *kelly.crossley@monash.edu*
Phone: 03 8572 2822 (A/Prof Polglase)

Project Description: Brain injury is common in preterm infants and is a major cause of long-term adverse neurodevelopment, including mental disability and cerebral palsy. Human data and animal studies have shown that brain injury pertaining to preterm birth occurs through two major mechanisms: 1) an inflammatory cascade in the brain and 2) alterations to cerebral blood flow. Our current research is focused on understanding events that occur in utero, during the time of birth, and upon subsequent respiratory support after birth, can lead to brain injury in preterm neonates. Several projects will focus on establishing techniques to reduce/prevent brain injury related to perinatal events. The experiments include whole-animal physiology, molecular biology and immunohistochemistry.



Infant and Child Health

Understanding ventilatory control in children with Arnold Chiari malformation

Suitability: Honours/Masters by Research
Location: Department of Paediatrics, Level 5 Monash Children's Hospital
Project Leaders: A/Prof Gillian Nixon, A/Prof Margot Davey, Prof Rosemary Horne, Dr Brad Edwards
Email: gillian.nixon@monashhealth.org,
Phone: 85723587

Project Description: Arnold Chiari malformation is a structural abnormality of the base of the brain where there is displacement of the lower portion of the cerebellum and/or brain stem through the foramen magnum. This may result in brainstem compression with various neurological effects including recurrent pauses in breathing during sleep known as central sleep apnoea, which is a type of ventilatory control instability.

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 apnoeas. However, it is not known if children with Arnold Chiari malformation have similarly high loop gain or whether the recurrent central apnoeas 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 Arnold Chiari malformation.

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

Suitability: Honours
Location: Department of Paediatrics, Level 5 Monash Children's Hospital
Project Leaders: Prof Rosemary Horne
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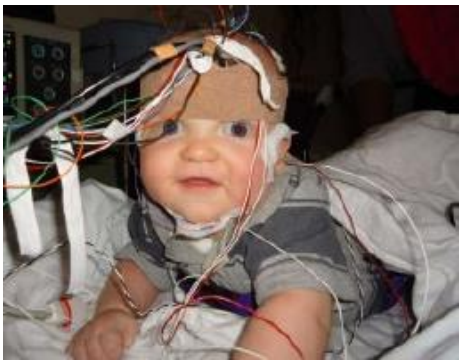
Phone: 8572 2827

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.



Infant and Child Health

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

Suitability: Honours/Masters by Research, PhD
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: 03 8572 2827 (Prof Horne)

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.

The impact of CPAP on quality of life and sleepiness in children

Suitability: Honours/Masters by Research
Location: Department of Paediatrics, Level 5 Monash Children's Hospital
Project Leaders: A/Prof Gillian Nixon, A/Prof Margot Davey, Prof Rosemary Horne
Email: gillian.nixon@monashhealth.org,
Phone: 85723587

Project Description: In adults, the first line of treatment for obstructive sleep apnoea (OSA) is continuous positive airway pressure (CPAP). CPAP effectively reduces snoring and the obstructive apnoea hypopnea index (OAHI), normalizes oxygen saturations and reduces arousals associated with the obstructive events. This improvement in respiratory disturbance has been associated with reduced daytime symptoms, but the relationship between the actual hours of usage and the degree of improvement in various symptoms may be different for different symptoms and reach a threshold of effect at different levels of usage.

OSA affects up to 4% of children, with even higher prevalence in children with certain conditions, such as obesity, Down Syndrome, Prader-Willi Syndrome and craniofacial abnormalities. OSA has a significant impact on daytime performance in children. The primary treatment is adenotonsillectomy, which is an effective treatment for the majority of children. However, in a minority of children surgical treatment is either insufficient or inappropriate, and in these children CPAP is also frequently used. Only one study has investigated the impact of CPAP on daytime sleepiness, neurobehavioral measures and quality of life, even with very low adherence to the treatment.

As the use of CPAP in paediatric populations continues to increase and new technologies become available, new studies are need to improve the evidence base for this treatment. We plan to investigate a range of cognitive, behavioural and quality of life measures at baseline and after CPAP treatment in children.

Infant and Child Health

Optimising daytime and cardiovascular function in children with Down syndrome through treatment of Obstructive Sleep Apnoea

Suitability: Honours/Masters by Research, PhD
Location: Department of Paediatrics, Level 5 Monash Children's Hospital
Project Leaders: Prof Rosemary Horne, A/Prof Gillian Nixon
Email: *rosemary.horne@monash.edu*
Phone: 03 8572 2827 (Prof Horne)

Project Description: Down Syndrome (DS) is one of the major causes of developmental disability in childhood. Obstructive sleep apnoea (OSA) is extremely common in children with DS, but investigation and treatment of OSA is not systematically carried out as part of clinical care, despite international recommendations. Given the significant impact of sleep disruption on learning, behaviour, the cardiovascular system and quality of life in typically developing children, a better understanding of the impact of OSA on daytime functioning in OS, especially adaptive functioning (skills of daily living), is urgently needed worldwide. We know that treatment of OSA in typically developing children leads to improvements in quality of life and cardiovascular functioning. Despite their existing intellectual disability and cardiovascular problems, children with DS stand to substantially benefit from early detection and appropriate treatment of OSA, ensuring maximisation of their potential and minimisation of the cardiovascular effects. This project will follow up children previously studied.

Temporal variations in clinical outcomes across international neonatal quality networks and effect

Suitability: Honours/PhD/BMedSc(Hons)
Location: The Nest (Monash Newborn) Level 5, Monash Children's Hospital
Project Leaders: A/Prof Kenneth Tan, Prof Kei Lui
Email: kenneth.tan@monash.edu
Phone: +61 3 85723650 (A/Prof Tan)

Project Description: The International Network for Evaluation of Outcomes (iNeo) is a collaboration of national neonatal network and registries from nine developed nations, namely Australia, New Zealand, Canada, United Kingdom, Sweden, Finland, Switzerland, Spain, Italy, Israel and Japan. A standardised neonatal intensive care database has been in operation for the iNeo since 2007. In a seminal study, the investigators investigated variations across these networks of a composite outcome of mortality before discharge, severe intraventricular hemorrhage or periventricular echodensity or echolucency, bronchopulmonary dysplasia, or retinopathy of prematurity that was treated. Important predictors for variations of the primary and secondary outcomes were identified and informed initiatives for improving care in the respective countries. The proposed project aims to investigate if intra-network variations across 12 years since inception of iNeo is associated with overall inter-network variations. The student working on this project will be co-supervised by Drs. Tan and Lui and will be working with biostatisticians and data officers from the Canadian Neonatal Network in Toronto where the iNeo database is housed.

Keywords
Neonatal outcomes, registry, collaborative networks

Infant and Child Health

Maternal health and neonatal outcomes – investigating secular trends and risk factors

Suitability: Honours/PhD/BMedSc(Hons)
Location: The Nest (Monash Newborn) Level 5, Monash Children's Hospital
Project Leaders: A/Prof Kenneth Tan, Dr Mary-Ann Davey
Phone: +61 3 85723650 (A/Prof Tan)

Maternal health affects newborn health, for example maternal diabetes is associated with large-for-gestational age infants who may suffer from respiratory distress or hypoglycaemia. The Victorian Perinatal Data Collection (VPDC) is a state health department mandated dataset recorded for all births. Similarly, the Australia and New Zealand Neonatal Network (ANZNN) a registry for infants who require intensive care has been in operation since 1994. The project will involve investigations of the two data repository to look into the secular trends of maternal health and weight and neonatal outcomes (including NICU admissions, birthweight and morbidities) initially in the Monash Health network. Through this project the student will acquire skills in managing datasets and biostatistical analyses. The project will be based at Monash Women's and Newborn.

Keywords
Maternal health, neonatal outcomes

Preterm Infants in The NICU – Mechanisms of Oxygen Desaturations

Suitability: Honours/PhD
Location: The Nest (Monash Newborn) Level 5, Monash Children's Hospital
Project Leaders: A/Prof Kenneth Tan, A/Prof Philip Berger
Email: kenneth.tan@monash.edu, *philip.berger@monash.edu*
Phone: +61 3 85723650 (A/Prof Tan)

Project Description: A number of factors render preterm infants susceptible to hypoxaemic events, including low lung oxygen stores, high metabolic rate and a strong tendency for apnoeas to recur, with brief periods of intervening breathing (e.g. periodic breathing). Management is by increased oxygen therapy which involves a strategy of adjusting inspired oxygen to maintain SpO_2 within a target range based on pulse oximetry (oxygen saturation targeting). This may lead to secondary hyperoxia, as manual adjustment of oxygen often overshoots what is required. There is evidence that these episodes (of hypoxia and hyperoxia) contribute to adverse outcomes such as retinopathy of prematurity, bronchopulmonary dysplasia and poorer long-term neurodevelopment. The aim of this study is to study hypoxia/hyperoxia events in preterm infants in the NICU and methods for improving delivery of oxygen including the role of automated oxygen delivery for preterm infants. This project will involve physiological measurements of infants receiving respiratory support (ventilation or CPAP) in the NICU, both from the ventilators and from additional research equipment.

This project will involve physiological measurements of infants receiving respiratory support in the NICU, both from the ventilators and from additional research equipment. The student will be conducting physiological measurements from infants in the NICU. This is part of the group's work on automated oxygen delivery to preterm infants.

Infant and Child Health

The early recognition of the deteriorating neonate - Investigating the utility of statistical or machine learning models

Suitability: Honours
Location: The Nest (Monash Newborn) Level 5, Monash Children's Hospital
Project Leaders: A/Prof Kenneth Tan, A/Prof Vincent Lee (Faculty of IT, Monash University)
Email: *kenneth.tan@monash.edu*
Phone: +61 3 85723650 (Dr Tan)

Project description: The early recognition of deteriorating patient and the timely administration of appropriate therapy saves lives and prevents long-term morbidity. The Australian Commission on Safety and Quality in Health Care (ACSQHC) has mandated to be an essential part of patient care. In adult and paediatric medical literature, there is good evidence that early warning systems (for recognition of patient deterioration) improves outcomes for condition such as sepsis. For the newborn infant, there is emerging data that early warning tools on routine charts may assist in early identification of the patient deterioration. Notable example being the "track and trigger chart" (manual observation charts) from the Plymouth group in the UK, which is increasingly adopted in delivery suites in the over there. With the introduction of electronic medical records (EMR) and networked (physiological vital signs) monitoring systems into use, we have the potential to develop real-time automated monitoring and alert systems.

The aim of the project will be to utilise currently available physiological signals and investigate the feasibility of 1) statistical risk prediction models and/or 2) machine learning algorithm to develop an electronic early warning system for newborn infants. Patient population: a) Infants who are convalescing in special care baby units or nursery after step-down from the intensive care section, preterm infants or term, b) Newborn infants being admitted for a primary indication to special care nursery within Monash Newborn. Physiological monitoring from cot-side monitors, specifically ECG data, pulse oximetry and plethysmograph, impedance respiratory, blood pressure, and temperature will be recorded from the monitor network. The work can will involve work in the NICU, data recording and interaction with IT engineers from Monash University and will be based at Monash Children's Hospital.

Keywords:
newborn infants, NICU, monitoring, early warning, prediction tools

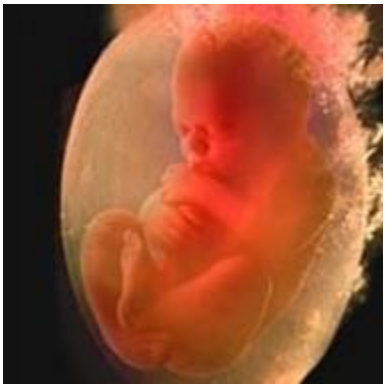
Infection, Inflammation and Immunity

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

Suitability: Honours or 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. Tim Moss
Email: *robert.galinsky@hudson.org.au, tim.moss@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 brain injury in preterm fetal sheep, using an FDA approved IL-1β receptor antagonist.

Research techniques: Fetal surgery, electronic fetal monitoring of brain activity, movement, breathing and cardiovascular function. Neuropathological assessment using immunohistochemistry and molecular biology. development of atherosclerosis in mice predisposed to development of the disease.



Amniotic fluid infection/inflammation: effects on brain development and postnatal behaviour

Suitability: Honours or PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: A/Prof Tim Moss, Dr Margie Castillo-Melendez, Dr Samantha Dando (Queensland University of Technology)
Email: *tim.moss@monash.edu*

Project description: Evidence of infection or inflammation within the uterus during pregnancy increases the risk of neurodevelopmental disorders like autism and cerebral palsy.
This project is aimed at identifying the effects of experimental amniotic fluid infection (using ureaplasmas, the microorganisms most commonly identified in amniotic fluid of women who deliver preterm) on brain development and postnatal behaviour in spiny mice (*Acomys cahirinus*). These animals are particularly suitable as a model of human pregnancy; postnatal outcomes can be assessed using a battery of neurobehavioural tests.

Research techniques: small animal experimentation (surgery, tissue collection, biometry); small animal neurobehavioral tests; histology; immunohistochemistry; molecular biology (RT-PCR); microbiology.

Infection, Inflammation and Immunity

Maternal immunisation against whooping cough: effect on fetal and postnatal brain development

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 Tim Moss, Dr Margie Castillo-Melendez
Email: *tim.moss@monash.edu*

Project description: Development of immunity to whooping cough by immunising babies after birth leaves them vulnerable to infection in early life. Immunisation of the mother during pregnancy allows development of immunity in the fetus, thus providing protection from birth. However, activation of the maternal immune system during pregnancy can influence brain development, leading to disorders such as autism and schizophrenia: whether maternal whooping cough immunization has this effect is unknown.
This project is aimed at assessing the effects on brain development in spiny mice, after maternal immunization against whooping cough.

Research techniques: histology; immunohistochemistry; molecular biology (RT-PCR); neuroanatomy

Maternal immunisation: potential effects on fetal growth and development

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 Tim Moss, Dr Miranda Davies-Tuck
Email: *tim.moss@monash.edu, robert.galinsky@hudson.org.au*

Project description: Immunisation of the mother during pregnancy allows development of immunity in the fetus, thus providing protection from birth. However, activation of the maternal immune system at particular stages during pregnancy may influence fetal growth and development.
This project is aimed at assessing the effects of timing of maternal immunization on fetal growth, by examining patient data from Monash Women's Hospital.
Research techniques: data extraction; epidemiology; biostatistics

SYNTRACK: Linking ED Data to Detect Outbreaks and Vaccine Safety Signals

Suitability: Honours/BMedSci/PhD
Location: Level 3, Monash Medical Centre, Clayton
Project Leaders: Prof Jim Buttery, A/Prof Franz Babl,
A/Prof Simon Craig
Email: *jim.buttery@monash.edu, franz.babl@rch.org.au, simon.craig@monash.edu*
Phone: 0403854179 (Prof Buttery)

Project Description: Direct clinical relevance: medium/high hands-on learning opportunities: clinical emergency datasets; real-time extraction and upload programming; geocoding; signal detection methodologies.
De-identified real-time surveillance systems operating from emergency department (ED) diagnostic coding have been effective in the early detection of influenza outbreaks and biological threats. This project will establish the feasibility of linking 3 Melbourne paediatric EDs to map in time and place syndromes consistent with epidemic infectious diseases and vaccine safety signals. This pilot BMedSci project could be expanded nationally using the PREDICT paediatric ED network as an "early warning" surveillance system for epidemic infectious diseases and vaccine safety signal in children.

Infection, Inflammation and Immunity

SNOTWATCH: Real Time Seasonal Viral Information for Health Providers

Suitability: BMedSci
Location: Level 3, Monash Medical Centre, Clayton
Project Leaders: Prof Jim Buttery, Dr Andrew Daley
Email: *jim.buttery@monash.edu*, *andrew.daley@rch.org.au*
Phone: 0403 854 179 (Prof Buttery)

Project Description: Direct clinical relevance: medium/high Hands-on learning opportunities: hospital microbiology datasets; real-time extraction and upload programming; geocoding; signal detection methodologies.
This project will develop an automated real-time presentation of respiratory and gastrointestinal viral detections from hospital and community pathology providers to help clinicians determine the probability of what is causing common illness syndromes in children presenting to them. The information would be uploaded and presented on a publicly available website and weekly updates provided to GPs and emergency departments. The geotemporal data will be examined to determine evidence of predictable state-wide spread of seasonal epidemic viruses.

Vaccine Safety in General Practice: Can Representation Rates Be Used as an Early Warning Surrogate for Adverse Event Rates?

Suitability: BMedSci
Location: Level 3, Monash Medical Centre, Clayton
Project Leaders: Prof Jim Buttery, Dr Nigel Crawford, Dr Jock Lawrie, A/Prof Chris Pearce
Email: *jim.buttery@monash.edu*, *nigel.crawford@rch.org.au*
Phone: 0403 854 179 (Prof Buttery)

Project Description: Direct clinical relevance: medium/high Hands-on learning opportunities: general practice and public health datasets; real-time extraction and upload programming; signal detection methodologies.
In 2010, one of the seasonal influenza vaccines had an unacceptable rate of fever and febrile convulsions, resulting in at least one child with severe neurological sequelae. This project will test whether using pooled GP presentation data extracted from GP software can act as an “early warning system” allowing potentially unsafe vaccines to be identified as soon as possible, minimizing harm to the public.

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
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
Phone: 03 8572 2775 (A/Prof C Nold), 03 8572 2815 (Dr Rudloff), 03 8572 2776 (Prof M Nold)

Project Description: 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..

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 alveolarisation 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 immunetherapies by histology and flow cytometry and by analysis of selected biochemical markers. In human specimen we will assess the underlying mechanism of disease.

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

Infection, Inflammation and Immunity

Molecular Characterisation of Regulation and Mechanism of Action of the Anti-inflammatory Cytokine Interleukin 37

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, Dr Devi Ngo
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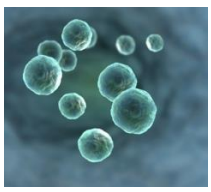
marcel.nold@hudson.org.au
Phone: 03 8572 2775 (A/Prof C Nold), 03 8572 2815 (Dr Rudloff), 03 8572 2776 (Prof M Nold)

Project Description: Direct clinical relevance: medium/low. Hands-on learning opportunities: Culture of primary human blood cells and cell lines, protein detection by ELISA, RNA detection by real-time PCR, flow cytometry, immunohistochemistry.

Interleukin (IL)-37 was discovered in silico in 2000, but it remained a neglected molecule, and nothing at all was known about its function until 2010, when we described the powerful anti-inflammatory properties of this cytokine. IL-37 belongs to the IL-1 family of cytokines and imparts a strong inhibition of the production of pro-inflammatory cytokines. Interestingly, this protection from inflammatory responses is not limited to one or a few triggers, but covers a wide spectrum of inflammatory assaults - a rare property, which renders IL-37 a prime candidate for clinical use. However, further research on the mechanism of action of this unusual cytokine is required before such steps can be taken. In this project, we will characterise several aspects of regulation and function of IL-37, in particular the mRNA and protein expression profile of IL-37 across a spectrum of cell types and the effect of IL-37 one of the key molecular regulator of inflammation, the inflammasome.

Keywords
medicine, immunology, inflammasomes, interleukin1 family, ELISA, PCR, flow cytometry, immunohistochemistry



The First In Vivo Exploration of IL-38 in Systematic Lupus Erythematous

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@hudson.org.au*, *ina.rudloff@hudson.org.au*, *marcel.nold@monash.edu*
Phone: 03 8572 2775 (A/Prof C Nold), 03 8572 2815 (Dr Rudloff), 03 8572 2776 (Prof M Nold)

Project Description: Direct clinical relevance: medium. Hands-on learning opportunities: Various aspects of work with mice and patient samples, workup of tissues for various downstream applications, flow cytometry, histology, immunohistochemistry, protein detection by ELISA, RNA detection by real-time PCR.

Interleukin (IL)-38 is a novel member of the IL-1 family of cytokines. The majority of IL-1 family members play important roles in inflammatory diseases – either as promoters or inhibitors of inflammation. IL-38, however, received almost no research attention until our group renamed the new IL-1 family cytokines in 2010. Thus, its function is still largely unknown. Recently, we discovered that IL-38 plays a role in systemic lupus erythematosus (SLE) – a very severe and potentially fatal autoimmune disease that mainly affects young women in their childbearing age. We found that SLE patients have elevated serum IL-38 concentrations and that IL-38 is predictive of disease severity and the development of major SLE-associated complications. Moreover, we have shown *in vitro* that IL-38 has anti-inflammatory properties and inhibits the production of cytokines that promote inflammation.

Now, we want to investigate the function of IL-38 *in vivo*. For this purpose, we have generated the very first IL-38 knockout mouse that is not available anywhere else in the world. In this exciting project we will undertake the first experiments using this mouse in a murine model of SLE but will also perform experiments on blood samples directly obtained from SLE patients. Applying techniques such as ELISA, flow cytometry, real-time PCR and histology we will aim to identify the role of IL-38 in SLE and potentially lay the foundation for a novel therapeutic approach for the treatment of SLE.

Keywords
Interleukin 1 family, knockout mice, human samples, systemic lupus erythematosus (SLE), flow cytometry, histology, immunohistochemistry, ELISA, real-time PCR

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 with option of 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*
Phone: 03 8572 2776 (Prof M Nold), 03 8572 2775 (A/Prof C Nold)

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

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.

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

The Role of IL37 in the pathogenesis of inflammatory bowel disease

Suitability: Honours/BMedSci with option of PhD
Location: Hudson Institute of Medical Research, Level 1, 27-31 Wright St, Clayton
Project Leaders: A/Prof Claudia Nold, Dr Rimma Goldberg, Prof Marcel Nold,
Email: *claudia.nold@hudson.org.au*
Phone: 03 8572 2776 (Prof M Nold), 03 8572 2775 (A/Prof C Nold)

Project Description: IL37 is a novel anti-inflammatory cytokine which is reduced in the circulation of patients with auto-immune diseases, including inflammatory bowel disease (1). Human peripheral blood mononuclear cells are capable of producing IL37, and in particular the T cell subset (2). Aberrant helper T cell responses play a key role in the pathogenesis of IBD (3-5). 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 look at characterising IL37 production in different cell subsets in the blood and lamina propria of patients with inflammatory bowel disease. Cells will be isolated from peripheral blood and colonic biopsies. Following appropriate processing or digestion and stimulation, flow cytometry will be used to characterise immune cell subsets and their capacity to produce IL37. Additionally, colonic biopsy samples will be collected and stored to create frozen sections for immunofluorescent staining. 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.

Keywords
preclinical study, inflammatory bowel disease, inflammation, immunology, interleukins,

Infection, Inflammation and Immunity

Exploration of IL-38 in inflammatory diseases

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@hudson.org.au*, *ina.rudloff@hudson.org.au*, *marcel.nold@monash.edu*
Phone: 03 8572 2775 (A/Prof C Nold), 03 8572 2815 (Dr Rudloff), 03 8572 2776 (Prof M Nold)

Project Description: Direct clinical relevance: medium. Hands-on learning opportunities: Various aspects of work with mice and patient samples, workup of tissues for various downstream applications, flow cytometry, histology, immunohistochemistry, protein detection by ELISA, RNA detection by real-time PCR. Interleukin (IL)-38 is a novel member of the IL-1 family of cytokines. The majority of IL-1 family members play important roles in inflammatory diseases – either as promoters or inhibitors of inflammation. IL-38, however, received almost no research attention until our group renamed the new IL-1 family cytokines in 2010. Thus, its function is still largely unknown. Recently, we discovered that IL-38 plays a role in systemic lupus erythematosus (SLE) – a very severe and potentially fatal autoimmune disease that mainly affects young women in their childbearing age. We found that SLE patients have elevated serum IL-38 concentrations and that IL-38 is predictive of disease severity and the development of major SLE-associated complications. Moreover, we have shown in vitro that IL-38 has anti-inflammatory properties and inhibits the production of cytokines that promote inflammation. Now, we want to investigate the function of IL-38 in vivo. For this purpose, we have generated the very first IL-38 knockout mouse that is not available anywhere else in the world. In this exciting project we will undertake the first experiments using this mouse in a murine model of SLE but will also perform experiments on blood samples directly obtained from SLE patients. Applying techniques such as ELISA, flow cytometry, real-time PCR and histology we will aim to identify the role of IL-38 in SLE and potentially lay the foundation for a novel therapeutic approach for the treatment of SLE.

Keywords
Interleukin 1 family, knockout mice, human samples, systemic lupus erythematosus (SLE), flow cytometry, histology, immunohistochemistry, ELISA, real-time PCR.

Evaluation of a Novel Allosteric IL-1R Inhibitor (Rytvela) in a Spiny Mouse Model of Infection in Pregnancy – a Study of Offspring Behavioural Outcomes.

Suitability: Honours
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Stacey Ellery and Dr Nadia Bellofiore
Email: stacey.ellery@hudson.org.au

Project description: *In utero* exposure to high levels of maternal immune cells (such as those produced to fight a bacterial or viral infection) has been linked to the development of mental illness disorders in offspring. Use of a novel allosteric inhibitor of the IL-1 receptor (Rytvela) has been proposed as a treatment to minimise the immune cascade in pregnancies complicated by infection; thus, protecting the fetus from adverse outcomes.

This study will use the spiny mice model of maternal immune activation to assess the effectiveness of Rytvela administration in pregnancy in reducing behavioural deficits in offspring. The study will involve running a series of behavioural tests, including open field, elevated plus maze, novel object recognition and social interaction in neonatal and juvenile spiny mice exposed to maternal immune activation at mid gestation, with and without Rytvela treatment. Applicants should be keen to develop skills in handling mice.

Infection, Inflammation and Immunity

Human amnion epithelial cells to prevent adverse outcomes of perinatal inflammation

Suitability: Honours
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: A/Prof Tim Moss, Prof Jane Pillow (UWA)
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Phone: 03 8572 2821 (A/Prof Moss)

Project description: Many preterm babies are exposed to inflammation before birth. This inflammation affects development and can cause life-threatening illness in newborns. The anti-inflammatory properties of epithelial cells from the amniotic membrane may be able to reduce the inflammation, normalize development, and prevent illness in these babies.
The aim of this project is to determine the effects of human amnion epithelial cells on inflammation and injury, and development, using tissues from preterm lambs. Individual projects may focus on particular aspects of development, inflammation or injury, using tissues including the brain and respiratory, immune, and gastrointestinal systems.

Targeting the inflammasome; the key to treating 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, Dr Jenifer Dowling, A/Prof Suzie Miller, A/Prof Michael Fahey
Email: courtney.mcdonald@monash.edu
Phone: 03 8572 2799

Project description: Inflammation plays a key role in the development of perinatal brain injury and cerebral palsy. However, the inflammatory mechanisms that lead to perinatal brain injury are not well understood. We have identified a pathway that is upregulated in perinatal brain injury that has not currently been investigated, the inflammasome. Using a rodent model, this project will explore the role of the inflammasome pathway, and through the use of small molecule inhibitors we will develop novel therapies to treat perinatal brain injury. This project will also explore the role of the inflammasome in human pregnancy complications adding a clinical aspect to this work. As part of this project you will learn cutting edge techniques like small animal surgery, motor control and cognitive behavioural testing, multicolour flow cytometry, molecular techniques including PCR and protein arrays, and brain immunohistochemistry.

Cell therapy and regenerative medicine

Isolation and Banking of Cord Blood Stem Cells and Placental Tissues for Future Clinical Therapies

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Graham Jenkin, A/Prof Suzie Miller, Prof Mark Kirkland, Dr Courtney McDonald, Dr Margie Castillo-Melendez
Email: *graham.jenkin@monash.edu*
Phone: 0419534101 (Prof Jenkin)

Project Description: Umbilical cord blood and the umbilical cord are a recognised source of a range of stem cells including mesenchymal stem cells (MSCs), hematopoietic stem cells (HSCs) and endothelial progenitor cells (EPCs), which have the potential to differentiate into a wide range of cell types and are also potentially neuroprotective, angiogenic, immunomodulatory and anti-inflammatory. The use of these cells is being explored in a number of therapeutic settings.

This project, carried out in collaboration with Cell Care, will validate methods for collection, processing, expansion, characterization and storage of umbilical cord blood and tissue containing these cells, and their viability and efficacy on retrieval post-thaw.

Activating the stem cell niche

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 Rebecca Lim, Prof Euan Wallace
Email: *rebecca.lim@monash.edu*
Phone: 03 8572 2794 (A/Prof Lim)

Project Description: Amnion stem cells have reparative potential in the lung. It is yet unknown how they trigger the regenerative process to improve lung function. We will use an animal model to mimic chronic lung disease and determine how amnion stem cell treatment can awaken the stem cell niche in the lung. Various techniques will be employed such as small animal surgery, stem cell culture, immunohistochemistry, ELISA, FACS, real-time PCR and western blotting. This project will provide valuable data on the mechanism of stem cell action as this work progresses to clinical trials.

Cord Blood Derived Stem Cells as Therapy for Brain and Lung Inflammation in Preterm Newborns

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 Suzie Miller, Prof Graham Jenkin, Dr Margie Castillo-Melendez, Dr Atul Malhotra **Email:**
graham.jenkin@monash.edu
Phone: 0419534101 (Prof Jenkin)

Project Description: Premature birth leads to lifelong complications of both brain and lung development. Cells isolated from umbilical cord blood have stem cell-like properties and other characteristics that make them attractive as a potential cell therapy. The aim of this project is to identify the effect of human UCBCs on inflammatory responses of newborn preterm lambs in order to develop clinical therapies for treatment of brain injury in preterm newborns. The experiments include whole-animal physiology, immunology, microscopy and molecular biology techniques.

Stem cell based nanomedicine

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 Rebecca Lim
Email: *rebecca.lim@monash.edu*
Phone: 03 8572 2794 (A/Prof Lim)

Project Description: This project looks to characterise the exosomes released by different stem cell types and assess their potential for regenerative medicine, and thus possibly pave the way for cell-free therapies. This area of research is newly emerging and highly novel in the stem cell field. Techniques employed include stem cell isolation, mass spectrometry, bioinformatics, tissue culture, electron microscopy, molecular biology, real-time PCR and western blotting.

Cell therapy and regenerative medicine

Do Cord Blood Stem Cells Reduce Cerebrovascular 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: A/Prof Suzie Miller, Dr Margie Castillo-Melendez,
Email: *suzie.miller@monash.edu*
Phone: 03 8572 2796 (A/Prof Miller)

Project Description: Babies that are born preterm are at the greatest risk of developing cerebral palsy. Indeed, up to 50% of children with cerebral palsy were born preterm. It is now appreciated that the parents of many Australian children with cerebral palsy are taking their children overseas to undertake cord blood stem cell therapy, despite a lack of published data that such therapy will be beneficial. We have identified that a principal component of brain injury in the preterm brain is instability of the blood vessels, which allows inflammatory and other blood products to enter the brain and damage cells. This project will examine whether cord blood stem cells can protect blood vessels within the brain, and in turn prevent brain injury. This project utilizes brain tissue that has already been collected and does not require the student to undertake animal work.
Keywords:
brain development, neuroprotection

Angiogenesis potential of exosomes

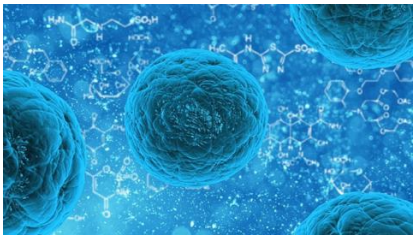
Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research, Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Mirja Krause, A/Prof Rebecca Lim
Email*: mirja.krause@hudson.org.au*
Phone: 03 8572 2874 (Dr Krause)

Project Description: It has been shown that exosomes can modulate angiogenesis (formation of new capillaries from pre-existing vasculature). This project looks to assess the angiogenesis potential of exosomes released by human amnion epithelial cells in more detail. Techniques employed include stem cell isolation and cultivation followed by exosomes isolation/ purification, tissue culture, exosome quantification and characterization, live cell fluorescence confocal microscopy.
Keywords:
human amnion epithelial cells, exosomes, angiogenesis

Bioengineering strategies to enhance stem cell therapeutics for vascular regeneration

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research, Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Gina Kusuma, A/Prof Rebecca Lim
Email*: gina.kusuma@hudson.org.au*
Phone: 03 8572 2876 (Dr Kusuma)

Project Description: The global burden of peripheral artery disease is at a dramatic increase due the prevalence of aging, obesity, diabetes, cardiovascular disorders, and autoimmune diseases. Stem cells have a significant promise for cell therapies and regenerative medicine applications. Stem cells serve as bio-factories releasing bioactive products including growth factors and exosomes and there is now increasing evidence that exosomes confer the therapeutic benefits of stem cells, thus accelerating the pathway for cell-free therapies. This project propose aims to enhance vascular regeneration potential of stem cell-derived exosomes by using cues from the cellular environment. Stem cells are highly sensitive to physical stimuli from their surrounding microenvironment and this project will evaluate this by comparing the traditional 2D static culture with dynamic 3D culture. Techniques employed include stem cell culture, immunofluorescence, proliferation assay, 3D culture, exosomes isolation, Western blotting, nanoparticle tracking analysis, and angiogenesis assays.
Keywords
stem cells, exosomes, regenerative medicine, angiogenesis



Cell therapy and regenerative medicine

Novel formulations of stem cell-derived exosomes for vascular regeneration

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research, Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Gina Kusuma, A/Prof Rebecca Lim
Email*: gina.kusuma@hudson.org.au*
Phone: 03 8572 2876 (Dr Kusuma)

Project Description: Peripheral artery disease (PAD) affects more than 200 million people globally and the main driving forces is the ageing of the population and increase in cardiovascular risk factors, such as smoking, diabetes mellitus, and hypertension. PAD is a severe medical condition commonly characterised by critical or acute limb ischemia that arises due to blockage of arteries in the lower limbs. Defective angiogenesis and wound healing capacities are the principal factors limiting tissue recovery in ischemic diseases and this project seeks to fine-tune the mechanisms controlling this process by employing targeted drug delivery system. Stem cell therapies are typically employed to repair tissue functions in the event of injury.

Stem cells also serve as bio-factories releasing bioactive products including growth factors and exosomes and there is now increasing evidence that exosomes confer the therapeutic benefits of stem cells, thus accelerating the pathway for cell-free therapies. Biomaterials such as hydrogels often used for drug delivery and we can tailor the release of biomolecules by altering their physicochemical properties such that in vivo the hydrogel can release the factors by different mechanisms such as swelling, degradation, or deformation. This project aims to develop formulations of stem cell-derived exosomes encapsulated in biomaterials to improve their stability and enhance vascular regeneration. Techniques employed include: murine peripheral artery disease model, stem cell culture, exosomes isolation, nanoparticle tracking analysis, biomaterials fabrication, in vitro angiogenesis and wound healing assays
Keywords
stem cells, vascular biology, extracellular vesicles, angiogenesis, biomaterials

Developing a combination stem cell therapy for preterm inflammation induced 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 Suzie Miller, Prof Graham Jenkin,
Email: courtney.mcdonald@monash.edu
Phone: 03 8572 2799

Project Description: Preterm birth and *in utero* inflammation (chorioamnionitis) place babies at high risk of neurodevelopmental deficits. White matter injury is the most common neuropathology in these infants, due to the vulnerability of developing oligodendrocytes. There are no established therapeutic interventions to protect or repair the immature brain after preterm birth. Stem cells derived from placental tissues have excellent neuroprotective potential. We have shown that stem cells, have the capacity to reduce inflammation and improve white matter cell survival and maturation. Using a preterm sheep model of inflammation induced brain injury, this project will test the combination of two stem cell types, UCB and MSCs with anti-inflammatory and/or white matter protective properties. As part of this project you will learn large animal surgery and monitoring, brain immunohistochemistry and molecular techniques using PCR and protein arrays.

Cell therapy and regenerative medicine

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

Suitability: Honours/PhD
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 Ashalyn Watt
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Phone: 0419534101 (Prof Jenkin)

Project Description: Umbilical cord blood (UCB) is one of the richest sources of "young" hematopoietic 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 molecular biology techniques and structural analysis of UCB stem cells.

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
Email: courtney.mcdonald@monash.edu
Phone: 03 8572 2799

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.

Development of a novel MRI method to deliver neural stem cells to the developing brain

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 Suzie Miller, Prof Graham Jenkin, A/Prof Michael Fahey
Email: courtney.mcdonald@monash.edu
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. A major challenge of NSC therapy for neurological conditions is getting the cells to the brain. Current intracerebral-delivery of NSCs is highly invasive and carries significant risks for the patient. We propose to develop a novel, non-invasive MRI-guided focused ultrasound (MRIgFUS) method for delivery of NSCs to the brain using a neonatal rodent model. MRIgFUS temporarily opens the blood brain barrier (BBB) allowing cells to directly access the brain, overcoming the need for invasive and high-risk brain or spinal administration.

This project will (a) optimise MRIgFUS for the delivery of clinically-compatible human NSCs that minimises collateral damage to the neonatal rat brain, and (b) examine the impact of MRIgFUS-NSC transplantation on long-term outcomes (cognition, memory, motor-skills) of stroke-affected rodents. As part of this project, you will learn small animal surgery, motor control and cognitive behavioural testing, MRI and ultrasound techniques and brain immunohistochemistry.

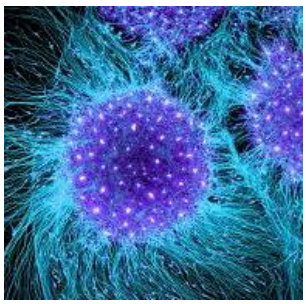
Cell therapy and regenerative medicine

Stem Cells and Tissue Scaffolds

Suitability: Honours/PhD
Location: Department of Surgery, Monash Medical Centre, Clayton & The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: A/Prof Tony Goldschlager, Prof Graham Jenkin
Email: *graham.jenkin@monash.edu*
Phone: 0419534101 (Prof Jenkin)

Project Description: In these studies, we are investigating the suitability of novel new biomimetic matrices to form tissue structures to produce biomimetic structures such as spinal discs and trapezium joints for repair of damage caused by trauma or degenerative processes. We will study the characteristics of biomatrices both in vitro and in vivo.

We will determine the appropriateness of our cellular scaffolds for the production of engineered tissues. We will determine the most appropriate polymer compositions and stem cell combinations that can be developed into the most viable scaffold for therapeutic use in clinical trials.



Derivation of Human Induced Pluripotent Stem Cells (iPSCs) using mRNA

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

Project Description: Human iPSCs may be derived using a range of methods. For clinical use, it is desirable to use non-genomic integrating methods for expressing the primary transcription factors (cMYC, OCT4, SOX2 and KLF4). It is possible to use mRNA (ReproCELLStemgent https://www.stemgent.com/products/227) to derive iPSCs from adherent cell types – blood or skin biopsy cell types (cord blood or cord tissue stem cells). Cord blood and cord blood MSCs will be obtained for generating adherent cell populations for the PhD studies through the Hudson Institute.

It is proposed that during the reprogramming step from somatic cells to iPSCs that it is more efficient to gene edit for other necessary changes at the same time. E.g. to introduce a chimeric antigen receptor (CAR) that can target cancer cells after differentiation to cytotoxic T cells. Or to knock-out or knock-in other edits useful for T cell function in killing solid tumor cells. This approach will be compared to single step iPSC conversion and iPSC gene editing. The use of cord blood cells verses cord tissue MSCs for iPSC production will also be evaluated.

The PhD will involve the production of iPSCs using mRNA and gene edits for CARs and a knockout of the PD1 gene, responsible for inhibition of T cell killing function. The iPSCs produced will be forward reprogrammed to cytotoxic T cells to confirm their targeted tumor killing ability. The studies will be undertaken Labs at the Monash Health & Translation Precinct.

Cell therapy and regenerative medicine

A novel biosystem for the induction of cytotoxic T cells from induced pluripotential stem cells

Suitability: Honours/PhD
Location: The Ritchie Centre / Cartherics, Hudson Institute of Medical Research; Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Richard Boyd and Prof Graham Jenkin, Co-supervisors: Dr Sacha Khong, Dr Nicholas Boyd, Technical support: Kelly Cartledge
Email: *graham.jenkin@monash.edu*
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Project description: The recent revolution in bioengineering of the cellular immune system offers a promising new frontier of personalized medicine with the potential to ultimately defeat cancer. This is best exemplified by being able to "Supercharge" the anti-cancer power of the immune system by genetically engineering killer T lymphocytes with Chimeric Antigen Receptors (CARs). These CAR-T cells are yielding unprecedented clinical success in some blood cancer. Currently, CAR-T cells are generated from the patients' own blood T cells. This is very problematic because the patients will have invariably had high dose chemotherapy, which is severely toxic to the immune system, limiting both the number and quality of cells which can be transduced to express the CAR receptor.

A pre-derived, highly defined 'off-the-shelf' CAR-T treatment that is compatible with a broad range of patients, is the future of CAR-T immunotherapy. The challenge is how to create such allogeneic CAR-T cells. The solution lies in using induced pluripotential stem cells (iPSC) which can be expanded infinitely in contrast to T cells which only have a limited number of divisions. This project will involve culturing iPSC, gene editing them to contain the CAR-DNA constructs, and then developing the methodology for inducing their differentiation into mainstream CD8+ T cells with the functional ability to induce lysis of cancer cells.

The project will not only vastly transform the utility of CAR-T cells for the clinic but also serve as a platform for creating polyclonal T cells for restoring immunity in immunosuppressive states such as following high chemo therapy and the effects of aging.

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

Suitability: Honours/PhD
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
Email: *graham.jenkin@monash.edu*
Phone: 03 8572 2801 (Prof Jenkin)

Project description: Chimeric antigen receptor (CAR-) T cells are designed to exploit the intrinsic cytotoxic function of T cells, whilst manipulating specificity by expressing a nominal antigen-specific receptor containing a cytoplasmic activation domain. CAR-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.

The project will utilize a variety of sophisticated technologies including the real-time impedence based xCelligence cytotoxicity and Luminex Multiplex cytokine arrays. 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.

Cell therapy and regenerative medicine

Next-generation micro-bead signalling systems for T-cell generation and cancer treatment

Suitability: PhD
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
Email: *graham.jenkin@monash.edu*
Phone: 0419534101 (Prof Jenkin)

Project description: The ability to genetically enhance a T lymphocyte with a cancer tracking surface antibody that activates a killing cascade upon binding to the target cancer cell, has revolutionised immunotherapy. This project aims to overcome a major practical problem – generating sufficient supply of these genetically "supercharged T cells" from stem cells. Aim: The ability to create an unlimited supply of CAR-T cells from iPSC unlocks access cancer immunotherapy to the masses. This requires an efficient iPSC to T-cell differentiation tissue culture system that is applicable to up-scale manufacture and clinical translation. The aim of this project is to provide a crucial element to this differentiation system by translating the highly coordinated set of signals provided by epithelial support cells within the thymus, into synthetic delivery system using microbeads and surface engineering.
The killing potency of in vitro generated T-cells is the primary target endpoint of this project and a major hurdle the field currently faces, beyond clinical applicability and T-cell conversion efficiency from iPSC. The ability for these in vitro generated T-cells to kill host different adenocarcinomas, in vitro and in mice will be assessed. This will be crucial for applying this technology into human clinical trials.

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

Suitability: PhD
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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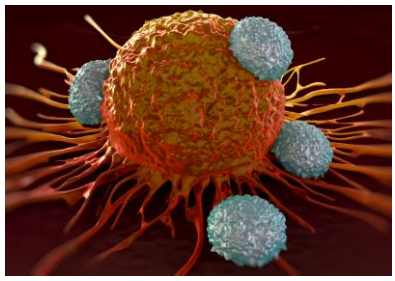
Phone: 0419534101 (Prof Jenkin)

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 invariable 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 induced human pluripotent stem cells (iPSC) offer great potential advantages in generating a self-renewing source of T cells that can be readily genetically modified for immunotherapy. The project is aiming to generate a genetically modified human stromal cell line from human Mesenchymal Stem Cells (MSC), for supporting the T cell in vitro differentiation.



Cell therapy and regenerative medicine

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

Suitability: PhD
Location: The Ritchie Centre / Cartherics, Hudson Institute of Medical Research; Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Alan Trounson, Prof Richard Boyd, Prof Graham Jenkin, Co-supervisors Dr Roland Shu, Dr Nicholas Boyd, Dr Ashalyn Watt
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Phone: 0419534101 (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.

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 in vivo models.

Elimination of cancer stem cells using chimeric antigen receptor T cells

Suitability: PhD
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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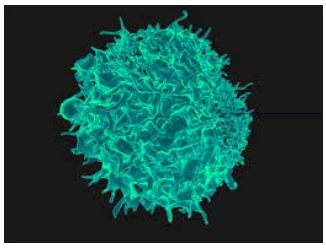
Project description: Disease relapse in CAR-T therapies of solid tumours suggests that current treatments lack the ability to eliminate the small subset of cells known as cancer initiating cells or cancer stem cells (CSCs). We propose to use the sophisticated specificity of immunotherapy to target surface 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.



Cell therapy and regenerative medicine

Re-engineering the function of natural killer cell receptors via CRISPR/Cas9: a new approach for 'off-the-shelf' immunotherapy

Suitability: PhD
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
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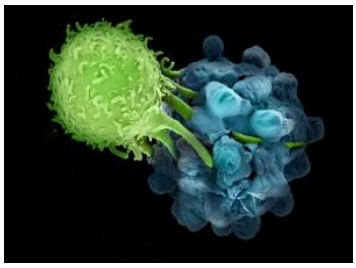

Project description:
Cellular immunotherapy with chimeric antigen receptors (CARs) have provided unprecedented results in treatment of liquid cancers. However, the few FDA approved autologous based therapies have been priced around $400,000 per patient. Inherently these face major challenges to reach 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.

This project 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.

Contact our supervisors

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

STEP 1: Find a project you are interested in.

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

All the information you need to enrol is on our website, or your supervisor can help you.

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

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