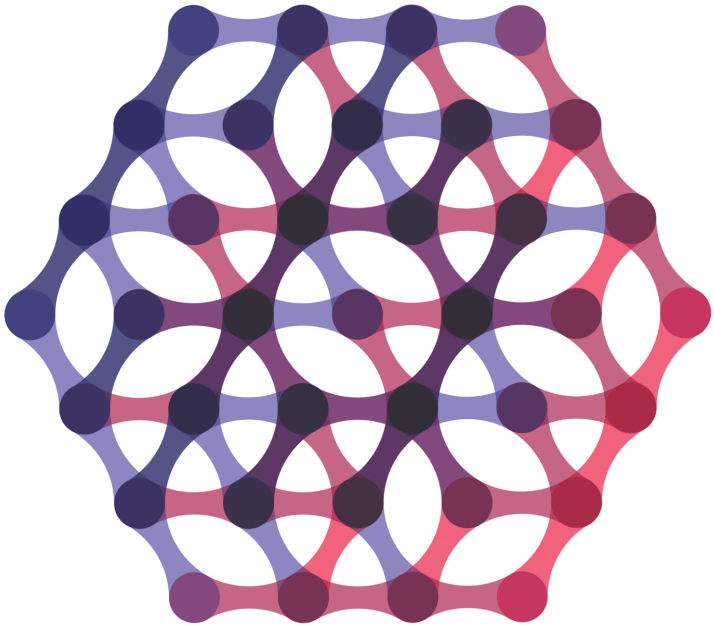
The Ritchie Centre

Student Research Projects 2017

Department of Obstetrics & Gynaecology
Department of Paediatrics



HUDSON INSTITUTE OF MEDICAL RESEARCH

MONASH University

MonashHealth

Monash Children's Hospital

Monash Newborn

melbourne children's sleep centre

MHTP Monash Health Translation Precinct

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
Professor Stuart Hooper, A/Professor Tim Moss

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

Infant and Child Health
Professor Rosemary Horne, A/Professor Jim Buttery

Cell Therapy & Regenerative Medicine
Professor Graham Jenkin, Professor Euan Wallace

web: http://hudson.org.au/research-centres/the-ritchie-centre/

Research Theme: 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: A/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 Perivascular Location of Human Endometrial Mesenchymal Stem Cells

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

Project Description: We discovered a small mesenchymal stem cell population in human endometrium (eMSC) likely responsible for its regeneration each month during the menstrual cycle. We also identified specific surface markers of eMSC: CD140b+CD146+ co-expression and SUSD2. Both markers show the perivascular location of eMSC. CD140b+CD146+ cells are pericytes closely associated with endothelial cells, but the precise location of SUSD2+ eMSC is unknown. In a sheep model, we found that CD271+ eMSC were also perivascular, located in the adventitia of larger vessels rather than pericytes. SUSD2+ cells are shed during menstruation and enter the pelvic cavity in greater numbers in women with endometriosis compared to normal, likely contributing to its pathogenesis. This project will undertake a detailed analysis of human endometrium using sophisticated microscopy to determine if the precise perivascular locations of eMSC. Colocalisation with other stem cell markers (OCT4, SOX2, NANOG) and estrogen and progesterone receptors from normal and endometriosis women will also be examined. This project will generate beautiful images showing precisely where eMSC reside.
Keywords: endometrium, mesenchymal stem/stromal cells; endometriosis; blood vessels; confocal microscopy

Do Endometrial Mesenchymal Stem Cells (MSC) Have Immunomodulatory Properties That Can Be Harnessed to Treat Human Disease?

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, A/Prof Caroline Gargett
Email: *james.deane@hudson.org.au*

Project Description: Mesenchymal stem cells (MSC) are rare populations of undifferentiated cells found in many tissues that are capable of self-renewal and differentiating into multiple mesodermal lineages. We first discovered a new and easily accessible MSC population in the endometrium, the highly regenerative lining of the uterus, (eMSC). MSC from other tissues such as bone marrow and fat have immunomodulatory properties which makes them ideal for treating diseases involving an over-exuberant or off target immune responses, and also allows their use in non-identical individuals. We have shown that eMSC inhibit mouse immune cells in an in vitro setting. We are now seeking to demonstrate the clinical utility of eMSC by confirming that they can inhibit human immune cells in an in vitro setting, and investigating their ability to inhibit a complete in vivo immune response in mouse models of inflammation.
Keywords: endometrium; mesenchymal stem/stromal cells; immunomodulation; mouse model; human

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

Suitability: Honours
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leader: A/Prof Caroline Gargett
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 overabundance 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

Research Theme: Women's Health

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 James Deane, A/Prof Caroline Gargett
Email: *james.deane@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 putative 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 cultured human endometrial 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

Telomerase activity as a stem cell marker in the endometrium

Suitability: **Honours**
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 A/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: Stem cells are believed to be responsible for the regenerative potential of the endometrium. Markers for mouse endometrial stem cells are required to study endometrial regeneration. To this end, we have investigated the endometrial activity of the telomerase complex which allows stem cells to divide indefinitely by maintaining telomere length. We have used transgenic mice expressing telomerase reporter constructs to identify putative stem cells in the endometrium. This project will use telomerase reporter mice to study stem cells in normal endometrial cycling, endometrial shedding and repair (as in the human menstrual cycle), and endometrial repair and regeneration after pregnancy.
Key Words: endometrium, stem cell, telomerase

Ex vivo perfusion of the term human placenta - establishing a technique for measuring placental creatine transport

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Hayley Dickinson, Dr Padma Murthi, Dr Stacey Ellery, Prof Rod Snow
Email: *hayley.dickinson@monash.edu*
Phone: 03 8572 2826 (Dr Dickinson)

Project Description: During pregnancy the increasing nutrient demands of the placenta and fetus impose a considerable metabolic load on the mother. As such, many problems in pregnancy, such as poor fetal growth and stillbirth, develop due to cellular energy failure arising from inadequate nutrient and/or oxygen supply to the fetus. We have compelling evidence that creatine is a critical cellular energy metabolite for pregnancy and high creatine supply protects the fetus from compromise and death. In identifying the main sources of creatine during pregnancy, we recently discovered that the term human placenta synthesises creatine.
This project will establish the technique, dual placental perfusion to determine the rate of creatine transport across the placenta. This study will involve out of hours work as it relies on delivery of human placentas, which can occur at any time (usually in the evening and the weekend). This project is recommended for a student who lives nearby and is willing to be flexible with time.

Uncovering Mechanisms Underlying Ethnic Disparities in Maternal and Perinatal Outcomes

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Miranda Davies-Tuck, Dr Padma Murthi, Prof Euan Wallace
Email: *miranda.davies@monash.edu*

Project Description: Despite growing evidence for an association between ethnicity and adverse perinatal and obstetric outcomes the possible mechanisms underlying the relationship(s) are unknown. Understanding why women of different ethnicities are at "higher risk" of adverse maternal and perinatal outcomes is important. A range of projects are available using routinely collected or recorded pregnancy and birth data as well as biological from the mother and baby at the birth

Research Theme: Women's Health

How does vitamin D influence feto-placental growth?

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Padma Murthi, Dr Hayley Dickinson, Dr Stacey Ellery, A/Prof David Walker
Email: padma.murthi@monash.edu
Phone: 03 8572 2874

Project Description: Maternal vitamin D supplementation during pregnancy improves fetal growth. However, the mechanism by which vitamin D promotes fetal growth is largely unknown. We aim to identify the effect of different vitamin D analogues and their mechanism of action in promoting placental growth in first trimester and term placental tissues. We will also define how vitamin D analogues influence placental blood flow and nutrient transport systems across the maternal and fetal compartments in term pregnancies using ex-vivo placental perfusion system and in vitro placental cell cultures.

How does placental insufficiency affect nutrient transport?

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Padma Murthi, Dr Hayley Dickinson, Dr Stacey Ellery, A/Prof David Walker
Email: padma.murthi@monash.edu
Phone: 03 8572 2874

Project Description: Placental maldevelopment and function lead to poor fetal growth, preterm labour, and increased neonatal morbidity. Placental insufficiency is often associated with preeclampsia, gestational diabetes, and fetal growth restriction. The placenta plays a critical role both in the synthesis and transport of nutrients including amino acids and micronutrients for the fetus. In this project we will determine if placental insufficiency is associated with alterations of amino acids and vitamin D transporters and their binding proteins in preeclampsia, fetal growth restriction and gestational-diabetes pregnancies using real-time PCR, immunoblotting, and immunocytochemistry techniques.

Novel Treatments for Preeclampsia

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Bryan Leaw, Prof Euan Wallace
Email*: bryan.leaw@hudson.org.au*
Phone: 03 8572 2797 (Dr Leaw)

Project Description: Preeclampsia is a serious pregnancy-specific condition affecting approximately 5% of pregnancies worldwide. It is a leading cause of maternal and fetal, morbidity and mortality. To date, there is no cure for preeclampsia. Resveratrol is becoming increasingly well known for its protective effects against cancer, cardiovascular disease, inflammation, obesity, age-related deteriorations and ischemic injuries, such as myocardial infarctions and stroke. Its potential as a therapeutic for preeclampsia is yet to be investigated in detail. Using a rat model of preeclampsia, we will determine the therapeutic benefits of several new anti-oxidative compounds. This project involves small animal surgery and molecular techniques.

Placental Pathology of births at Monash Health

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Hayley Dickinson, Dr Padma Murthi, Dr Miranda Davies-Tuck
Email: *hayley.dickinson@monash.edu*
Phone: 03 8572 2826 (Dr Dickinson)

Project Description Placentae are routinely sent for pathological assessment at Monash Health after an adverse pregnancy outcome such as preterm birth, fetal growth restriction, pre-eclampsia and stillbirth. This project will access these previously collected data, review the histology and clinical notes, and determine relationships between these and the available pregnancy data, maternal demographics and baby outcomes data. This study will describe the relationship between placental health and adverse pregnancy events at Monash Health.

How does maternal vitamin D deficiency during pregnancy contribute to neurocognitive deficits in infants and children?

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Padma Murthi, Prof Peter Ebeling
Email: padma.murthi@monash.edu
Phone: 03 8572 2874

Project Description: Maternal vitamin D deficiency during pregnancy has been linked to impaired neurocognitive and language development in children. The mechanism by which vitamin D affects childhood neurocognitive outcomes is unclear but may be via interactions between vitamin D and the serotonin pathway. Serotonin is an important neurotransmitter involved in fetal brain development. Vitamin D modulates serotonin synthesis. We hypothesise that vitamin D deficiency contributes to disruption in fetal serotonin signalling during pregnancy. We aim to understand the biological mechanism(s) by which vitamin D regulate fetal serotonin signalling pathways using human term placental tissues. We will define molecular pathways by which vitamin D regulate serotonin synthesis using molecular and protein analyses in placental cell cultures (in vitro) and in placental perfusion system (ex-vivo).

Research Theme: Fetal and Neonatal Health

Supplementing the Diet with Creatine at the End of Pregnancy: A Possible Treatment to Prevent Perinatal Brain Damage in Preterm and Term Lambs?

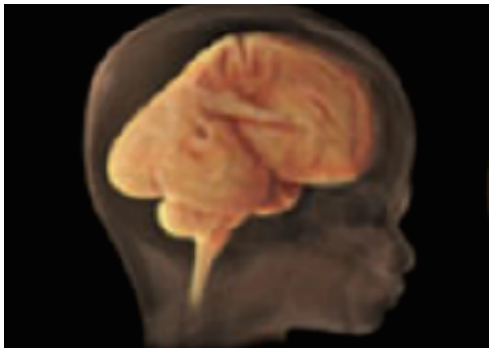
Suitability: Honours/PhD
Location The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: A/Prof David Walker, A/Prof Suzie Miller, Dr Hayley Dickinson, Dr Graeme Polglase
Email: *david.walker@monash.edu*
Phone: (03) 8572 2823 (David Walker)

Project Description: The aetiology of brain damage that manifests itself in some infants after prolonged labour or hypoxic birth is still not understood. Current treatments such as head cooling, or use of noble gases such as xenon or argon are 'rescue' treatments with limited effectiveness. Our recent work in pregnant sheep and a precocial rodent shows that adding creatine to the maternal diet in the latter stages of pregnancy protects the fetal brain against the effects of severe hypoxia at birth. The aim of our on-going studies is to show that this creatine treatment improves the resuscitation and development of locomotor function in lambs delivered preterm or at term, with or without the additional challenge of birth hypoxia.

Establishing the placental phenotype in a spiny mouse model of reduced fetal growth

Suitability: Honours/Masters
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Hayley Dickinson, Dr Stacey Ellery, Dr Padma Murthi
Email: *hayley.dickinson@monash.edu*
Phone: 03 8572 2826 (Dr Dickinson)

Project Description Fetal growth restriction (FGR) is a major obstetric problem, contributing to neonatal morbidity and mortality. FGR continues to present problems due to difficulty of antenatal detection and no effective preventative or interventional strategy.
We've developed a model of FGR in the spiny mouse by restricting uterine blood flow for the last 25% of gestation. Once validated and characterised we will use this model to test preventative and interventional strategies to improve outcomes for the fetus. This project will describe the structure and molecular profile of the term placenta from this model.



Brain creatine levels in preterm infants

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton / Monash Newborn
Project Leaders: Dr Hayley Dickinson, A/Prof Flora Wong, A/Prof Michael Fahey, A/Prof David Walker, Prof Rod Snow
Email: *hayley.dickinson@monash.edu*
Phone: 03 8572 2826 (Dr Dickinson)

Project Description Preterm birth is associated with long-term neurological deficits and currently no effective treatment exists to lessen these burdens. We have discovered that creatine is produced in large amounts by the human placenta, implying an importance to the developing fetus, and our animal studies demonstrate that fetal creatine synthesis develops only very late in gestation (0.9 in a precocial rodent species). In this context, preterm birth has the effect of removing the fetus (premature neonate) from the protective environment where the mother and placenta supply creatine to it. The very low level of creatine in breast milk, formula milk, and parenteral nutrition cannot prevent the possibility that preterm infants become creatine deficient, with detrimental effects on brain function and development. The known syndromes of cerebral creatine deficiency are associated with significant neurological impairment of the neonate and child, including mental retardation, expressive speech and language delay, autism-like behaviour and epilepsy. These conditions are frequently misdiagnosed as cerebral palsy. We propose to determine plasma and urine creatine concentrations in preterm and term infants throughout the duration of their hospital stay, and to measure brain creatine content using MRI.

Assessing behavior in spiny mouse offspring*: effects of birth asphyxia and effectiveness of creatine to prevent injury*

Suitability: Honours/Masters
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Hayley Dickinson, Dr Stacey Ellery, A/Prof David Walker
Email: *hayley.dickinson@monash.edu*
Phone: 03 8572 2826 (Dr Dickinson)

Project Description Over the past 8 years we've developed and validated a model of birth asphyxia in the spiny mouse that mimics many features of the clinical condition hypoxic-ischemic encephalopathy HIE. This project will analyse, interpret and visualise behavioural data collected from a large cohort study performed by previous PhD students in our laboratory. This project will determine whether behaviour is altered in offspring exposed to birth asphyxia and whether maternal dietary creatine supplementation is protective, as we have shown it is for brain structure, kidney structure and function and muscle structure and function.

Research Theme: Fetal and Neonatal Health

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 9594 5482 (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 9594 5482 (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
Email: *flora.wong@monash.edu*
Phone: 03 9594 5482 (A/Prof Wong)

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).

Use of Activated Protein C (Apc) To Reduce Brain Injury from Birth Asphyxia

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: A/Prof Flora Wong, A/Prof David Walker, Dr Hayley Dickinson
Email: *flora.wong@monash.edu*
Phone: 03 9594 5482 (A/Prof Wong)

Project Description: Birth asphyxia leads to significant brain injury and long term neurodevelopmental problems including cerebral palsy, cognitive and other neurological dysfunction. Activated Protein C (aPC) is a vitamin K-dependent plasma glycoprotein, and has been shown to be neuroprotective in adult animal models of brain injury and stroke. We propose to explore aPC as a possible new therapy for brain injury following birth asphyxia. We will use our well-validated model of birth asphyxia in the spiny mouse to determine if treatment of birth-asphyxiated pups with aPC prevents the neuropathology in brain slides, and improves postnatal behavioural deficits.

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, A/Prof David Walker
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 relatively common; they are powerful predictors of long-term cognitive and developmental impairment. There is also a significant concern about current anti-seizure therapies, which can cause brain injury as they have the potential to be neurotoxic. We will investigate the effects of the synthetic $GABA^{A}$ 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, new born, brain activity

Research Theme: Fetal and Neonatal Health

Sildenafil treatment in growth restricted fetuses; What are the effects on brain structure

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, A/Prof Suzie Miller, Dr Graeme Polglase
Email: beth.allison@hudson.org.au, suzie.miller@monash.edu graeme.polglase@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, sildenafil citrate (Viagra) is currently being trialed during human pregnancy. Sildenafil is thought to increase the blood flow through the placenta and increase nutrient and oxygen delivery to the developing baby. Despite it's promise for growth restricted babies, sildenafil may also have effects in the fetus as it crosses the placenta. This project will be undertaken in pregnant sheep exposed to sildenafil and use techniques such as histology, inflammatory assays, rtPCR and western blotting to investigate brain structure following exposure to sildenafil.

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
Location: Hudson Institute of Medical Research, Level 1, 27-31 Wright St, Clayton
Project Leaders: A/Prof Marcel Nold, Dr Claudia Nold
Email: *marcel.nold@monash.edu*, *claudia.nold@hudson.org.au*
Phone: 03 8572 2776 (A/Prof Nold), 03 8572 2775 (Dr Nold)

Project Description: Direct clinical relevance: high Hands-on learning opportunities: Multi-color flow cytometry, protein arrays, cell culture of primary human blood cells.
The immune and coagulation systems of preterm infants are largely unknown, a problematic blank page for clinicians, a true frontier for researchers. The dearth of information on preterm immunity and coagulation is explained by our inability until recent times to extract large amounts of information from the 0.5 ml samples available from the tiny patients, remembering they have as little as 35 ml of blood. Our laboratory is conducting an exciting study on blood taken from extremely premature infants at 5 time points, thus allowing for a unique longitudinal view of plasmatic and cellular immunity as well as coagulation. To explore these systems in depth, we use cutting edge methods such as protein arrays and multi-colour flow cytometry, which students will learn. Access to the babies' clinical data we enable us to perform correlation analyses to probe the relevance of our findings to the major diseases of prematurity such as bronchopulmonary dysplasia, intracranial haemorrhage and necrotising enterocolitis. These insights may identify biomarkers and/or new therapeutic targets, which are direly needed as several of these diseases are life-threatening and currently untreatable.

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, Dr Claudia Nold, Dr Kirstin Elgass, Dr Devi Ngo
Email: *marcel.nold@monash.edu, claudia.nold@hudson.org.au* kirstin.elgass@hudson.org.au, *devi.ngo@hudson.org.au*
Phone: 03 8572 2775 (Dr Claudia Nold), 03 8572 2776 (A/Prof Nold), 03 8572 2790 (Dr Kirstin Elgass)

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.

Research Theme: Fetal and Neonatal Health

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: Dr Claudia Nold, A/Prof Marcel Nold, A/Prof Philip Berger
Email: *claudia.nold@hudson.org.au*, *marcel.nold@monash.edu* *philip.berger@monash.edu*
Phone: 03 8572 2775 (Dr Claudia Nold), 03 8572 2776 (A/Prof Nold), 03 8572 2833 (A/Prof Berger)

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 quantify 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-1R

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: Dr Claudia Nold, Dr Ina Rudloff, A/Prof Marcel Nold
Email: *claudia.nold@monash.edu*, *ina.rudloff@hudson.org.au* marcel.nold@hudson.org.au, *devi.ngo@hudson.org.au*
Phone: 03 8572 2775 (Dr Nold), 03 8572 2815 (Dr Rudloff), 03 8572 2776 (A/Prof Nold)

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

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

The First In Vivo Exploration Of IL-3

Suitability: Honours/BMedSci/PhD
Location: Hudson Institute of Medical Research, Level 1, 27-31 Wright St, Clayton
Project Leaders: Dr Claudia Nold, Dr Ina Rudloff, A/Prof Marcel Nold
Email: *claudia.nold@hudson.org.au*, *ina.rudloff@hudson.org.au*, *marcel.nold@monash.edu*
Phone: 03 8572 2775 (Dr Nold), 03 8572 2815 (Dr Rudloff), 03 8572 2776 (A/Prof Nold)

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

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

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

Research Theme: Fetal and Neonatal Health

Transition to Life After Birth

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Stuart Hooper, Dr Kelly Crossley, Dr Graeme Polglase, Dr Lauren Kerr
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 Lauren Kerr, 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.

Fetal Lung 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 Leader: Dr Megan Wallace, Dr Annie McDougall
Email: *megan.wallace@monash.edu*
Phone: 03 8572 2812 (Dr Wallace)

Project Description: At birth the lungs must take on the role of gas-exchange, a role they have never performed before. To survive, the lungs must be appropriately grown and mature by the time of birth. Babies born prematurely, before the lungs have had time to develop, are at high risk of death or disease. To improve the outcome for these babies we must understand the mechanisms that regulate normal lung development, so that we can find new ways to accelerate it. This project will investigate factors that are likely candidates for mediating lung growth using cell culture and molecular biology approaches.

Interrogating the NO pathway in the growth-restricted fetus?

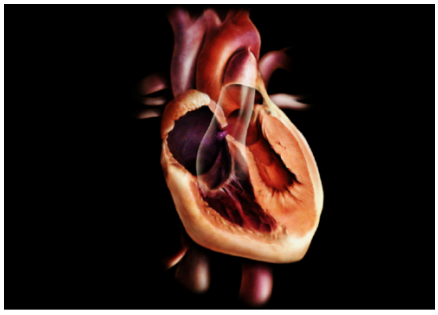
Suitability: Honours
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Beth Allison, A/Prof Suzie Miller, Dr Graeme Polglase
Email: *tamara.yawno@hudson.org.au*, *beth.allison@hudson.org.au*, *graeme.polglase@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 offspring of a sub-optimal pregnancy have an increased susceptibility of cardiovascular disease as they age. One of the leading causes of a sub-optimal pregnancy is fetal hypoxia leading to oxidative stress. It is because of this that nitric oxide pathways are thought to be involved. Despite this, little is understood about the role of the nitric oxide pathway during chronic fetal hypoxia, and therefore this will become the aim of this current project. This project will be using an array of techniques including in vitro wire myopgraphy, real-time PCR, histology, immunohistochemistry and image analysis.

Preventing Lung Disease in Very Premature Babies

Suitability: Honours/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. Several projects are possible to prove the involvement of these factors and could involve studies in premature rabbits and/or cell culture, together with molecular biology and immunohistochemical approaches.



Research Theme: Fetal and Neonatal Health

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 remodeling 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.

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, Dr Annie McDougall, Dr Mary Tolcos
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 features critical for 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 analyzing 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.

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

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 Hayley Dickinson, A/Prof David Walker
Email: *tim.moss@hudson.org.au, hayley.dickinson@hudson.org.au, david.walker@hudson.org.au*
Phone: 03 8572 2821 (A/Prof Moss)

Project description: Evidence of infection or inflammation within the uterus during pregnancy increases the risk of neurodevelopmental disorders like autism and cerebral palsy. The spiny mouse (*Acomys cahirinus*) is particularly suitable as a model of human pregnancy, and postnatal outcomes can be assessed using a battery of neurobehavioural tests.
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 behavior in spiny mice.
Research techniques: small animal experimentation (surgery, tissue collection, biometry); small animal neurobehavioral tests; histology; immunohistochemistry; molecular biology (RT-PCR); microbiology

Gestation-dependent Effects of Virus-like Illnesses in Fetal Brain Development in the Spiny Mouse

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 David Walker
Email : *david.walker@monash.edu*
Phone: (03) 8572 2823 (David Walker)

Project description: Rodent models of maternal infection during pregnancy (also known as maternal immune activation [MIA]) reproduce many behavioural, cognitive and neurochemical changes in the offspring that signify major changes in brain development have occurred. The current epidemic of 'microcephaly' in Brazilian women infected with the Zika virus has lent urgency to understanding how viral infections affect brain development during pregnancy. We now want to see if a virus-like illness induced in early, mid, or late pregnancy affects fetal brain development. Specifically, we want to determine the effects of Poly I:C treatment on development of the cerebral cortex in the spiny mouse fetus, to see if there is evidence of microcephaly at the end of pregnancy in this animal model.

Research Theme: Fetal and Neonatal Health

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

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 Hayley Dickinson
Email: *tim.moss@hudson.org.au, hayley.dickinson@hudson.org.au*
Phone: 03 8572 2821 (A/Prof Moss)

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 and postnatal behavior, and may lead to disorders such as autism and schizophrenia: whether maternal immunization has this effect is unknown.
This project is aimed at assessing the effects on brain development and postnatal behavior in spiny mice, after maternal immunization against whooping cough.
Research techniques: small animal experimentation (injection, tissue collection, biometry); small animal neurobehavioral tests; histology; immunohistochemistry; molecular biology (RT-PCR)

Early life inflammation and cardiovascular disease

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, Prof David Burgner (MCRI)
Email: *tim.moss@hudson.org.au, david.burgner@mcri.org.au*
Phone: 03 8572 2821 (A/Prof Moss)

Project description: Atherosclerosis, a major cause of cardiovascular disease, is an inflammatory condition that has its origins in early life. Atherosclerosis develops for decades before becoming clinically apparent. Early life is therefore a potential but largely over-looked window of opportunity for interventions to prevent or slow the development of atherosclerosis. The early life determinants of the initiation and progression of atherosclerosis are poorly understood. Animal and human data clearly indicate that postnatal inflammation and infection accelerate the development of atherosclerosis and are associated with adverse clinical outcomes.
The aim of this project is to determine the effect of inflammation before and soon after birth on the development of atherosclerosis in mice predisposed to development of the disease.
Research techniques: small animal experimentation (surgery, injection, tissue collection, biometry); histology; immunohistochemistry; molecular biology (RT-PCR)

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: Dr Graeme Polglase, Prof Stuart Hooper
Email: graeme.polglase@monash.edu
Phone: 03 8572 2822 (Dr 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.

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: Dr Graeme Polglase, Dr Kelly Crossley
Email: *graeme.polglase@monash.edu*, *kelly.crossley@monash.edu*
Phone: 03 8572 2822 (Dr 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.

Research Theme: Fetal and Neonatal Health

Tracking the movement of creatine between maternal and fetal compartments in sheep using stable isotopes

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 David Walker, Dr Hayley Dickinson, Prof Rod Snow (Deakin U.)
Email*: david.walker@hudson.org.au*
Phone: 03) 8572 2823 (David Walker)

Project Description: Our recent studies using creatine infused into either the maternal or fetal circulations provided no evidence for transplacental passage of creatine. However, the sheep placenta and chorio-amniotic membranes are richly endowed with the creatine transporter protein, CrT1. Possible explanations are: (1), the CrT1 transporter is fully saturated at normal creatine concentrations found in maternal plasma; or (2) placental CrT1 functions to distribute creatine between the placenta and fetus. We will use a stable isotope of creatine (^{13}C-methyl-creatine) to: (i) measure the rate of isotope transfer across the placenta in pregnant sheep near term; (ii) use ex vivo methods to determine isotope uptake by placental samples; and (iii) transfer of isotopic creatine across isolated segments of chorion/amnion using an Ussing chamber.

Effect of Maternal Asthma On Fetal/Neonatal Lung Development and Function

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Rob Bischof, A/Prof Tim Moss, Dr Megan Wallace
Email: *rob.bischof@monash.edu, tim.moss@monash.edu*

Project Description: Asthma is a common chronic disease affecting pregnant women and is a well-known risk factor for adverse outcomes in mother and baby. This project aims to investigate the effects of maternal asthma on fetal lung development and neonatal lung function in sheep, and identify mechanisms responsible for increased risk of neonatal lung disease. The outcomes of corticosteroid use in maternal asthma and in antenatal care on fetal/neonatal lung development and function will also be examined. The project will involve live animal studies, immunology, cell and molecular biology.

Mediators of fetal lung surfactant production

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, Dr Alana Westover
Email: *alana.westover@hudson.org.au*

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 preterm lung 'maturation' are not known.

We have demonstrated that exposing fetal lung fibroblast cells to inflammatory stimuli can increase surfactant in fetal lung epithelial cells. It is unclear how fibroblasts are communicating with epithelial cells to increase surfactant. This project will investigate the species mediating communication between these lung cells using fetal mice, cell culture and molecular biology.

Identifying the impact of Viral Illness in Pregnancy on the Fetal Brain using the Spiny Mouse

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 David Walker, Dr Rachel Hill
Email: *david.walker@monash.edu*
Phone: (03) 8572 2823 (David Walker)

Project Description: Schizophrenia is a severely debilitating neuropsychiatric disorder that affects approximately 1% of the population. Epidemiological data identify maternal infection (i.e., activation of the immune system) during pregnancy as a strong aetiological risk factor for schizophrenia. Rodent models of maternal immune activation (MIA) produce many of the behavioural, cognitive and neurochemical features of schizophrenia in the offspring, and so provide highly tractable tools for testing new therapeutic approaches. Our goal is to explore potential preventative strategies that can be implemented antenatally in the event of maternal infection, ***before*** critical disruptions to brain development have taken place. This behavioural neuroscience project will determine whether antenatal treatments based on preventing MIA after induction of a maternal viral-like illness will prevent behavioural dysfunctions that otherwise occur in the adult 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
Email: *tamara.yawno@monash.edu*, *suzie.miller@monash.edu*
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.

Research Theme: Infant and Child Health

A Clinical Tool for the Detection of Children at High Risk of Obstructive Sleep Apnoea

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: A/Prof Gillian Nixon, Prof Rosemary Horne
Email: *gillian.nixon@monashhealth.org*
Phone: 03 9594 5586 (A/Prof Nixon)

Project Description: Obstructive sleep apnoea (OSA) affects 1-3% of children and is a major health issue in childhood, with significant impacts on cognition, behaviour and cardiovascular health. The cardinal symptom of OSA is snoring. Approximately 35% of children snore- over one million children in Australia- but only about 10% of snoring children (1-3% of the population) will have OSA. Formally defining the presence of OSA in a snoring child requires polysomnography, a technically challenging and expensive (about $1000 each) test only available in paediatric tertiary referral hospitals. Such facilities could never meet the demand if all snoring children were referred. We are finalizing development of a clinical scoring tool that will help predict children at highest risk of OSA without the need for polysomnography. In 2017 we will be testing the new tool for usability and accuracy. Is it helpful for GPs, ENT surgeons and paediatricians at the coal face?

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

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Prof Rosemary Horne, A/Prof Gillian Nixon, Dr Lisa Walter
Email: *rosemary.horne@monash.edu*
Phone: 03 8572 2827 (Prof Horne)

Project Description: Children born preterm are 3-5 times more likely to be diagnosed with obstructive sleep apnoea (OSA) than those born at term. We have previously shown in children born at term that OSA has significant effects on the cardiovascular system with increased blood pressure and impaired autonomic control of heart rate. In our studies of infants born preterm we have shown that they have impaired control of blood pressure and heart rate which continues for at least the first 6 months after term equivalent age, but to date we have not carried out longitudinal studies into childhood. In this study we will analyse overnight polysomnographic studies of children referred to the Melbourne Children's Sleep Centre to identify if the severity and consequences of OSA are exacerbated in those children who were born preterm. Students will learn how to set up and record polysomnographic studies and to use spectral analysis techniques to assess heart rate control and cardiovascular responses to respiratory events.

Obstructive sleep apnoea in children with Down Syndrome

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: A/Prof Gillian Nixon, Prof Rosemary Horne
Email: *gillian.nixon@monashhealth.org*
Phone: 03 9594 5586 (A/Prof Nixon)

Project Description: Obstructive sleep apnoea (OSA) affects 30%-80% of children with Down Syndrome (DS). Different countries have proposed different guidelines to clinicians for screening for the condition, with American guidelines recommending routine sleep studies at 4 years of age and British guidelines recommending simpler overnight oximetry at home. As OSA can occur at any age, a single sleep study at a given age is an expensive and poorly targeted intervention. In addition, the benefits of treatment for OSA are poorly defined in children with DS, raising questions about the value of aggressive screening. We have recently shown that normally developing children benefit from treatment of OSA in terms of IQ, particularly in tasks associated with spatial visualisation, visual-motor coordination, abstract thought, and nonverbal fluid reasoning, and that elevated blood pressure returns to control levels. We now postulate that improvements in similar domains in children with DS might make substantial differences to their health and well-being. In this study we will quantify the impact of OSA on children with DS, especially in terms of adaptive functioning, quality of life and cardiovascular functioning, and determine the effect of treatment of OSA on these parameters. This will provide crucial information to guide clinical recommendations for screening and treatment of OSA in DS. Collection of relevant clinical data will secondarily allow us to develop screening tools for OSA in this population.

Mobile phone video clips to aid diagnosis of obstructive sleep apnoea in children

Suitability: Honours
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: A/Prof Margot Davey, A/Prof Gillian Nixon, Prof Rosemary Horne
Email: *margot.davey@monashhealth.org*
Phone: 03 9594 5572 (A/Prof Davey)

Project Description: When parents attend a Paediatric Sleep Clinic outpatient appointment for assessment of their child's suspected obstructive sleep apnoea (OSA), they often bring a short video recorded on their mobile phone that they have taken at home of their child sleeping, to demonstrate the problem to their doctor. Currently the diagnosis of OSA is achieved by performing overnight polysomnography (PSG), which time-consuming, costly, and has limited availability nationwide. A previous study has used prolonged VHS video recordings to predict the presence or severity of OSA diagnosed on PSG. IN this study we will ask parents to record a video clip of their child during sleep according to specific instructions, and to send the recording to a designated e-mail address. The video clips will be scored in a standardised fashion using a scoring sheet. PSG will then be performed as per usual clinical procedure. The relative risk of OSA given an abnormal video score will then be determined. If we can validate the use of home videos for predicting patients with OSA, then this tool could be used as a screening tool to prioritise clinic appointments, rationalise the use of further investigations and plan treatment

Research Theme: Infant and Child Health

Bright Light Therapy to Improve Sleep and Quality of Life in Children with Cancer

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Lisa Walter, Prof Rosemary Horne
Email: *lisa.walter@hudson.org.au*
Phone: 8572 2834 (Dr Walter)

Project Description: Childhood cancer can disrupt sleep through the direct effect of the disease and/or a consequence of treatment. Poor sleep in children with cancer impacts on their perception of, and the ability to cope with the emotional and physical challenges associated with both the disease and its treatment. Sleep disruption in these children is an added burden on their quality of life that can last many years beyond diagnosis and treatment. Bright light therapy has been shown to improve sleep and the quality of life in adults with cancer. A similar study has not been conducted in children. This study will investigate the efficacy of using bright light therapy in children with acute lymphoblastic leukaemia during chemotherapy, utilizing actigraphy and validated questionnaires, to improve sleep and the quality of life of these children.

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

Suitability: Honours
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Lisa Walter, Prof Rosemary Horne
Email: *lisa.walter@hudson.org.au*
Phone: 8572 2834 (Dr Walter)

Project Description: A particular phenomenon of the electroencephalography (EEG) wave form is the sleep spindle, believed to function as mechanism through which long-term changes are made in the neocortex and as a mechanism for maintaining sleep. Sleep spindles have also been associated with different aspects of cognitive performance in healthy children. Sleep disordered breathing (SDB), is a very common condition in children, and has been associated with neurocognitive deficits. To date, it is not known whether the poor neurocognition in children with SDB is related to a loss of sleep spindles. This study will investigate sleep spindles in children with SDB and determine if there is an association between sleep spindle numbers and neurocognitive deficits. The student will be involved in conducting sleep studies (polysomnography) and analysis of electroencephalography data.

Identifying pathways for new treatment strategies for children with primary snoring

Suitability: PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Sarah Biggs, Prof Rosemary Horne
Email: *sarah.biggs@hudson.org.au*
Phone: 03 8572 2835 (Dr Biggs)

Project Description: Children with primary snoring (PS) represent the greatest proportion of children with SDB and are often untreated, leaving them at risk of continued or even increasing cognitive and behavioural deficit. An understanding of the mechanisms of the association between behaviour and learning will provide vital information regarding potential new, non-surgical treatment strategies. The aim of this project is to, for the first time, separate out the behavioural influence on cognitive potential in children with PS by examining the independent effect of SDB-related sleep disturbance on learning ability. This study will also provide novel data which may identify sleep-related brain activity as an underlying mechanism linking SDB with daytime neurocognitive and behavioural deficits in children with PS and obstructive sleep apnoea.

Preterm Infants in The NICU – Mechanisms of Oxygen Desaturations

Suitability: Honours/PhD
Location: Level 5, Block B, Monash Medical Centre, Clayton & Monash Newborn, Monash Medical Centre, Clayton
Project Leaders: Dr Kenneth Tan, Dr Atul Malhotra, A/Prof Philip Berger
Email: *kenneth.tan@monash.edu, atul.malhotra@monash.edu, philip.berger@monash.edu*
Phone: 03 9594 5191 (Dr Tan), 03 95945191 (Dr Malhotra), 03 9594 5398 (A/Prof Berger)

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

Research Theme: Infant and Child Health

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
Email: *jim.buttery@monash.edu, franz.babl@rch.org.au, simon.craig@monash.edu*
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.

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
Email: *jim.buttery@monash.edu*, *andrew.daley@rch.org.au*
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 statewide 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
Email: *jim.buttery@monash.edu*, *nigel.crawford@rch.org.au*
Phone: 0403 854 179 (A/Prof Buttery)

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

Research Theme: 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

The Effects of cord blood stem cells on the lungs following fetal inflammation

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, Prof Graham Jenkin, Ms Madison Paton
Email: *beth.allison@hudson.org.au*, *suzie.miller@monash.edu*
Phone : 03 8572 2488 (Dr Allison), 03 9902 2796 (A/Prof Miller)

Project Description: Intrauterine inflammation is recognized as a major cause of preterm birth and pulmonary complications in the developing lung. This study aims to examine whether human Amnion Epithelial Cells (hAECs) can be used as a potential therapeutic agent to reduce lung injury induced by inflammation (lipopolysaccharide, LPS) in preterm fetal sheep. This project will utilize techniques to investigate lung injury, such as lung histology, inflammatory assays, rtPCR, western blotting and stem cell tracking.

Do Cord Blood Stem Cells Reduce Cerebrovascular Brain Injury?

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: A/Prof Suzie Miller, Dr Margie Castillo-Melendez, Prof Graham Jenkin, Dr Courtney McDonald,
Email: *margie.castillo-melendez@monash.edu*, *suzie.miller@monash.edu*
Phone: 03 8572 2796 (A/Prof Miller), 03 8572 2803 (Dr Castillo-Melendez)

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

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
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 potently 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 and storage of umbilical cord tissue containing these cells, and their retrieval post-thaw, to enable patients to have the option to store umbilical cord tissue at birth, in addition to cord blood.

Research Theme: 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: Dr Abhilasha Tiwari, Prof Graham Jenkin, Dr Courtney McDonald, A/Prof Mark Kirkland (Deakin University)
Email: *graham.jenkin@monash.edu*
Phone: 03 8572 2801 (Prof Jenkin)

Project Description: Umbilical cord blood (UCB) is one of the richest sources of "young" hematopoietic stem cells. Currently, more than 3000 UCB stem cell transplants are performed each year. However, these are mostly restricted to children, as UCB samples usually do not contain sufficient stem cells to treat adults. The umbilical cord and cord blood also contains multiple potentially efficacious cell types for a range of diseases. Hence, this research project aims to develop and refine methods for expanding the number of stem cells obtained from human UCB and umbilical cord under laboratory conditions and translation of this research to the clinic. This stem cell research could help save lives of people suffering from blood disorders, cancers and auto-immune diseases. The experiments will include cell culture and molecular biology techniques and transplantation of UCB stem cells to mice to determine their efficacy.

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)
Email : *tim.moss@hudson.org.au, jane.pillow@uwa.edu.au*
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.

How do umbilical cord blood stem cells reduce neuroinflammation 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
Phone: 03 8572 2799

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 that 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.

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 Courtney McDonald
Email: *graham.jenkin@monash.edu*
Phone: 03 8572 2801 (Prof Jenkin)

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

Research Theme: Cell therapy and regenerative medicine

How Do Umbilical Cord Blood Stem Cells Reduce Neuroinflammation 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*
Phone: 03 9902 4816

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 that 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.

Do Cord Blood Stem Cells Promote Neurorestoration in Preterm Brain Injury?

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: A/Prof Suzie Miller, Dr Margie Castillo-Melendez, Prof Graham Jenkin, Dr Courtney McDonald,
Email: *margie.castillo-melendez@monash.edu*, *suzie.miller@monash.edu,*
Phone: 03 8572 2796 (A/Prof Miller), 03 8572 2803 (Dr Castillo-Melendez)

Project Description: One of the most devastating pathologies that occur in preterm births are brain hemorrhages which increases an infant's probability of being diagnosed with CP, emphasizing the involvement of the cerebral vasculature in the etiology of neonatal brain injury. It is now appreciated that the parents of many Australian children with cerebral palsy are taking their children overseas to undertake cord blood stem cell therapy, despite a lack of published data that such therapy will be beneficial. Umbilical cord blood (UCB) represents a useful source of blood stem cells. UCB is enriched with a number of different progenitor cells thus it has the potential to generate a variety of cell types and produce restoration of the brain via the formation of new blood vessels (angiogenesis) and the generation of new neurons (neurogenesis) and synapses (synaptogenesis). In adult brain injury, the generation of new blood vessels is known to facilitates neuro-restorative processes including neurogenesis and synaptogenesis, which in turn lead to improved functional recovery. This project will determine if UCB cell transplantation prevents injury in the preterm brain by stimulating the brain restorative capacity – by promoting angiogenesis, neurogenesis and synaptogenesis. This project utilizes brain tissue that has already been collected and does not require the student to undertake animal work.

Stem Cells and Pregnancy: What Women Want

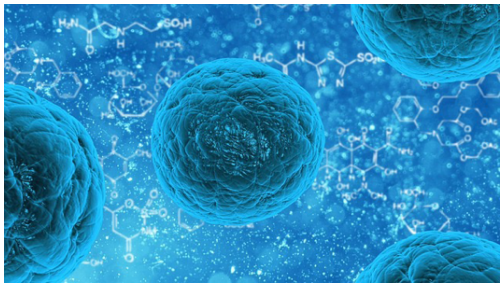
Suitability: Honours
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Prof Euan Wallace, Prof Graham Jenkin
Email: *graham.jenkin@monash.edu*
Phone: 03 8572 2801 (Prof Jenkin)

Project Description: As a component of a program of stem cell and cell therapy research, the student will explore women's views about stem cell therapies and their application to their baby's health, using validated surveys The project will be based at Monash Medical Centre where the student will interview new mothers who have just had a baby at either Monash or Jessie McPherson Private Hospital, exploring their attitudes to the collection of cord blood stem cells and placental stem cells. Skills in questionnaire development, data analyses, and bioethics will be gained in this project as well as participation in stem cell research.

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.



Research Theme: Cell therapy and regenerative medicine

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, Dr Jean Tan
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.

Treatment of Critical Limb Ischemia with 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: Jean Tan, Dr Rebecca Lim
Email: *jean.tan@hudson.org.au*
Phone: 03 8572 2794 (Dr Lim)

Project Description: Critical limb ischemia (CLI) affects 15% of the population of every socioeconomic scale. Arteriosclerotic plaque build up causes occlusion of oxygen and nutrient supply to the limb leading to tissue death, leaving amputation as the only option. Amnion stem cell derived nanomedicine have shown significant vasculogenesis potential making them a viable source for therapy. We will use an animal model to mimic CLI and determine how naturally occurring nanoparticles released by stem cells can help revascularise necrotic limb and prevent amputation. Techniques involved include small animal surgeries, cell culture, MRI and SPECT imaging, immunohistochemistry, ELISA, FACS, real-time PCR and western blotting.

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
Email: *rob.bischof@monash.edu*, *tim.moss@monash.edu*

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

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.

Research Theme: Cell therapy and regenerative medicine

Stem Cells and Tissue Scaffolds

Suitability: Honours/PhD
Location: Department of Surgery, Monash Medical Centre, Clayton & The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: A/Prof Tony Goldschlager, Prof Graham Jenkin
Email: *graham.jenkin@monash.edu*
Phone: 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 spinal discs for repair of discs damaged by trauma or degenerative processes. We will study the characteristics of biomatrices both in vitro and in vivo, in collaboration with the commercial company, Mesoblast. We will determine the appropriateness of our cellular scaffolds for the production of engineered tissues. We will determine the most appropriate polymer compositions and stem cell combinations that can be developed into the most viable scaffold for therapeutic use in clinical trials.

Amnion cells for the treatment of cerebral palsy

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research, Level 3, 27-31 Wright St, Clayton & Monash University, Clayton
Project Leaders: Dr Bryan Leaw, Dr Rebecca Lim, Prof Euan Wallace
Email*: bryan.leaw@hudson.org.au*
Phone: 03 8572 2797 (Dr Leaw)

Project Description: Cerebral palsy affects 1 in 500 babies, and every 15 hours a baby is diagnosed with cerebral palsy. Cerebral palsy is a group of motor and cognitive impairments, where patients may never develop the ability to walk and experience delayed learning. Unfortunately, these symptoms are life-long and there is no cure. Amnion cells are an exciting part of the emerging cell therapy field, and we have previously shown in other models that amnion cell administration results in reduced inflammation and cell death after brain injury. Using a new rat model of cerebral palsy, we will assess whether amnion cells have long-lasting protective effects, and for the first time assess whether they improve long-term motor and learning outcomes. This project involves small animal surgery and molecular techniques.