Student Research Projects 2019

Department of Obstetrics & Gynaecology
Department of Paediatrics
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The Ritchie Centre

Director
Professor Stuart Hooper

University Department Heads
Professor Euan Wallace, Professor Nick Freezer

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 Themes:

Women’s Health
A/Professor Caroline Gargett

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

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

Infant and Child Health
Professor Rosemary Horne

Infection, Inflammation and Immunity
A/Professor Tim Moss, Prof Jim Buttery

Cell Therapy & Regenerative Medicine
Dr 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 James Deane
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 adenomyosis 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

Immunomodulatory function of Endometrial Mesenchymal Stem Cells (MSC) Around Implanted Biomaterials

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Saeedeh Darzi, Dr James Deane, Prof Caroline Gargett
Email: james.deane@hudson.org.au; saeedeh.darzi@hudson.org.au

Project Description: Our proposed tissue engineering approaches for treating pelvic floor disorders involves implantation of a mesh biomaterial with endometrial MSC, which have immunomodulatory properties. Bone marrow derived monocytes and macrophages contribute to the unwanted foreign body response and are the target cells of the immunomodulatory MSC. Using 2 mouse models implanted with mesh/MSC, this project will determine the main source of macrophages mediating the foreign body response using a variety of experimental approaches. The interaction between T regulatory cells and endometrial MSC will also be investigated using reporter mouse models.

Keywords: endometrium; mesenchymal stem/stromal cells; immunomodulation; mouse model;
Women’s Health

Role of Endometrial Stem/Progenitor Cells in Endometrial Injury-Induced Doubling of Pregnancy Rates in IVF Procedures

**Suitability:** Honours/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 Caitlin Filby  
**Email:** caroline.gargett@hudson.org.au

**Project Description:** Recently it was discovered that an endometrial biopsy taken during the cycle before embryo transfer in in vitro fertilization (IVF) procedures doubles the pregnancy rate. However, the reason for this is not known. This project will examine whether biopsy-induced tissue damage activates endometrial stem/progenitor cells which produce an over-abundance of new endometrial cells generating an endometrium thick enough to support pregnancy in subsequent cycles. Flow cytometry will be the method of analysis.  
**Keywords:** endometrium; stem/progenitor cells; IVF; pregnancy rate; tissue damage

Role of Hedgehog signalling in the endometrial stem/progenitor populations that cause endometriosis

**Suitability:** Honours/PhD  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project Leaders:** Dr James Deane, Dr Fiona Cousins and Prof Caroline Gargett  
**Email:** james.deane@hudson.org.au, fiona.cousins@hudson.org.au, caroline.gargett@hudson.org.au  
**Phone:** 03 8572 2792 (Dr James Deane)

**Project Description:** Endometriosis occurs when the endometrium (the highly regenerative lining of the uterus) escapes and causes painful lesions on other organs. The Hedgehog and Notch signalling pathways control stem cell activity and are over activated in endometriotic lesions. The inappropriate activation of endometrial stem/progenitor cells by these pathways may promote the establishment and persistence of endometriosis. This project will block the Notch and Hedgehog signalling pathways in mouse models of endometriosis to test whether this reduces stem/progenitor cell activity and lesion growth. The aim is to identify new approaches that can be used to treat endometriosis in women.

How Are Endometrial Stem Cells Regulated?

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

**Project Description:** Stem cells are believed to be responsible for the regenerative potential of the endometrium. We have used markers to identify endometrial stem/progenitor cells in the human and mouse uterus, but how the growth and differentiation of these cells is controlled is unclear. Hedgehog signalling is a developmental pathway that is modulated during endometrial regeneration and over-activated in endometrial cancer. We have evidence that Hedgehog signalling exerts its influence on endometrial growth by influencing stem/progenitor cells. This project will use human endometrial organoids stem/progenitor cells and mouse models of endometrial regeneration using telomerase reporter mice to examine the role of Hedgehog signalling in regulating endometrial stem cells.  
**Keywords:** endometrium; stem/progenitor cells; transgenic mouse models; Hedgehog signalling; regeneration
Women’s Health

Large Animal Pre-Clinical Model for Assessing the Effect of a Cell Based Therapy to Prevent the Development of Pelvic Organ Prolapse

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 incontinence 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 approach to improve treatment outcomes using cell-based therapy delivered in novel materials fabricated by CSIRO. There is a pre-clinical project available to examine the effect of using autologous endometrial mesenchymal stem cells (eMSC) labelled with a lentivirus vector to treat or prevent POP. This project examines the effect of eMSC in a hydrogel injected into the vaginal wall of sheep following Bakri balloon induced injury (simulating birth injury). 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

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 James Deane, 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. This aim of this project is to develop organoids from
• human endometrial epithelial progenitor cells using our specific marker
• mouse endometrial epithelial progenitors from the telomerase reporter mouse 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. Another project will involve the overexpression of variants endometriosis susceptibility genes identified by Genome Wide Association Studies to assess function and effects on stem/progenitor cells. This will involve RNAseq studies to identify gene pathways involved. 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
Women’s Health

Can humidified/warm CO2 insufflation be used to reduce the development of lesions in endometriosis?

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

**Project description:**  
Insufflation (inflating the abdominal cavity) with dry/cold CO2 is routinely used during laparoscopic surgery to diagnose and treat endometriosis. Dry/cold CO2 desiccates the peritoneum causing inflammation and angiogenesis that increases the attachment and survival of colorectal cancer cells. Endometriotic lesions exist in an inflammatory and proangiogenic environment, making it likely they will also thrive on a peritoneal layer that has been damaged by dry/cold CO2. Thus standard laparoscopic surgery techniques using dry/cold CO2 insufflation are likely to promote the progression and recurrence of endometriotic lesions. Insufflation with humidified/warm CO2 minimises peritoneal damage and may represent an avenue to reduce the recurrence of endometriotic lesions after laparoscopic surgery. A mouse model will be used to assess whether dry/cold CO2 insufflation promotes endometrial lesion formation in a manner that can be prevented by substituting humidified/warm CO2 insufflation.  
**Keywords:** endometrium; endometriosis; insufflation; mouse

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 affects 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
Women’s Health

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.

**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

**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 (eg 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,
Women’s Health

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
Fetal & Neonatal Health: Respiratory & 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 & 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:** Dr Megan Wallace, Prof Stuart Hooper
**Email:** megan.wallace@monash.edu
**Phone:** 03 8572 2812 (Dr 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.

The Role of Trop2 in Trophoblast invasion, Placental Development and Preeclampsia

**Suitability:** Honours/PhD
**Location:** The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
**Project Leader:** Dr Megan Wallace, A/Prof Evdokia Dimitriadis and Dr Annie McDougall
**Email:** megan.wallace@monash.edu
**Phone:** 03 8572 2812 (Dr Wallace)

**Project Description:** During placental development trophoblasts from the developing embryo invade into the maternal uterine lining aiding placental development and remodelling the maternal spiral arteries to increase blood flow and nutrient supply to the developing fetus. Preeclampsia is a disease of pregnancy that is associated with poor trophoblast invasion and inadequate remodelling of the spiral arteries; this leads to maternal systemic endothelial cell dysfunction, hypertension and proteinuria. If untreated, preeclampsia can cause seizures and maternal death. The only treatment is to deliver the placenta and therefore the fetus, which places the newborn infant at increased risk of death or developing diseases of prematurity. Trop2 is a protein that was originally identified in trophoblasts but its role in trophoblast cells is not known. In other cell types Trop2 regulates cell proliferation, migration and invasion and our pilot data suggests that its levels in the placenta are altered in preeclampsia.

We hypothesise that Trop2 regulates trophoblast cell proliferation and invasion and that it is important for placental development. We also hypothesise that low Trop2 levels will be associated with abnormal placentation, which contributes to the development of preeclampsia. This project will involve the manipulation of Trop2 levels using small-interfering RNA to decrease Trop2 levels and overexpression vectors to increase Trop2 levels, in cultured human trophoblast cell lines, to assess the role of Trop2 in trophoblast proliferation and invasion. It will also involve the assessment of placental development in Trop2 knockout mice using histological techniques. If time permits, Trop2 levels will also be assessed in placentas from women with preeclampsia and from gestational-age matched placentas.

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:** Dr Megan Wallace and Assoc. Prof. Tim Cole
**Email:** megan.wallace@monash.edu
**Phone:** 03 8572 2812 (Dr 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.
Fetal & Neonatal Health: Respiratory & Cardiovascular

Characterising the role of Trop2 in fetal development

**Suitability:** Honours  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project Leaders:** Dr Megan Wallace and Dr Annie McDougall  
**Email:** megan.wallace@monash.edu  
**Phone:** 03 8572 2812 (Dr Wallace)

**Project Description:** Trop2 is a protein that regulates cell proliferation and migration in tumours. Cell proliferation and migration are also critical features during fetal development. We have shown that Trop2 is highly expressed in most fetal organs and that it regulates cell proliferation and migration in the developing lung and brain. The aim of this project is to determine if Trop2 also regulates cell proliferation and migration in other fetal organs by analysing fetal and neonatal organ development in Trop2 knockout mice. Students will be able to select their organ of interest for this project. The project will combine small animal work, histology, immunohistochemistry and molecular biology to characterise the role of Trop2 in organ development before and after birth.

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

Impact of Dopamine in The Immature Brain

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

Project Description: Dopamine is commonly prescribed to preterm babies to raise their blood pressure, but its effect in the immature brain is uncertain. New data suggests that dopamine may improve brain oxygenation. This project aims to define the effects of dopamine in the immature brain using a preterm lamb model, to evaluate the therapeutic potential of dopamine in improving brain oxygenation and reducing brain injury in preterm babies. In preterm lambs receiving dopamine, we will correlate changes in blood pressure, cerebral blood flow and metabolism with histopathology in brain slides, in order to assess the effect of dopamine in reducing brain injury.

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.

Are Sick Preterm Infants Sleeping in Prone Position at Risk of Low Brain Oxygen Levels?

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: A/Prof Flora Wong, Prof Rosemary Horne
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Project Description: It is common practice for sick, preterm babies receiving intensive care to sleep on both their front (prone) and back (supine) alternatively while in hospital. However, our recent study shows that healthy term babies sleeping prone have lower brain oxygen levels. Preterm babies receiving intensive care are particularly vulnerable to brain injury due to low brain oxygen levels. We therefore aim to determine whether the current practice of prone sleeping in sick babies is compromising the developing brains of these vulnerable babies, by measuring brain oxygen at the babies’ bedside with a spectrometer (Near infrared spectroscopy).

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 2798 (Dr Yawno), 03 8572 2796 (Dr 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.

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

Dietary intervention to improve growth and brain development in pregnancies complicated by intrauterine 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 Margie Castillo-Melendez, Dr Amy Sutherland, Dr Beth Allison
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Phone: 03 8572 2796 (A/Prof Miller), 03 8572 2803 (Dr Castillo-Melendez)

Project Description: Intrauterine growth restriction (IUGR) is a common pregnancy complication, affecting up to 1 in 10 pregnancies worldwide. IUGR describes a fetus that fails to grow to its full potential, principally caused by poor placental function (termed placental insufficiency) such that the supply of oxygen and nutrients to the developing fetus is restricted. The prolonged lack of oxygen has profoundly detrimental effects on the growing fetal brain, with IUGR infants at high risk of brain injury and cerebral palsy. We propose that a simple dietary supplementation of lactoferrin to mum during pregnancy will normalize brain development in IUGR fetuses, and reduce long-term neurological deficits associated with IUGR. Lactoferrin is a simple, cost effective treatment that could be readily adopted into routine clinical care anywhere in the world, and we have pilot evidence that lactoferrin will be neuroprotective for the brain of growth restricted offspring.

The Effects of Betamethasone in Single and Repeat Doses on 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: A/Prof Suzie Miller, Dr Tamara Yawno, Prof Graham Jenkin
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Phone: 03 8572 2796 (A/Prof Miller), 03 8572 2798 (Dr Yawno)

Project Description: Betamethasone is routinely administered to pregnant women in preterm labour to mature the fetal lungs and aid preterm survival of the neonate. In this regard, betamethasone is accepted as a life-saving treatment. However, betamethasone has other non-pulmonary effects, particularly on the cardiovascular system and brain. We will administer betamethasone in single or repeat doses to pregnant sheep carrying either a well-grown or IUGR fetus and examine cerebral physiological and cellular responses, to correlate with neuropathology. We hypothesise that brain growth and development will be adversely affected in IUGR fetuses, particularly with repeat betamethasone. Neuroprotective options for IUGR fetuses will be considered.

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
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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

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: Dr Lisa Walter, Prof Rosemary Horne
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Project Description: A particular phenomenon of the electroencephalography (EEG) wave form is the sleep spindle, believed to function as a 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

Can treatment of sleep disordered breathing in children normalise alterations to brain regions associated with adverse behavioural, neurocognitive and cardiovascular effects?

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

The most common sleep disorder in children, affecting over 1.5 million Australian children, is that of sleep disordered breathing, with the hallmark symptom of snoring. In children sleep disordered breathing is primarily due to enlarged tonsil and adenoid tissue. Sleep disordered breathing forms a spectrum of severity from simple or primary snoring, which is not associated with clinically significant oxygen desaturation or sleep fragmentation (using current techniques) to obstructive sleep apnoea. The apnoeas which are a feature of sleep disordered breathing are associated with repetitive falls in peripheral and cerebral oxygen saturation and the arousals which occur to terminate these events disrupt sleep.

These two features are thought to underpin both the cardiovascular and neurocognitive consequences of the disorder. Our recent studies have examined the integrity of brain tissue with non-invasive diffusion tensor imaging in non-snoring control children and children with sleep disordered breathing. We have identified that sleep disordered breathing is accompanied by predominantly acute brain changes in areas that regulate autonomic, cognitive, and mood functions, and chronic changes in frontal cortices essential for behavioural control.

This is the first time that these changes have been identified in children and likely result from the repetitive hypoxia falls in cerebral oxygenation that we have shown are associated with sleep disordered breathing. What we need to understand now is if these acute and chronic brain changes can be normalised following treatment and whether these changes are disease severity dependent.

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, Dr Lisa Walter, A/Prof Flora Wong  
**Email:** rosemary.horne@monash.edu  
**Phone:** 03 8572 2827 (Prof Horne)

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.
Infant and Child Health

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
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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.

Bad Sleep is bad for your cardiovascular health

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

Project Description: The research of my group focuses on sleep in infants and children. This is of the utmost importance to the health of every baby and child. Sleep is the primary activity of the brain during early development. By the age of 2 years a child has spent a total of 13 months sleeping! Between 2 and 5 years of age children spend equal amounts of time asleep as awake. A common cause of sleep disruption in childhood is partial or complete upper airway obstruction, termed sleep disordered breathing, with the hallmark feature being snoring. The repetitive airway obstruction leads to intermittent periods of hypoxia, with perhaps even more damaging rapid re-oxygenation after release of the obstruction, which is known to lead to brain injury. Repetitive events also cause surges in blood pressure, which leads to hypertension.

In this project we will examine the effects of sleep disordered breathing on vascular stiffness. Vascular stiffness reflects the compliance of the large conductance vessels and is an important contributor to increased cardiac stress and a risk factor for adverse cardiovascular events. It is a non-invasive method of assessing vascular dysfunction.

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

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, Dr Atul Malhotra, A/Prof Philip Berger

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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 SpO2 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.

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)

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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 it 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.


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 (Anatomy & Developmental Biology)
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
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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
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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

Identifying mediators of inflammation-induced fetal lung surfactant production

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research, Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Alana Westover, A/Prof Tim Moss
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Project Description: Intrauterine inflammation is a major cause of preterm birth, which is associated with an increased risk of respiratory distress syndrome (RDS), a condition caused by a lack of surfactant in the lungs. However, preterm babies that are exposed to intrauterine inflammation are less likely to develop RDS. The underlying mechanisms whereby inflammation induces precocious production of surfactant by the preterm lungs are not known.

Research techniques: cell culture; molecular biology

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

Suitability: Honours/BMedSci/PhD
Location: Level 3, Monash Medical Centre, Clayton
Project Leaders: A/Prof Jim Buttery, A/Prof Franz Babl, Dr Simon Craig
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Phone: 0403854179 (A/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: A/Prof Jim Buttery, Dr Andrew Daley*

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*Phone: 0403 854 179 (A/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: A/Prof Jim Buttery, Dr Nigel Crawford, Dr Jock Lawrie, A/Prof Chris Pearce*

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*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: IL-1Ra and IL-37 In 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, A/Prof Marcel Nold, Dr Ina Rudloff*

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*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, synchrotron X-ray imaging. 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 two innovative anti-inflammatory mediators, interleukin 1 receptor antagonist (IL-1Ra) and IL-37, protect against BPD and NEC. In newborn mice with a BPD-like lung disease, we will quantitate whether increased levels of IL-1Ra or IL-37 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 IL-1Ra and IL-37 by histology and flow cytometry and by analysis of selected biochemical markers.
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, A/Prof Marcel Nold, Dr Devi Ngo
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**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.

The First In Vivo Exploration of IL-38

**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, A/Prof Marcel Nold
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**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 *vivo* 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.
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: A/Prof Marcel Nold, A/Prof Claudia Nold
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Phone: 03 8572 2776 (A/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 untreated.

Molecular Tracking of the Cytokine IL-37 In Anti-inflammatory Signalling

Suitability: Honours/PhD
Location: Hudson Institute of Medical Research, Level 1, 27-31 Wright St, Clayton
Project Leaders: A/Prof Marcel Nold
Email: marcel.nold@monash.edu,
Phone: 8572 2776 (A/Prof Nold)

Project Description: Direct clinical relevance: medium/low. Hands-on learning opportunities: Confocal microscopy, molecular engineering (cloning), cell culture of primary human blood cells and cell lines.

Many of the major diseases of prematurity, and of old age, are typified by an intense and run-away inflammation. In this program we plan to elucidate the molecular signalling cascades triggered by what is perhaps the most powerful anti-inflammatory cytokine so far discovered, interleukin 37 (IL-37). The two leaders of the Nold laboratory were central figures in discovering the anti-inflammatory actions of IL-37 in 2010. Over the past 5 years we discovered the receptor through which IL-37 operates and we have been systematically laying the foundations for developing new and much-needed anti-inflammatory drugs based on IL-37. Our work recently identified the molecular features that endow IL-37 with its powerful beneficial effects, and in this program we will extend that understanding to exploit its therapeutic potential. This project continues our approach of utilising sophisticated high-resolution microscopy and live cell imaging techniques to observe and track IL-37 and its signalling cascades in real time. Students will have the opportunity to learn and use methods involving tissue/cell culture, molecular engineering, micrometer-scale resolution imaging as well as statistical analysis of the results.
Infection, Inflammation and Immunity

Therapeutic Application of Human Amnion Epithelial Cells in Allergic Asthma

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Rob Bischof, A/Prof Tim Moss, Prof Euan Wallace
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Project Description: Allergic asthma is a chronic inflammatory disease of the airways that has a significant impact on affected people of all ages. Human amnion-derived epithelial cells (hAECs) have stem cell-like properties as well as possible anti-inflammatory or immunomodulatory characteristics that make them attractive as a potential cell therapy.

The aim of this project is to investigate the therapeutic efficacy of airway hAEC administration, in blocking or reducing the asthmatic airway responses in a sheep model of asthma. These experiments will include whole-animal physiology, immunology, cell biology, microscopy and molecular biology techniques.

Keywords: asthma, inflammation, stem cell therapy

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.
Cell therapy and regenerative medicine

Cell based therapy for the ex-vivo reconditioning of donor lungs prior to lung transplantation

Suitability: Honours/PhD
Locations: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton and Faculty of Medical Sciences, Newcastle University Medical School, Newcastle UK
Project Leaders: Professor Graham Jenkin & Dr Rebecca Lim, Monash University, Professor Andrew Fisher & Dr Lee Borthwick, Newcastle University UK.
Email: graham.jenkin@monash.edu
Phone: 03 8572 2801 (Prof Jenkin)

Project Description: An opportunity exists to undertake a collaborative program of research, jointly at Monash University and Newcastle University UK, under the auspices of the Monash-Newcastle Partnership Alliance. The project would be suitable for BMedSc Hons and/or PhD students. The research program brings together the therapeutic potential of placental derived stem cells and their conditioned media, developed at Monash, with the platform offered by Ex Vivo Lung Perfusion (EVLP) to ameliorate lung injury and inflammation in donor lungs before transplantation, developed at Newcastle. The research will involve in vitro cell and tissue culture and perfusion experiments to ascertain the timing, dose and nature (cells or conditioned media) of this novel biological therapy during EVLP to reduce inflammation, endothelial injury and immunogenicity of donor lungs immediately before organ transplantation. This approach could revolutionise ex-vivo organ perfusion procedures and significantly increase the conversion rate of unusable to suitable donor lungs for increased lung transplant activity, protect against primary graft dysfunction and improve outcomes of this life saving intervention.

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

Suitability: Honours
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, Dr Ashalyn Watt
Email: graham.jenkin@monash.edu
Phone: 03 8572 2801 (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 retrieval post-thaw.

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
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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. The experiments include whole-animal physiology, immunology, microscopy and molecular biology techniques.
Cell therapy and regenerative medicine

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

**Suitability:** Honours

**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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**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.

How do umbilical cord blood stem cells reduce neuro-inflammation and 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 Suzie Miller, Prof Graham Jenkin

**Email:** courtney.mcdonald@monash.edu

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**Project description:** Cerebral Palsy (CP) is the most common cause of physical disability in children and there is no cure. Inflammation is known to play a key role in the development of brain injury, however the immune cells or mechanisms in which they are involved in perinatal brain injury (which leads to CP) are not well understood. This proposal will explore a new therapy that holds much promise for treating children with CP; stem cells isolated from umbilical cord blood. Using a rodent model of perinatal brain injury, this project we will explore the mechanism of how specific cord blood stem cells can reduce brain inflammation and damage caused by hypoxia-ischemia, an event known to lead to cerebral palsy. This project will also use cutting edge technology including magnetic resonance imaging techniques, to track the fate of umbilical cord blood stem cells in the brain, and extensive multicolour flow cytometry to examine the mechanisms by which stem cells reduce perinatal brain injury.
Cell therapy and regenerative medicine

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

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:** Dr Rebecca Lim  
**Email:** rebecca.lim@monash.edu  
**Phone:** 03 8572 2794 (Dr 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.

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, Dr 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

Identifying mechanical cues in lung stem cells

**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, Dr Rebecca Lim  
**Email:** gina.kusuma@hudson.org.au  
**Phone:** 03 8572 2876 (Dr Kusuma)

**Description**  
Lung fibrosis is characterised by scarring of the lungs and impaired repair is associated with excess extracellular matrix. This results in lung stiffness and compromises gas exchange. We will engineer a cell culture platform that mimics this environment in order to study how lung stem cells contribute to repair processes in these settings and how the stiffness of the lung can influence injury and repair processes. Hydrogels of different levels of stiffness can be fabricated and used to promote cell adhesion and growth, as well as to test the impact of stiffness on the stem cell function. We will investigate how differences in stiffness as seen in fibrotic and healthy lungs will affect the regeneration process of lung stem cells. We will identify the defective repair mechanisms of lung stem cells and target these stiffness-related pathways to restore the repair mechanisms. Techniques employed include stem cell culture, flow cytometry, real-time PCR, immunohistochemistry, confocal imaging, proliferation assay, and hydrogel fabrication.  
**Keywords**  
stem cells, lung fibrosis, regenerative medicine
Cell therapy and regenerative medicine

Engineering the therapeutic effect of stem cells

**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, Dr Rebecca Lim  
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**Phone:** 03 8572 2876 (Dr Kusuma)

**Project Description:** Stem cell therapies are typically employed to repair tissue functions in the event of injury. Mesenchymal stem cells (MSCs) hold significant promise for tissue engineering and cell therapy applications due to their unique properties such as extensive proliferation ability, multilineage differentiation, ease of isolation, immune-privileged status, and paracrine activity. It has been proposed that MSCs may act as injury drug stores by secreting bioactive molecules and regulating immune response to establish a regenerative microenvironment. MSCs are commonly cultured as monolayers on conventional tissue culture plastic. We hypothesise that the environment surrounding MSCs is of critical importance to direct the paracrine activity. 3D culture system provides a better recapitulation of cell-cell interactions than conventional 2D cultures. Approaches to generate 3D spheroids using MSC could open new opportunities to enhance paracrine activity of MSCs, for example, by improving the immunomodulatory, anti-inflammatory, and angiogenic properties. Techniques employed include stem cell culture, immunofluorescence, proliferation assay, 3D spheroids formation assay, exosomes isolation, Western blotting, nanoparticle tracking analysis.

**Keywords**  
stem cells, lung fibrosis, extracellular vesicles

Stem cells as a novel therapy for Perinatal Stroke

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

**Project Description:** Perinatal stroke is a common problem that results in seizures, behavioural difficulties and cerebral palsy. Despite the remarkable ability of newborns to survive a stroke, there are no drug treatments proven for infants unlike adults. Stem cells offer a promising solution. The “holy grail” of treatments for perinatal stroke would be an off the shelf stem cell product that could both halt brain injury and repair damaged brain tissue. This proposal will explore a new therapy that is very promising for infants that have suffered a stroke at or around the time of birth. Using a rodent model of perinatal stroke, in this project we will explore the mechanism of how different types of stem cells can reduce brain inflammation and damage caused by perinatal stroke. This project will use cutting-edge technology, including magnetic resonance imaging techniques and extensive multi-colour flow cytometry to examine the mechanisms by which stem cells reduce stroke induced brain injury. This project will also include long term behavioural testing to understand the benefits of stem cell therapies to improve outcomes after treatment of perinatal stroke.

Tracking Stem Cells In Vivo in Regenerative Medicine

**Suitability:** Honours  
**Location:** The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton  
**Project Leaders:** Dr Courtney McDonald, Prof Graham Jenkin, A/Prof Tony Goldschlager, Dr Rebecca Lim, Prof Euan Wallace  
**Email:** graham.jenkin@monash.edu  
**Phone:** 03 8572 2801 (Prof Jenkin)

**Project Description:** We are exploring the use of human amnion epithelial cells (hAECs), Mesenchymal Stromal Cells and Mesenchymal Progenitor Cells (MPCs) as cellular regenerative therapy for a variety of diseases, including bronchopulmonary dysplasia, chronic lung disease of the preterm infant, multiple sclerosis and spinal disc repair. This project will utilise novel labelling techniques, including MRI, that will allow us to track the migration profile of stem cells in real-time.
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
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Phone: 03 8572 2801 (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 polymeric compositions and stem cell combinations that can be developed into the most viable scaffold for therapeutic use in clinical trials.

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
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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.

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
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Phone: 03 8572 2801 (Prof Jenkin)

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. For example 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 pluripotent 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
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Project summary
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. A significant challenge is to make the CAR-T’s effective in solid cancers. As exciting as this is, a practical problem is how to create sufficient numbers of CAR-T cells for meaningful clinical application. Currently by necessity the 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 pluripotent stem cells (iPSC) which can be expanded infinitely in contrast to T cells which only have a limited number of divisions.

Using xenofree, clinic ready conditions, 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+, CD4+ T cells with the functional ability to induce lysis of cancer cells. The differentiation signals to be investigated include the initial specification into haemopoietic lineage, the sequential and quantitative delivery of a panel of strategically chosen transcription factors closely aligned with CD8+ T cells, functionalized beads and stromal cell supporting cells which will be transduced to express important signaling molecules, and cytokines linked to T cell differentiation, proliferation and function. The need for 3 dimensional biomatries to better mimic the in vivo T cell differentiation in the thymus will also be investigated. The success of the T cell differentiation will be monitored by multi-parameter flow cytometry for stage specific surface markers. The proof of functionality will be assessed by stimulation through CD3/CD28 cross-linking, release of cytokines (using Luminex multiplex arrays) and ability to kill cancer versus normal cells.

If successful 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

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 summary
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. Such cells have recently revealed remarkable success in the clinic, with multiple studies reporting the ability to ameliorate certain blood malignancies in particular. However, transitioning this technology to the treatment of solid tumours has posed many challenges, in particular the identity of appropriate target antigens and the need to penetrate the protective cancer stromal microenvironment. Accordingly, we developed second generation CAR-T constructs against an ovarian cancer antigen TAG-72 using lentiviral transduction of T cells from donated healthy blood. The resultant CAR-T cells were able to kill ovarian cancer cells in vitro. As exciting as this is, there are several parameter of these CAR-T cells which need to be optimized before any clinical studies can be undertaken. The important questions include: what is the best type of T cell (CD8+, CD4+, naive, effector memory, central memory, combinations); the role of cytokines and serum supplements in activation and proliferative expansion of CAR-T cells; the synergy or complication of combining the CAR- with the endogenous T Cell Receptor (TCR). The project will utilize a variety of sophisticated technologies including the real-time impedance based xCelligence cytotoxicity and Luminex Multiplex cytokine arrays.

Through sensitive, label-free, real-time cell monitoring, thus study will identify a collection of culture conditions which augment CAR-T function in vitro and in vivo. The studies highlight the importance of the production process in the ability to achieve the fine balance between highly antigen-specific but potent cytotoxicity CAR-T cells for the eradication of cancer.
Information for Prospective Students

https://www.monash.edu/medicine/scs/education/prospective

Science (Honours)
https://www.study.monash/courses/find-a-course/2017/science-s3701

Biomedical Science (Honours)
https://www.study.monash/courses/find-a-course/2017/biomedical-science-m3702

Bachelor of Medical Science (Honours)
https://www.monash.edu/medicine/scs/education/prospective/bmedsci-prospective

Doctorate/PhD