MONASH University

Department of Obstetrics and Gynaecology

and

Department of Paediatrics

The Ritchie Centre Student Projects 2015

mimr-phi institute

the RITCHIE CENTRE

The Ritchie Centre

The Ritchie Centre is affiliated with the newly merged MIMR-PHI Institute of Medical Research as well as with Monash University Faculty of Medicine, Nursing and Health Sciences. It is the principal research centre of the Monash University Department of Obstetrics and Gynaecology and Department of Paediatrics at the School of Clinical Sciences and the principal research partner of Monash Children's Hospital and Monash Women's Services at Monash Health. The Centre aims to improve the health of women and children through innovative research that informs better healthcare.

The Ritchie Centre is now acknowledged as the leading perinatal research centre in Australia and is one of the country's leading women's health medicine research clusters. 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 lead to rapid translation of its basic research into clinical trials and clinical practice. The Centre has, in a very short time, clearly demonstrated the value of bringing together a critical mass of dedicated scientists and clinicians to undertake translational research. The Centre has also initiated an innovative annual "Public Forum" to inform and educate the general public on women's health issues.

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.

THEME: WOMEN'S HEALTH

How does the Endometrium (Lining of the Uterus) Regenerate?

Suitability: Honours
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: A/Prof Caroline Gargett, Dr James Deane
Email: caroline.gargett@mimr-phi.org
Phone: 03 9902 4712 (A/Prof Gargett)

Project Description: Human endometrium is highly regenerative, growing 1 cm of mucosal tissue each menstrual cycle. The thin endometrium of postmenopausal women also regenerates and can support pregnancy after hormone replacement therapy. It is likely that endometrial epithelial progenitor cells and mesenchymal stem cells that we recently identified are responsible for this remarkable regenerative capacity. A microarray study comparing human endometrial epithelial cells from pre-and post-menopausal women identified 22 differentially expressed WNT signalling genes, which have important roles in stem cell function and in development. This project will examine the role of the Wnt signalling pathway in regulating endometrial epithelial progenitor cell populations.

Index: Endometrium, stem cells, Wnt signalling

Testing the In Vivo Regenerative Potential of Putative Stem Cell Populations from the Endometrium

Suitability: Honours
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: A/Prof Caroline Gargett, Dr James Deane
Email: caroline.gargett@mimr-phi.org
Phone: 03 9902 4712 (A/Prof Gargett)

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.

Index: Endometrium, stem cells, transplantation

Role of Human Endometrial Stem/Progenitor Cells in Endometriosis

Suitability: Honours/PhD *(role of Wnt4, identified as a susceptibility gene will also be examined)*
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: A/Prof Caroline Gargett, Dr Kjiana Schwab
Email: caroline.gargett@mimr-phi.org
Phone: 03 9902 4712 (A/Prof Gargett)

Project Description: We discovered that human endometrium has a population of epithelial progenitor cells and mesenchymal stem cells (MSC), which can be identified by several novel markers: W5C5 for endometrial MSC and H3D12 and AdM2 are candidates for epithelial progenitor cells. Our preliminary data shows that $W5C5^+$, $H3D12^+$ and $AdM2^+$ cells are shed in menstrual blood and that significantly more of these cell populations gain access to the pelvic cavity in women with endometriosis than normal, suggesting that these cells initiate endometriosis. This project will undertake gene profiling on endometrial stem/progenitor cells purified with our markers from endometrial samples of women with and without endometriosis a common disease affecting 6-15% of young women.

Index: Endometrium, adult stem cells, endometriosis

Do Endometrial Mesenchymal Stem Cells (MSC) have Immunomodulatory Properties that can be Harnessed to Treat Human Disease?

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Dr James Deane, A/Prof Caroline Gargett
Email: james.deane@mimr-phi.org, caroline.gargett@mimr-phi.org
Phone: 03 99024778 (Dr Deane), 03 9902 4712 (A/Prof Gargett)

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.

Index: Mesenchymal stem cells, cell-based therapy, regenerative medicine

THEME: WOMEN'S HEALTH

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

Suitability: Honours
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leader: A/Prof Caroline Gargett
Email: caroline.gargett@mimr-phi.org
Phone: 03 9902 4712 (A/Prof Gargett)

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.

Index: Mesenchymal stem cells, epithelial progenitors, IVF

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

Suitability: Honours/BMedSci/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: A/Prof Caroline Gargett, A/Prof Anna Rosamilia, Dr Jerome Werkmeister (CSIRO), Prof John (Arkwright, Flinders University, Adelaide)
Email: caroline.gargett@mimr-phi.org
Phone: 03 9902 4712 (A/Prof Gargett)

Project Description: Pelvic organ prolapse (POP) results from childbirth injury, affecting 25% of all women. It causes incontinence and sexual dysfunction. POP is treated by surgery, frequently augmented by mesh, but failure and complication rates are high. We are investigating a regenerative medicine approach to improve treatment outcomes using cell-based therapy delivered in novel materials fabricated by CSIRO. There are 2 pre-clinical projects available to examine the effect of using autologous endometrial mesenchymal stem cells (eMSC) labeled with a lentivirus vector to treat or prevent POP. One project examines the effect of eMSC surgically delivered in novel meshes in sheep with POP (detected by a novel fibre optic device) and the second examines the effect of eMSC in a hydrogel injected into the vaginal wall of sheep following Bakri balloon induced injury (simulating birth injury). Flow cytometry, histological, immunohistochemistry, biochemical and biomechanical analyses will be undertaken.

Index: Animal model, mesenchymal stem cells, prolapse

Pelvic Organ Prolapse – Computer Simulation of New Treatments

Suitability: Honours/PhD
Location: Anatomy & Cell Biology, Monash University, Clayton & MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Dr Colin McHenry, A/Prof Caroline Gargett
Email: colin.mchenry@monash.edu, caroline.gargett@mimr-phi.org
Phone: 03 9902 4712 (A/Prof Gargett)

Project Description: Pelvic organ prolapse (POP) results from childbirth injury, affecting 25% of all women. It causes incontinence and sexual dysfunction. POP is treated by surgery, but failure rates are high. We are investigating a regenerative medicine approach to improve treatment outcomes using cell-based therapy delivered in novel scaffold materials fabricated by CSIRO. This project will use virtual testing of the scaffolds to examine the impact of biomechanical loads simulating daily activities on their performance. Normative data will be collected from a sheep and human pelvis using high resolution MRI and CT imaging to generate models predicting biomechanical responses of the pelvic tissues. This multidisciplinary project involves the use of engineering software and supercomputers.

Index: Prolapse, computational biomechanics, simulation

Telomerase Activity as a Stem Cell Marker in the Endometrium

Suitability: Honours
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Dr James Deane, A/Prof Caroline Gargett
Email: james.deane@mimr-phi.org, caroline.gargett@mimr-phi.org
Phone: 03 99024778 (Dr Deane), 03 9902 4712 (A/Prof Gargett)

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.

Index: Endometrium, stem cell, telomerase

THEME: WOMEN'S HEALTH

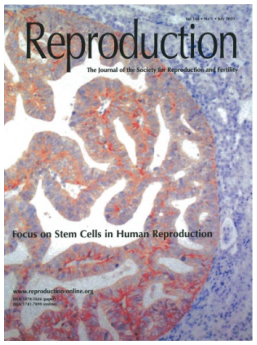
Are there Prenatal Factors that Reduce Ovarian Reserve and therefore Fertility?

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Hayley Dickinson, A/Prof Peter Temple-Smith, Dr Suzie Miller, A/Prof Beverley Vollenhoven
Email: hayley.dickinson@monash.edu
Phone: 03 9594 4760 (Dr Dickinson)

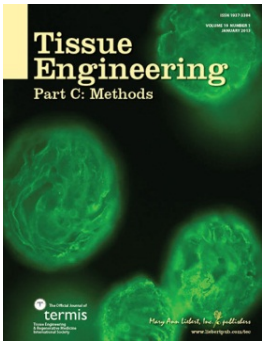
Project Description: This study will explore the novel idea that prenatal events associated with oxidative stress will have profound negative effects on ovarian reserve and oocyte quality in the adult ovary. We will explore this in 2 models of perinatal oxidative stress, birth asphyxia and IUGR. We will identify the mechanisms by which birth asphyxia reduces the OvR in the spiny mouse and determine if this impacts on fertility. Determine the mechanisms by which creatine protects follicle loss from the ovary in this model and whether fertility is normal in these animals. Determine if IUGR reduces OvR in the spiny mouse and whether melatonin protects the ovary from follicle loss.

Additionally we will perform a retrospective study, identifying women with reduced fertility due to poor OvR and access their birth records to determine whether they were exposed to an adverse prenatal event.

Index: Intrauterine growth restriction, fetal development, long-term health outcomes, ovarian reserve, fertility, birth asphyxia



Critical Windows of Organ Development Susceptible to Maternal Stress



Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Hayley Dickinson, Prof David Walker, Dr Tracey Quinn
Email: hayley.dickinson@monash.edu
Phone: 03 9594 4760 (Dr Dickinson)

Project Description: We propose to identify when during pregnancy fetal organ systems are susceptible to the effects of excess maternal stress hormones. This knowledge would give a rational basis for knowing more about how to handle and treat illnesses during pregnancy. For these studies we use the spiny mouse, a precocial rodent species in which the maternal hormonal environment closely mimics that of the human.

We will administer betamethasone, cortisol or saline to pregnant spiny mice for 60h on days 15, 25, 30 or 35 of gestation (term is 39 days) and determine the fetal, newborn and adult consequences for the offspring.

Index: Stress, pregnancy, fetal development, long-term health outcomes

THEME: FETAL & NEONATAL HEALTH

Intrauterine Growth Restriction (IUGR) in the Spiny Mouse

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Hayley Dickinson, Dr Suzie Miller, Dr Mary Tolcos, Prof David Walker
Email: hayley.dickinson@monash.edu
Phone: 03 9594 4760 (Dr Dickinson)

Project Description: We have very recently developed a model of IUGR in the spiny mouse using a unique experimental approach. Our model is associated with asymmetric growth restriction, such that the growth of organs of high priority, such as the brain are preserved, whilst other organs, such as the kidney, are more severely affected, as is most commonly observed clinically. The aim of this project is to characterize the development of the organs systems (brain, heart, kidney, lung, adrenal gland, gonads) in these IUGR offspring. Once characterized, we will then use this model to test a range of therapeutic strategies to improve the growth of the fetus for improved postnatal outcomes.

Index: Intrauterine growth restriction, fetal development, long-term health outcomes

Overcoming the 4-Cell Block in Spiny Mouse Embryo Culture

Suitability: Honours/PhD *(project will be expanded for PhD)*
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Hayley Dickinson, Prof David Walker
Email: hayley.dickinson@monash.edu
Phone: 03 9594 4760 (Dr Dickinson)

Project Description: In vivo, the spiny mouse embryo cleaves at a similar rate to the human embryo, making it an ideal model to study human embryogenesis. In vitro, spiny mouse embryos readily cleave from the 1- to 4-cell stages and from the 8-cell stage through to blastocyst hatching. However, spiny mouse embryos will not cleave from 4- to 8-cells. We hypothesize, that this '4-cell block' coincides with embryonic genome activation (EGA) in this species.

This project will determine when EGA occurs in the spiny mouse embryo, and develop culture conditions to support the development of spiny mouse embryos.

Index: Embryo, in vitro, culture, embryonic genome activation

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: Level 5, Monash Medical Centre, Clayton
Project Leaders: Prof David Walker, Dr Syed Baharom, Dr Suzie Miller, Dr Graeme Polglase
Email: david.walker@monash.edu
Phone: 03 9594 5372 (Prof Walker)

Project Description: The aetiology of brain damage that manifests itself in some infants after 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.

Index: Bone marrow, stem cells, brain repair, cerebral palsy

Endothelial Progenitor Cells (EPCs) in Fetal Blood and Brain – Role in Repair and Recovery from Developmental Brain Injury

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Dr Margie Castillo-Melendez, Dr Suzie Miller, Prof Graham Jenkin
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Phone: 03 9905 2195

Project Description: We hypothesize that EPCs from bone marrow are recruited in the developing brain following hypoxia and/or ischaemic (HI) injury, and determine the capacity of the fetal and newborn brain to limit and repair this damage caused by HI and inflammation. Specifically, we propose that EPCs are mobilized from fetal bone marrow following HI and limit brain damage by promoting vascularization of injured regions. EPCs derived from umbilical cord blood may be useful for therapeutic repair of brain injury in the postnatal brain following HI. By investigating preterm and term fetal sheep, we will provide new insights into the role of circulating EPCs in the developing brain under hypoxic conditions, explore the potential of circulating EPCs to serve as a prognostic marker of brain injury, and determine the therapeutic potential of EPCs for promoting recovery from perinatal brain injury.

Index: Bone marrow, stem cells, brain repair, cerebral palsy

THEME: FETAL & NEONATAL HEALTH

Impact of Dopamine in the Immature Brain

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

Index: Preterm, Brain injury, infants

Novel Approaches to Bedside Monitoring of Cerebral Oxygenation in Infants with HIE Undergoing Therapeutic Hypothermia

Suitability: Honours
Location: Level 5, Monash Medical Centre, Clayton
Project Leader: Dr Flora Wong
Email: flora.wong@monash.edu
Phone: 03 9594 5482 (Dr Wong)

Project Description: Hypoxic ischaemic encephalopathy (HIE) is major problem worldwide with significant mortality and morbidity. Based on recent evidence that therapeutic hypothermia is beneficial to term newborns with HIE, neonatal units now offer cooling as recommended therapy. This project aims to improve and refine the cooling therapy, by using the Tissue Oxygenation Index measured by Near Infrared Spectroscopy (NIRS). We plan to continuously monitor the cerebral oxygenation of HIE infants by NIRS, and relate the measurements to neurodevelopmental outcome. The study will provide bedside information to aid clinical assessments with the potential to guide therapeutic interventions in these critically ill infants.

Index: Brain injury, Infants, birth asphyxia

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: Dr Flora Wong, Prof Rosemary Horne
Email: flora.wong@monash.edu
Phone: 03 9594 5482 (Dr 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).

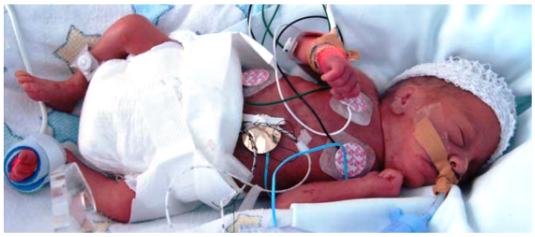
Index: Preterm, brain injury, infants

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: Dr Flora Wong, Prof David Walker, Dr Hayley Dickinson
Email: flora.wong@monash.edu
Phone: 03 9594 5482 (Dr 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.

Index: Brain injury, infants, birth asphyxia



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THEME: FETAL & NEONATAL HEALTH

Novel Treatments for Preterm Brain Injury (1)

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton & Large Animal Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Suzie Miller, Prof Graham Jenkin, Dr Margie Zakhem, Dr Tamara Yawno, Dr Beth Allison
Email: suzie.miller@monash.edu, graham.jenkin@monash.edu
Phone: 03 9902 4795 (Dr Miller), 03 9902 4736 (Prof Jenkin)

Project Description: In Australia, a baby is born with the brain injury that underlies cerebral palsy every 15 hours. Improvements in newborn care mean that most babies that are born preterm will survive, but prematurity remains linked to cerebral palsy. This project will examine whether melatonin, a free radical scavenger and steroid derived neuroprotectants can reduce brain damage caused by preterm lack of oxygen. Treatments will be administered to preterm (fetal) lambs following hypoxia in vitro.

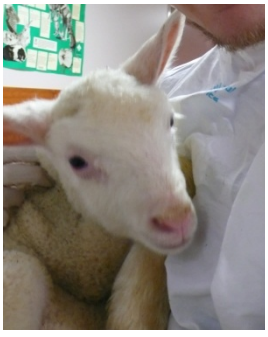
Index: Prematurity, cerebral palsy, melatonin

Do Cord Blood Stem Cells Reduce Brain Injury After Birth Asphyxia?

Suitability: Honours/ PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton & Large Animal Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Suzie Miller, Prof Graham Jenkin
Email: suzie.miller@monash.edu, graham.jenkin@monash.edu
Phone: 03 9902 4795 (Dr Miller), 03 9902 4736 (Prof Jenkin)

Project Description: 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 plan to undertake a project that will directly address the question of whether cord blood stem cells reduce perinatal brain injury, caused by a severe asphyxic event at birth, and the mechanisms of protection. This project will utilise our established term lamb model of birth asphyxia, with state-of-the-art neonatal care and magnetic resonance imaging to track the cells.

Index: Perinatal brain injury, stem cells, newborn lambs



The Effects of Betamethasone in Single and Repeat Doses on the Developing Brain

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton, Large Animal Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Suzie Miller, Dr Tamara Yawno, Prof Graham Jenkin
Email: suzie.miller@monash.edu,graham.jenkin@monash.edu, tamara.yawno@mimr-phi.org
Phone: 03 9902 4795 (Dr Miller), 03 9902 4736 (Prof Jenkin), 03 9902 4797 (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.

Index: Antenatal glucocorticoids, obstetrics, brain injury, IUGR

Novel Treatments for Preeclampsia

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton & Monash University, Clayton
Project Leaders: Dr Rebecca Lim, Prof Euan Wallace
Email: rebecca.lim@monash.edu
Phone: 03 99024775 (Dr Lim)

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 efficacy of resveratrol as a novel therapy. This project involves small animal surgery and molecular techniques.

Index: Preeclampsia, pregnancy, oxidative stress

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THEME: FETAL & NEONATAL HEALTH

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: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: A/Prof Marcel Nold, Dr Claudia Nold
Email: marcel.nold@monash.edu, claudia.nold@monash.edu
Phone: 03 9902 4763 (A/Prof Nold), 03 9902 4723 (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.

Surprisingly little is known about the immune and coagulation system of preterm infants, which therefore represent problematically blank pages for clinicians on the one hand, but a true frontier for researchers on the other. Another reason why preterm immunity and coagulation represent a new frontier is that technology has advanced enough only recently to allow us to extract large amounts of information from sample volumes as small as 0.5 ml - which in fact is a significant volume of blood to take from the tiny patients, considering that the total blood volume is as small as 35 ml in some of the babies. Our laboratory has obtained approval to conduct an exciting study in which blood is taken from extremely premature infants at 5 timepoints, thus allowing for a unique longitudinal view at 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. Since we also have access to the babies' clinical data, we will be able to perform correlation analyses and draw conclusions about the relevance of our findings to the major diseases of prematurity such as bronchopulmonary dysplasia, intracranial haemorrhage and necrotising enterocolitis. These insights may lead to the identification of biomarkers and/or new therapeutic targets, which are direly needed as several of these diseases are clinically highly problematic and currently untreatable.

Index: Preterm babies, immune system, coagulation, clinical study

Molecular Tracking of the Cytokine IL-37 in Anti-Inflammatory Signalling

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: A/Prof Marcel Nold, Dr Claudia Nold, Dr Camden Lo
Email: marcel.nold@monash.edu, claudia.nold@monash.edu, camden.lo@monash.edu
Phone: 03 9902 4763 (A/Prof Nold), 03 9902 4723 (Dr Nold), 03 9902 4710 (Dr Camden)

Project Description: The focus of this study is on elucidating the molecular mechanism of signalling cascades triggered by the anti-inflammatory cytokine interleukin 37 (IL-37). We have recently described IL-37's powerful beneficial effects, which endow this cytokine with a vast potential for therapeutic application. This project continues our research on IL-37 by 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.

Index: New anti-inflammatory interleukin, high-resolution microscopy, live cell imaging

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THEME: FETAL & 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/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Dr Claudia Nold, A/Prof Marcel Nold, A/Prof Philip Berger
Email: marcel.nold@monash.edu, claudia.nold@monash.edu, philip.berger@monash.edu
Phone: 03 9902 4763 (A/Prof Nold), 03 9902 4723 (Dr Nold), 03 9594 5477 (A/Prof Berger)

Project Description: The severe chronic lung disease bronchopulmonary dysplasia (BPD) of the preterm newborn causes considerable suffering for affected children and families and contributes substantially to health care costs. Necrotising enterocolitis (NEC) is a disease of the premature gut that is very poorly understood and that carries a high mortality. Importantly, no effective therapy is known for either of these devastating diseases. Neonatal immunity has been neglected by biomedical research; therefore, the immense importance of inflammation for BPD and NEC is only beginning to be recognised. In this study, we will assess the therapeutic potential of two innovative anti-inflammatory mediators, interleukin 1 receptor antagonist (IL-1Ra) and IL-37, in established animals models of BPD and NEC. A BPD-like lung disease will be triggered in newborn mice and we will investigate whether increased levels of IL-1Ra or IL-37 can protect the young mice from developing lung pathology. To assess such BPD-like pathology, we will analyse biochemical and cellular markers of inflammation as well as histological slides for alveolarisation and vascularisation on day 3 and 28 of life. To mimick NEC, newborn mice will not be allowed to breast-feed, but will be fed an equivalent to formula for 3 days. In addition, they will briefly be exposed to cold and hypoxia. The resulting pathology in the gut resembles human NEC, and again we will assess the protective properties of IL-1Ra and IL-37 on the cellular level by histology and flow cytometry and on the molecular level by analysis of various biochemical markers.

Index: Animal models of disease, preterm babies, anti-inflammatory interventions

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

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Dr Claudia Nold, Dr Ina Rudloff, A/Prof Marcel Nold
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Phone: 03 9902 4763 (A/Prof Nold), 03 9902 4723 (Dr Nold), 03 9905 3105 (Dr Rudloff)

Project Description: Interleukin (IL)-37 was discovered in silico in 2000, but received very little attention (not even 10 publications) in general and nothing at all was known about its function until 2010, when our group 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, including the mRNA and protein expression profile of IL-37 across a spectrum of cell types and the effect of IL-37 on an important molecular regulator of inflammation, the inflammasome.

Index: New anti-inflammatory interleukin, RNA and protein detection, inflammasome

THEME: FETAL & NEONATAL HEALTH

The First In Vivo Exploration of IL-38

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Dr Claudia Nold, Dr Ina Rudloff, A/Prof Marcel Nold
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Project Description: Like interleukin (IL)-37, IL-38 was discovered in silico in 2000, but received even less attention until our group renamed the new IL-1 family cytokines in 2010. There is some evidence that IL-38 has anti-inflammatory properties, but confirmation of the function of this cytokine is needed. We have generated the first IL-38 knockout mouse in the world and in this exciting project will undertake the first experiments that involve this mouse. In addition to employing the simple endotoxic shock model, we will study the effects of IL-38 in autoimmune disease.

Index: New anti-inflammatory interleukin, RNA and protein detection, autoimmune disease

Transition to Life After Birth

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Prof Stuart Hooper, Dr Kelly Crossley, Dr Graeme Polglase, Lauren Kerr
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Phone: 03 9594 5013 (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.

Index: Onset of air-breathing at birth, premature birth, cardiovascular changes at birth.

Imaging the Entry of Air into the Lungs at Birth

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Prof Stuart Hooper, Lauren Kerr, Dr Marcus Kitchen (Physics)
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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.

Index: Onset of air-breathing at birth, premature birth, lung imaging

Preventing Lung Disease in Very Premature Babies

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Dr Megan Wallace, Prof Stuart Hooper
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Phone: 03 9902 4761 (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 cell culture.

Index: Fetal and neonatal development, lung injury, lung disease

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THEME: FETAL & NEONATAL HEALTH

Fetal Lung Growth and Development

Suitability: Honours/PhD
Location: MIMR-PHI - Level 3, 27-31 Wright St, Clayton
Project Leader: Dr Megan Wallace, Dr Annie McDougall
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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.

Index: Fetus, newborn, lung development

Characterising a Novel Factor, Trop2, in the Developing Brain

Suitability: Honours
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton & Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Annie McDougall, Dr Mary Tolcos, Dr Megan Wallace
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Project Description: Abnormal development of the brain is linked with adverse neurological outcomes, such as motor, cognitive, and learning deficits and can lead to autism, schizophrenia and cerebral palsy. A thorough understanding of the mechanisms underlying normal brain development are important for generating better, more specific treatments to prevent these disorders. We have identified a novel factor, Trop2 that regulates lung and cerebellar development by controlling cell proliferation and migration. This project will combine small animal work, histology, immunohistochemistry and molecular biology to characterise the role of Trop2 throughout the developing brain.

Index: Brain development, neuronal migration, Trop2

Amniotic Fluid Infection/Inflammation: Effects on Brain Development and Postnatal Behaviour

Suitability: Honours/PhD
Location: The Ritchie Centre, Level 5, B Block, Monash Medical Centre, Clayton
Project Leaders: A/Prof Tim Moss, Dr Hayley Dickinson, Dr Mary Tolcos, Dr Graeme Polglase
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Phone: 03 9594 5392 (A/Prof Moss)

Project description: Bacterial infection of amniotic fluid is a major cause of preterm birth, and is associated with a number of adverse neurodevelopmental outcomes including cerebral palsy and autism.

At present there is no animal model of amniotic fluid infection that allows investigation of the neurodevelopmental and postnatal behavioural outcomes. 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 determining the effects of experimental amniotic fluid infection on brain development and postnatal neurobehavior in spiny mice.

Index: Neurodevelopment, infection, inflammation

Fetal Anti-Inflammatory Effects of Human Amnion Epithelial Cells

Suitability: Honours/PhD
Location: The Ritchie Centre, Level 5, B Block, Monash Medical Centre, Clayton & MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: A/Prof Tim Moss, Prof Graham Jenkin
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Phone: 03 9594 5392 (A/Prof Moss)

Project Description: Epithelial cells from the amniotic membrane have the pluripotent capacity of embryonic stem cells, and several other characteristics, which make them an attractive option for cell therapy. Amnion epithelial cells appear to exert their effects by modulating the immune response.

This project is aimed at determining the effect of amnion epithelial cells on the fetal lung and systemic immune responses to intra-amniotic injection of lipopolysaccharide (LPS) in sheep.

Index: Inflammation, stem cells, fetus

THEME: FETAL & NEONATAL HEALTH

Early Life Immunisation and Cardiovascular Disease

Suitability: Honours
Location: The Ritchie Centre, Level 5, B Block, Monash Medical Centre, Clayton
Project Leaders: A/Prof Tim Moss, Prof David Burgner (MCRI)
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Phone: 03 9594 5392 (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. In humans, mycobacterial infections, including tuberculosis, are associated with elevated rates of atherosclerosis. In rabbits fed a high fat diet, administration of the BCG vaccine against tuberculosis worsens atherosclerosis. A recent study in mice, however, suggests that early life BCG vaccination may protect against the development of atherosclerosis.

The BCG vaccine is administered routinely worldwide to infants at risk of contracting tuberculosis. The effect of this procedure on development of atherosclerosis is unknown. While data from adult humans and rabbit experiments suggest that BCG vaccine might accelerate the progression of atherosclerosis, it is possible that administration early in life might be protective.
The aim of this project is to determine the effect of BCG vaccination on the development of atherosclerosis in mice predisposed to development of vascular disease.

Index: Inflammation, cardiovascular

Developing a Model of Cerebral Palsy for Rapid Clinical Translation of Therapies

Suitability: Honours/PhD
Location: The Ritchie Centre, Level 5, B Block, Monash Medical Centre, Clayton & the Australian Primate Facility, Monash University Churchill Campus.
Project Leaders: Dr Graeme Polglase, A/Prof Tim Moss, Dr Mary Tolcos
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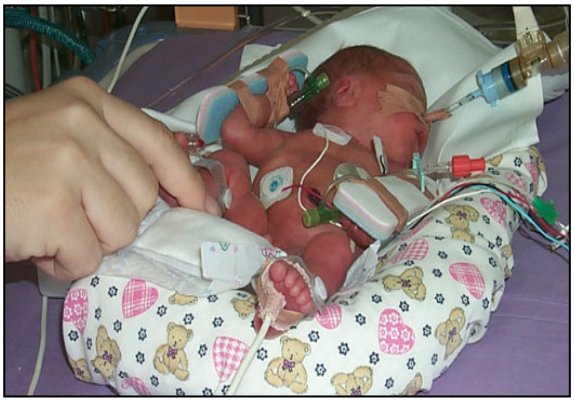
Phone: 03 9594 5675 (Dr Polglase)

Project description: Cerebral Palsy is a major complication of preterm birth, with 10% of infants born <30 weeks gestation being diagnosed. Exposure to inflammation within the womb is one of the main known causes of cerebral palsy. There are many antenatal therapies, including stem cells, melatonin and erythropoietin, that may prevent brain damage in preterm infants exposed to inflammation within the womb. However, current animal models are unsuitable for rapid translation of treatments into clinical practice, due to species differences in brain development. This project is aimed at developing a primate model of cerebral palsy, using first-world primates. We will assess the effect of inflammation on cardiovascular and brain inflammation and injury.

Index: Neurodevelopment, inflammation, cardiovascular



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THEME: FETAL & NEONATAL HEALTH

Protecting the Brain from Injury at Preterm Delivery

Suitability: Honours/PhD
Location: The Ritchie Centre, Level 5, B Block, Monash Medical Centre, Clayton
Project Leaders: Dr Graeme Polglase, Dr Kelly Crossley
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Phone: 03 9594 5675 (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.

Index: Circulation, cardiovascular, preterm birth

How Does the Fetal Cerebral Cortex Fold?

Suitability: Honours, PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Mary Tolcos, Prof David Walker, Dr Joanne Britto (Florey Neuroscience Institute)
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Phone: 03 9594 5379 (Dr Tolcos)

Project Description: The cerebral cortex is involved in high-level cognitive functions and intelligence. During normal brain development the growth of the cortex is accompanied by the onset of surface folding to produce sulci (grooves) and gyri (ridges). Brain folding is disturbed by premature birth, fetal hypoxia, and alcohol consumption during pregnancy but how these factors interfere with cortical development is unknown. This study will combine large animal surgery, immunohistochemistry, and nerve fiber tracing with MRI, to better understand cortical folding in the fetal brain following normal and abnormal pregnancies.

Index: Brain development, brain folding, fetal brain injury

Effects of Intrauterine Growth Restriction on Cortical Laminar Development: Relevance to Autism

Suitability: Honours
Location: Level 5, Monash Medical Centre, Clayton
Project Leader: Dr Mary Tolcos
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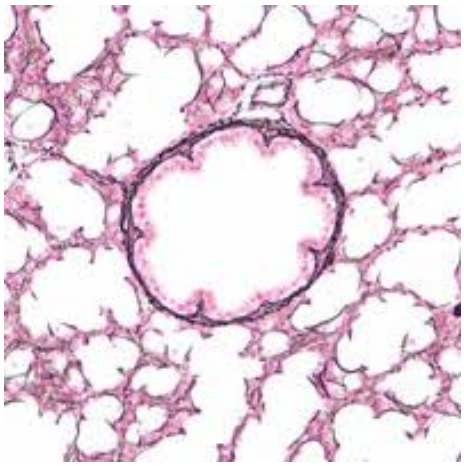
Phone: 03 9594 5379 (Dr Tolcos)

Project Description: Babies born intrauterine growth restricted (IUGR) have an increased risk of developing autism later in life. Recent evidence now suggests that cortical layering is disrupted in autistic brains and that this accounts for abnormal functioning of the brain. It is also thought that these changes manifest in fetal life. We have a rodent model of IUGR, where the brain, although spared relative to other organs, is still retarded in growth and development. The aim of this project is to assess layering of the cerebral cortex in control and IUGR fetuses. This project will combine paraffin sectioning, histology, immunohistochemistry and image analysis.

Index: Intrauterine growth restriction, brain development, autism



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THEME: FETAL & NEONATAL HEALTH

Investigating the Effects of Sustained High Dose Caffeine Treatment on the Development of the Cerebellum

Suitability: Honours
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Mary Tolcos, Dr Robert De Matteo
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Project Description: Babies born premature often develop apnoea of prematurity (AOP), a condition where breathing ceases for up to 20 seconds. AOP is treated with caffeine, however if apnoea continues, clinicians will often use higher doses. However it is not known what high doses of caffeine may be doing to the developing brain. This project will use an ovine model to determine the effects of high dose chronic caffeine exposure on the developing cerebellum in the short-term. This project will combine brain histology, immunohistochemistry, image analysis, immunofluorescence, and confocal microscopy.

Index: Perinatal brain injury, preterm, brain development

Cerebellar Development Following Fetal Inflammation: Is Erythropoietin Neuroprotective?

Suitability: Honours
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Mary Tolcos, Dr Annie McDougall
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Phone: 03 9594 5379 (Dr Tolcos)

Project Description: Erythropoietin (EPO) is a naturally occurring hormone that controls erythropoiesis. EPO also prevents brain injury and promotes brain repair in preterm and term infants. In 2010 we published a paper to show that EPO prevents brain injury in the fetal sheep brain following the induction of inflammation using the endotoxin LPS. Specifically, we found EPO prevented lesions in the white matter, a pathology commonly seen in babies with cerebral palsy. The development of the cerebellum is also disrupted following fetal inflammation. The aim of this project is to determine whether EPO can protect against impaired cerebellar development following fetal inflammation. This project will combine paraffin sectioning, histology, immunohistochemistry and image analysis.

Index: Fetal inflammation, perinatal brain injury, neuroprotection

Investigating the Effects of Fetal Hypoxia on Hippocampal Neurogenesis

Suitability: Honours
Location: Level 5, Monash Medical Centre, Clayton
Project Leader: Dr Mary Tolcos
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Phone: 03 9594 5379 (Dr Tolcos)

Project Description: Lack of oxygen to the fetal brain during pregnancy is one of the main causes of brain injury in newborns. Some of these infants will suffer neurodevelopmental and behavioural problems including decreased intelligence and cognition, learning difficulties, poor memory and attention deficits. It is likely that these deficits are associated with neuronal alterations in the hippocampus. This project will investigate the effect of fetal hypoxia on neurogenesis and cell death in the hippocampus using an array of techniques including brain histology, immunohistochemistry, image analysis, immunofluorescence, and confocal microscopy.

Index: Perinatal brain injury, fetal hypoxia, neurogenesis

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THEME: FETAL & NEONATAL HEALTH

Regulation of Myelination in Brain of the Growth Restricted Fetus: Identification of Targets and Potential Therapies

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Mary Tolcos, Prof David Walker
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Phone: 03 9594 5379 (Dr Tolcos)

Project Description: Intrauterine growth restricted (IUGR) babies are often born with brain damage, and then grow up with disabilities such as cerebral palsy and/or learning and behavioural problems. This project will study the impact of IUGR on the developing oligodendrocyte, the cell responsible for myelin formation in the brain. We propose that the mechanisms which control oligodendrocyte development are impaired and that these mechanisms can be targeted therapeutically to promote myelination in the IUGR brain. This project combines small animal surgery, brain histology, immunohistochemistry, western blot analysis and qPCR.

Index: Perinatal brain injury, growth restriction, myelination

Erythropoietin as a Protective and Reparative Therapy for Brain Injury in the IUGR Fetus

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Mary Tolcos, Dr Graeme Polglase.
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Phone: 03 9594 5379 (Dr Tolcos)

Project Description: Erythropoietin (EPO) has been shown to be neuroprotective in numerous preclinical animal models of perinatal brain injury and is currently being trialed for use in term and preterm babies with hypoxic-ischemic brain injury. However, there is no study examining EPOs neuroprotective potential in a model of brain injury associated with fetal growth restriction – one of the most well-recognised causes of perinatal brain injury. This project aims to show that administration of EPO to growth-restricted fetuses in utero can prevent the establishment of brain injury. It will combine large animal surgery, fetal physiology, brain histology, immunohistochemistry, western blot analysis and qPCR.

Index: Perinatal brain injury, growth restriction, neuroprotection

THEME: INFANT & CHILD HEALTH

Postnatal Consequences of Intrauterine Growth Restriction on Cardiovascular Control During Sleep in Infants

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Stephanie Yiallourou, Prof Rosemary Horne
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Phone: 03 9594 5100 (Prof Horne)

Project Description: Intrauterine growth restriction (IUGR) has been associated with increased risk of hypertension later in life. The causes of this increased susceptibility remain unclear, however impaired autonomic cardiovascular control may play a role. Autonomic control undergoes dramatic maturational changes within the first 6 months of life which can be assessed during sleep in infants. To date there has been no description of the consequences of IUGR on the maturation of cardiovascular control within this window of maturation. In these novel studies we will utilise clinical sleep studies to examine the effects IUGR on cardiovascular control within the first 6 mo of life in an effort to identify underlying mechanism/s that contribute to cardiovascular complications later in life.

Index: Infant, Sleep, Intrauterine growth restriction, blood pressure

Understanding the Relationship Between Childhood Obesity and Obstructive Sleep Apnoea

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 9594 5100 (Prof Horne)

Project Description: Childhood obesity is reaching epidemic proportions in Western societies, with 1 in 4 Australian children being either overweight or obese. While obesity is well recognised as the primary cause of obstructive sleep apnoea (OSA) in adults, the relationship between the two disorders is less straightforward in childhood. In children, airway obstruction results primarily from enlarged adenoids and tonsils. With the rise in childhood obesity, however, more children are being seen clinically in whom obesity could significantly contribute to OSA, but the extent of this contribution is unclear. This study will answer important clinical questions. Does the added burden of OSA worsen any existing adverse cardiovascular or psychological outcomes in children with obesity? What factors are associated with a higher risk of OSA in obese children? The study involves polysomnography and MRI in obese and control children.

Index: Sleep, children, obesity

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
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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 2015 we will be testing the new tool for usability and accuracy. Is it helpful for GPs, ENT surgeons and paediatricians at the coal face?

Index: Sleep, children

Executive Function and Frontal Lobe Activity in Children with Sleep Disorders

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Prof Rosemary Horne, Dr Sarah Biggs
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Phone: 03 9594 5100 (Prof Horne)

Project Description: Research by our group has revealed that sleep disorders are associated with deficits in executive function, in particular working memory and planning ability. Debate exists as to whether the mechanism for executive function deficit is due to neurological changes in frontal lobe function or is a symptom of daytime sleepiness caused by disrupted sleep. This study will examine executive function and sleep-related frontal lobe activity in children with sleep disorders and for the first time provide objective evidence as to the association between frontal lobe activity during sleep and executive function in children.

Index: Children, sleep disorders, brain activity, executive function

THEME: INFANT & CHILD HEALTH

Long-Term Consequences of Intrauterine Growth Restriction on Cardiovascular Control and Function

Suitability: Honours/ PhD

Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: Dr Stephanie Yiallourou, Prof Rosemary Horne
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Phone: 03 9594 5399 (Dr Yiallourou), 03 9594 5100 (Prof Horne)

Project Description: Intrauterine growth restriction (IUGR) is associated with significantly increased risk of cardiovascular morbidity and mortality in adulthood. Despite these epidemiological findings, as yet we do not fully understand the mechanism(s) linking IUGR to later cardiovascular morbidity, or indeed which babies are most at risk. There is now strong evidence to suggest that cardiovascular dysfunction that occurs in utero in the IUGR fetus persists after birth. To date, long-term cardiovascular control and function has not been assessed in severe IUGR. In a cohort of children who were born with severe IUGR (ages 5 to 12) this study will utilise state of the art physiological recording to assess 1) autonomic cardiovascular control during sleep 2) vascular stiffness and 3) cardiac structure and function. This study will involve performing overnight polysolmnography, applanation tonometry and echocardiography. Findings from this study will determine the long-term cardiovascular outcomes in children born with severe IUGR. Early identification of cardiovascular dysfunction in children born IUGR may allow targeted interventions that offer the prospect of significantly better life-long health outcomes.

Index: Children, sleep, intrauterine growth restriction, cardiovascular function

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, A/Prof Philip Berger
Email: kenneth.tan@monash.edu, philip.berger@monash.edu
Phone: 03 9594 5191 (Dr Tan), 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 administration which often leads to a 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.

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 and could take part in adult human and infant studies conducted by Dr Berger's team from the Ritchie Centre. This is part of the group's work on automated oxygen delivery to preterm infants.

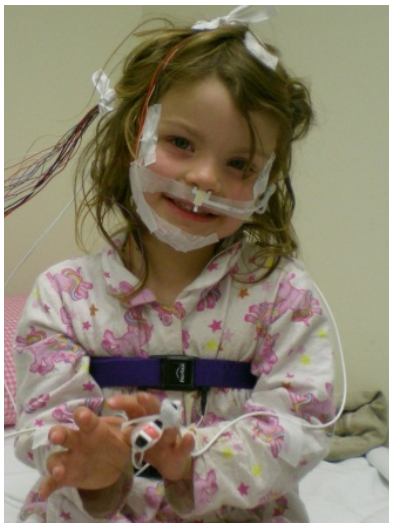
Index: Respiratory distress, oxygenation, hypoxia, hyperoxia, oxygen delivery

Sleep 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@monash.edu
Phone: 03 9594 5474 (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, and yet current research investigating the prevention and treatment of sleep disorders in children with cancer is sadly lacking. This study will examine sleep in children with cancer during the year following completion of treatment, utilizing actigraphy and validated questionnaires to provide a sound basis for clinical intervention to improve the quality of life of these children.

Index: Children, cancer, sleep



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THEME: INFANT & 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.

Index: Epidemiology; communicable disease surveillance; vaccine safety

NOTWATCH: 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.

Index: Epidemiology; communicable disease surveillance; clinician education

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THEME: CELL THERAPY & REGENERATIVE MEDICINE

Do Cord Blood Stem Cells Reduce Brain Injury After Birth Asphyxia?

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton, & Large Animal Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Suzie Miller, Prof Graham Jenkin
Email: suzie.miller@monash.edu, graham.jenkin@monash.edu
Phone: 03 9902 4795 (Dr Miller), 03 9902 4736 (Prof Jenkin)

Project Description: 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 plan to undertake a project that will directly address the question of whether cord blood stem cells reduce perinatal brain injury, caused by a severe asphyxic event at birth, and the mechanisms of protection. This project will utilise our established term lamb model of birth asphyxia, with state-of-the-art neonatal care and magnetic resonance imaging to track the cells.

Index: Perinatal brain injury, stem cells, newborn lambs

Novel Treatments for Preterm Brain Injury (2)

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton & Large Animal Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Suzie Miller, Prof Graham Jenkin, Dr Margie Zakhem, Dr Tamara Yawno, Dr Beth Allison
Email: suzie.miller@monash.edu, graham.jenkin@monash.edu
Phone: 03 9902 4795 (Dr Miller), 03 9902 4736 (Prof Jenkin)

Project Description: In Australia, a baby is born with the brain injury that underlies cerebral palsy every 15 hours. Improvements in newborn care mean that most babies that are born preterm will survive, but prematurity remains linked to cerebral palsy. Although umbilical cord blood derived stem cells are being used to treat cerebral palsy, there is currently insufficient evidence that such treatment will improve the underlying brain injury. This project will examine whether melatonin, a free radical scavenger, steroid derived neuroprotectants and/or umbilical cord blood stem cells can reduce brain damage caused by preterm lack of oxygen. Treatments will be administered to preterm (fetal) lambs following hypoxia. The active constituents of cord blood will also be investigated in vivo and in vitro.

Index: Prematurity, cerebral palsy, stem cells

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

Suitability: Honours
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Dr Courtney McDonald, Dr Chris Siatskas, Prof Graham Jenkin
Email: graham.jenkin@monash.edu
Phone: 03 9902 4736 (Prof Jenkin)

Project Description: Umbilical cord blood and the umbilical cord are a recognised source of mesenchymal stem cells and the cord is lined by amnion epithelial cells, which have the potential to differentiate into a wide range of cell types and are also potently 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.

Index: Stem cell isolation and storage, regenerative medicine

Tracking Stem Cells In Vivo in Regenerative Medicine

Suitability: Honours
Location: Monash Biomedical Imaging, Clayton & MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Dr Courtney McDonald, Prof Graham Jenkin, Dr Tony Goldschlager
Email: graham.jenkin@monash.edu
Phone: 03 9902 4736 (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.

Index: Cell tracking, stem cells, regenerative medicine

THEME: CELL THERAPY & REGENERATIVE MEDICINE

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

Suitability: Honours
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Dr Abhilasha Tiwari, Dr Chris Siatskas, Prof Graham Jenkin, Dr Courtney McDonald, A/Prof Mark Kirkland (Deakin University)
Email: graham.jenkin@monash.edu
Phone: 03 9902 4736 (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.

Index: Stem cell isolation and expansion, regenerative medicine

Treatment of Cystic Fibrosis with Stem Cells

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Dr Rebecca Lim, Prof Euan Wallace, Prof Graham Jenkin
Email: rebecca.lim@monash.edu
Phone: 03 99024775 (Dr Lim)

Project Description: There is a dire need for a cell type therapy to replace dysfunctional lung epithelial cells in patients with cystic fibrosis. We aim to produce functional lung epithelial cells from placental stem cells or by iPS derived cells using synthetic mRNA technology. We will utilize a novel method of delivering these cells into the lungs of mouse or sheep models of cystic fibrosis to incorporating the functional lung epithelial cells into the respiratory conducting airway and the lung. We will track placental stem cell-derived lung epithelial cells in the lung using novel Imaging techniques and assess their effectiveness in repairing lung function of mice with cystic fibrosis.

Index: Cystic fibrosis, amnion stem cells, iPS

Human Amnion Epithelial Cells as Therapy for Lung Inflammation in Preterm Newborns

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton & Level 5, Monash Medical Centre, Clayton
Project Leaders: A/Prof Tim Moss, Prof Graham Jenkin, Prof Euan Wallace
Email: graham.jenkin@monash.edu
Phone: 03 9902 4736 (Prof Jenkin)

Project Description: Bronchopulmonary dysplasia (BPD) is a life-threatening chronic lung disease that affects many infants born very preterm. Lung inflammation likely underlies the pathogenesis of BPD. Epithelial cells isolated from the amniotic membrane 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 amnion epithelial cells on inflammatory responses of newborn preterm lambs. The experiments include whole-animal physiology, immunology, microscopy and molecular biology techniques.

Index: Bronchopulmonary dysplasia, newborn lung disease, amnion stem cells

Do Cord Blood Stem Cells Reduce Brain Injury After Birth Asphyxia?

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton &Large Animal Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Suzie Miller, Prof Graham Jenkin
Email: suzie.miller@monash.edu, graham.jenkin@monash.edu
Phone: 03 9902 4795 (Dr Miller), 03 9902 4736 (Prof Jenkin)

Project Description: 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 plan to undertake a project that will directly address the question of whether cord blood stem cells reduce perinatal brain injury, caused by a severe asphyxic event at birth, and the mechanisms of protection. This project will utilise our established term lamb model of birth asphyxia, with state-of-the-art neonatal care and magnetic resonance imaging to track the cells.

Index: Perinatal brain injury, stem cells, newborn lambs

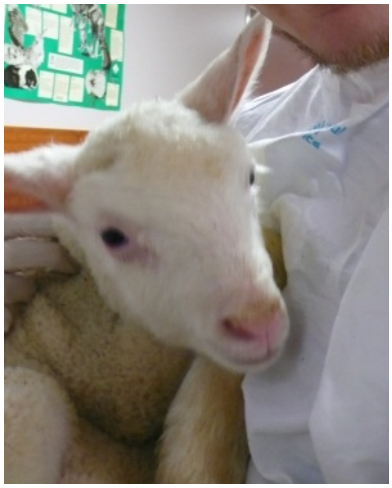
THEME: CELL THERAPY & REGENERATIVE MEDICINE

Isolation and Banking of Placental Tissues for Future Clinical Therapies

Suitability: Honours
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Prof Graham Jenkin, Dr Courtney McDonald
Email: graham.jenkin@monash.edu
Phone: 03 9902 4736 (Prof Jenkin)

Project Description: The umbilical cord is a recognised source of Mesenchymal Stem Cells and is lined by Amnion Epithelial Cells, which have the potential to differentiate into a wide range of cell types and are also potently immunomodulatory and anti-inflammatory. The use of these cells are being explored in a number of therapeutic settings. This project, carried out in collaboration with Cell Care, will validate method for collection, processing, 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.

Index: Stem cell isolation and storage, regenerative medicine



Stem Cells and Tissue Scaffolds

Suitability: Honours/PhD
Location: Department of Surgery, Monash Medical Centre, Clayton & MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Dr Tony Goldschlager, Prof Graham Jenkin
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Phone: 03 9902 4736 (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.

Index: Cell tracking, stem cells, regenerative medicine

Tracking Human Amnion Epithelial Cells In Vivo in Regenerative Medicine

Suitability: Honours
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Prof Graham Jenkin, Prof Euan Wallace
Email: graham.jenkin@monash.edu
Phone: 03 9902 4736 (Prof Jenkin)

Project Description: We are exploring the use of human amnion epithelial cells (hAECs) and Mesenchymal Progenitor Cells (MPCs) as cellular regenerative therapy for a variety of diseases including bronchopulmonary dysplasia and chronic lung disease of the preterm infant and spinal disc repair. This project will utilise novel labeling techniques that will allow us to track the migration profile of stem cells in real-time.

Index: Cell tracking, stem cells, regenerative medicine

THEME: CELL THERAPY & REGENERATIVE MEDICINE

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 9902 4736 (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.

Index: Stem cell survey, pregnancy, baby health

A Model of Viral Illness in Pregnancy in the Spiny Mouse: The Possible Prenatal Origin of Mental Illness?

Suitability: Honours
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton
Project Leaders: Prof David Walker, Dr Hayley Dickinson, Dr Udani Ratnayake (Florey)
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Phone: 03 9594 5372 (Prof Walker)

Project Description: While the etiology of mental illnesses such as schizophrenia and autism remains unknown, many epidemiological and animal studies have identified a potential neurodevelopmental origin of these disorders. Our animal model, the precocial spiny mouse (*Acomys cahirinus*), is developmentally more advanced by term than conventional rodents, having largely completed organogenesis, and they are capable of coordinated motor activity and thermoregulation. The aim of this study is to determine if offspring born to pregnant spiny mice that are exposed to a prenatal infection show behavioural abnormalities which are comparable to symptoms of mental illness disorders such as schizophrenia and autism, as measured by a comprehensive battery of behavioural tests.

Index: Mental illness, spiny mice, prenatal infection

Activating the Stem Cell Niche

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton & Monash University, Clayton
Project Leaders: Dr Rebecca Lim, Prof Euan Wallace
Email: rebecca.lim@monash.edu
Phone: 03 99024775 (Dr Lim)

Project Description: Amnion stem cells have reparative potential in the lung. It is yet unknown how the amnion cells trigger the regenerative process to improve lung function. We will use an animal model to mimic bronchopulmonary dysplasia 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.

Index: Neonatal lung injury, stem cells, regenerative medicine

THEME: CELL THERAPY & REGENERATIVE MEDICINE

Understanding the Stem Cell Sheddome

Suitability: Honours/PhD
Location: MIMR-PHI Institute, Level 3, 27-31 Wright St, Clayton & Monash University, Clayton
Project Leader: Dr Rebecca Lim
Email: rebecca.lim@monash.edu
Phone: 03 9902 4775 (Dr Lim)

Project Description: Exosomes are nano-sized particles shed by cells. They contain bioactive cargo such as microRNAs and proteins, which can exert effects on specific tissues and cell types. This project looks to characterise the exosomes released by amnion stem cells 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, tissue culture, electron microscopy, molecular biology, real-time PCR and western blotting.

Index: Stem cells, regenerative medicine