HUDSON
INSTITUTE OF MEDICAL RESEARCH

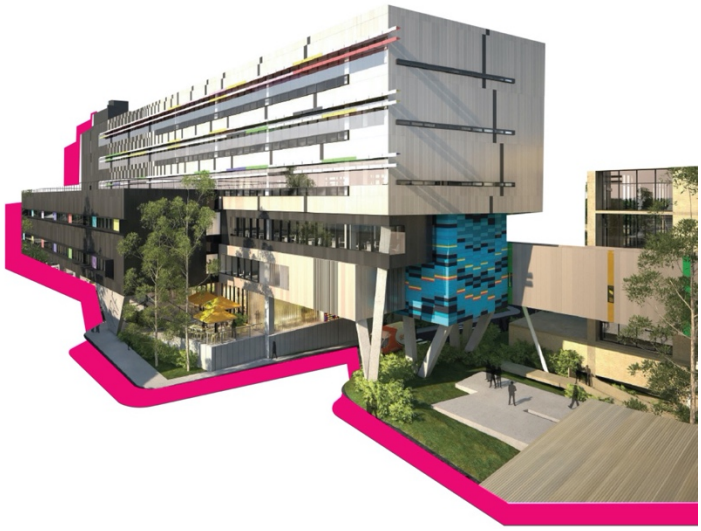
THE RITCHIE CENTRE

2021 Student Research Projects

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

Contents

Contents	**2**
Welcome to Hudson Institute	**3**
The Ritchie Centre	**4**
Women's Health	**5**
Fetal & Neonatal Health: Respiratory and Cardiovascular	**16**
Fetal & Neonatal Health: Brain Injury and Neurodevelopment	**20**
Infant and Child Health	**22**
Infection, Inflammation and Immunity	**23**
Cell therapy and regenerative medicine	**29**
Contact our supervisors	**38**



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

Welcome to Hudson Institute

Hudson Institute specialises in discoveries in four areas of medical need

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

Our 448 scientists and students focus on laboratory discovery science, plus translational research – taking discoveries to patients and industry for real-world impact.

296 STAFF

152 STUDENTS

50 RESEARCH GROUPS

283 RESEARCH PUBLICATIONS

Students at a glance 2019

58 POSTGRADUATE AND HONOURS STUDENTS COMPLETED

152 STUDENTS 113 PHD 4 MASTERS 35 HONOURS

28 STUDENTS WITH MEDICAL TRAINING

We educate and train more than 150 students through our academic affiliation with Monash University. Our postgraduate training is predominantly through the School of Clinical Sciences at Monash Health, part of the Faculty of Medicine, Nursing and Health Sciences at Monash University.

Our students

- Are exposed to university, institute and hospital research
- Attend national and international conferences
- Publish their research (there were 43 student first author publications in 2019)
- Are mentored by leading supervisors and their teams
- Regularly win prestigious prizes and awards
- Take part in regular networking and learning and development programs.

All work and no play …

Our students can join in a range of student networking and social events organised by Hudson Institute Student Society (HISS), including being part of the management committee.

Our precinct

Hudson Institute is a leading Australian medical research institute recognised internationally for discovery science and translational research into infant and child health, reproductive health and pregnancy, inflammation, and cancer.

Our Institute is home to 448 world-class scientists, who push the boundaries of scientific knowledge to answer complex questions about human disease, including prevention and treatment.

We are a founding member of the Monash Health Translation Precinct with partners Monash Health and Monash University. Our close ties with clinicians and industry enable us to translate our discoveries into new preventative approaches, therapies and devices for patients.

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

Working alongside clinicians in Melbourne hospitals for more than 50 years, our scientists pioneered IVF and stem cell discoveries and are now leading developments in cell therapies, paediatric cancer and the human microbiome. Our worldwide scientific and medical collaborations provide a foundation for transformative healthcare programs across the globe.

The Ritchie Centre

Location

Hudson Institute of Medical Research
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Centre Head

Professor Stuart Hooper

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

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

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

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

Research Groups Heads

Women's Health
Prof Caroline Gargett

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

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

Infant and Child Health
Prof Rosemary Horne

Cell Therapy & Regenerative Medicine
A/Prof Rebecca Lim

Women's Health

Characterising novel targets for the treatment of endometriosis

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

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

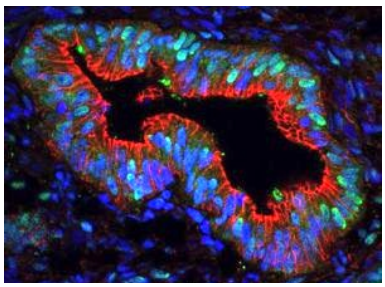
Interferon epsilon (IFNε) is a novel cytokine and immunomodulator that is constitutively expressed and only in the female reproductive tract (FRT) epithelium. IFNε exerts its protective effects in the FRT to prevent bacterial/viral infections and cancers. IFNε exerts a protective effect against the development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

Keywords: endometriosis; immune system; immunomodulation; endometrium; women's health; disease;

A novel non-invasive diagnostic for endometriosis/adenomyosis

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

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



Women's Health

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

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

Project Description: Pelvic organ prolapse (POP) is a debilitating condition affecting 1 in 4 women. It results from incomplete repair of pelvic tissues following vaginal birth which often progresses to POP years later. We are developing tissue engineering approaches using endometrial mesenchymal stem cells (eMSC) we discovered together with nan biomaterials to treat and prevent POP. As we prepare our eMSC for clinical translation, we need to ensure the novel culture methods we have developed are safe. This project will use integrated ATAC-seq (Assay for Transposase-Accessible Chromatin using sequencing) and RNA-seq in serum-free-culture media containing a unique small molecule inhibitor that keeps the eMSC in the undifferentiated state. This project will reveal the changes in the transcriptional landscape and gene pathways involved in maintaining eMSC self-renewal, the reversibility of this culture method and any oncogene activation, generating safety and mechanistic data for applying to regulatory authorities for licencing our eMSC product for clinical use in treating and preventing POP. This project has NHMRC funding and will provides an opportunity to develop skills in molecular sequencing, analysing vast quantities of data and interact with bioinformatician collaborators at Warwick University, UK. Other techniques are primary cell isolation, eMSC purification and culture, flow cytometry, PCR, cell proliferation and apoptosis assays.

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

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

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

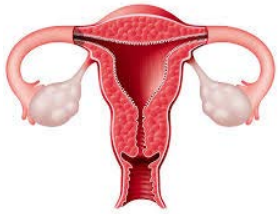
Project description:
Pelvic organ prolapse (POP) results from childbirth injury, affecting 25% of all women. It causes bladder, bowel and sexual dysfunction. POP is treated by surgery, frequently augmented by mesh, but failure and complication rates are high. We are investigating a regenerative medicine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

1. The first project looks at the foreign body response to implanted meshes in aged parous sheep

2. The second examines the effect of varying design aspects of 3D printing such as porosity, mesh fiber thickness etc on the surgical performance of meshes.

3. We are also examining the biomechanics of the tissues at the nanoscale using atomic force microscopy to understand the overall strength of the tissues after treatment.

Keywords:
3D Printing, Nanofabrication, Cell culture, Flow cytometry, histological, immunofluorescence and confocal microscopy, biochemical and biomechanical analyses will be undertaken. This project is supported by NHMRC funding



Women's Health

Decoding the significance of endometriosis risk

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

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

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

Endometrial organoids: novel tools for precision gynaecological medicine

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

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

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

Women's Health

Tissue clearing microscopy in endometrium and uterine fibroids

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

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

Methods: tissue preparation, two photon microscopy, light sheet microscopy, immunostainings (immunofluorescence), image analysis.
If no lab access can be granted because of COVID-19 lockdown measures, a systematic review of available studies will be carried out, and own data will be analysed.

Keywords: Imaging, tissue clearing microscopy, light sheet microscopy, immunofluorescence

Exosome population concordance within sample species

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

Project description: Exosomes are small, nanosized vesicles produced by most cells and readily found in bodily fluids which carry surface markers and genetic material from their cell of origin (Colombo 2014). This makes exosomes an attractive candidate diagnostic and therapeutic tool, and they have recently seen increased attention as potential biomarkers for diseases such as obesity and diabetes, pre-eclampsia, and cancer.

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

This project will investigate exosomes in uterine fluid and peritoneal fluid within the same patients in order to determine the potential for substitution of exosomes isolated from one or the other fluid as biomarkers. If available, blood samples will be added to the analysis, to compare exosomes found in circulation to the species found in uterine and peritoneal fluids.

Methods: Exosome isolation, ultracentrifugation, nanosight tracking analysis, immunoblotting, RNA extraction, proteomics, microarrays.
If no lab access can be granted because of COVID-19 lockdown measures, a systematic review of available studies will be carried out, and own data will be analysed.

Keywords: Exosomes, endometriosis, biomarkers.

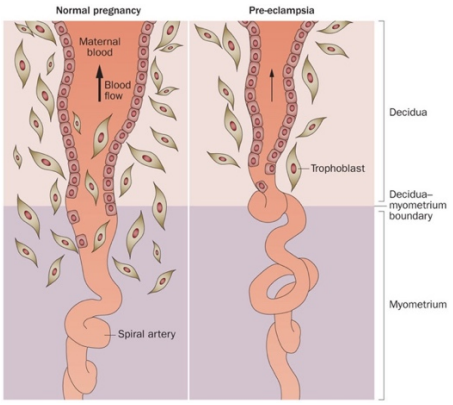
Women's Health

Assessing the Beneficial effects of Cruciferous Vegetable Extracts

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

Project description: Early in pregnancy, the maternal vasculature undergoes dramatic adaptations to help support both the mother and the developing baby throughout pregnancy. However, failure of the maternal vasculature to fully adapt can result in the pregnancy disease known as pre-eclampsia (PE). PE affects approximately 1/20 pregnancies and is a leading cause of maternal and foetal morbidity and mortality worldwide. Unfortunately, disease severity often results in premature babies. Recently, it has become apparent how important the maternal vasculature is for disease development, making it a target to alleviate the clinical symptoms of PE and prolong pregnancy. Cruciferous vegetables, such as broccoli, provide a variety of beneficial health effects. So far, evidence suggests that novel compounds found in green leafy vegetables may have beneficial affects throughout the body, including the vasculature. Therefore, this project aims to identify whether these extracts can promote systemic health and be potential novel treatments for women with pre-eclampsia.

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



Assessing survival and viability of human placental (trophoblast) cells

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

Project description: Preeclampsia is a pregnancy disorder characterised by hypertension with proteinuria, maternal organ dysfunction or fetal growth restriction. Each year preeclampsia is the cause of death in over 60,000 women and in more than 500,000 babies globally. The pathophysiological mechanisms underlying the disease are not entirely clear, however we do know that placental (trophoblast) cells are major contributors to this disorder. Therefore, the trophoblast cells of the placenta are very important research tools to help us better understand preeclampsia and to help us identify potential treatments for this disorder. This project will involve the collection and culturing of trophoblast cells from the placenta of women undergoing elective caesarean. Then, survival and viability of these cells will be assessed after treatment with new compounds that could be future treatments for preeclampsia

Key words: Pregnancy, preeclampsia, placenta, trophoblast, cell culture, novel treatment

Understanding drivers of stillbirth to inform prevention

Suitability: **Honours/PhD/Masters**
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leader: Dr Miranda Davies-Tuck
Email: *miranda.davis@hudson.org.au*

Description
This project seeks to uncover new drivers or stillbirth amenable to clinical practice change and assess the impacts of interventions.

Keywords
Stillbirth, maternal ethnicity, risk factors, clinical practice

Women's Health

Reducing stillbirth in Victoria

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

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

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

The impact of labour and birth factors on breastfeeding

Suitability: **Honours**
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leader: Dr Mary-Ann Davey, Dr Miranda Davies-Tuck
Email: *mary-ann.davey@monash.edu*

Description
Many women intend to breastfeed their baby but discontinue sooner than they wanted. A number of interventions in labour and birth are associated with early breastfeeding problems. This project will use routinely-collected, linked data to explore the impact up to 6 months of age.
Keywords
Perinatal breastfeeding intervention

Reducing preterm birth

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

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

Keywords: preterm, premature, perinatal, birth, pregnancy, labour, fetus, newborn, baby, paediatrics, obstetrics, NICU

Elective induction of labour and caesarean section – do we really have all the answers?

Suitability: **Honours/PhD**
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leader: Dr Mary-Ann Davey, Dr Miranda Davies-Tuck
Email: *mary-ann.davey@monash.edu*

Description
A recent publication on the relationship between induction of labour in uncomplicated pregnancies, and birth by caesarean section reports a lower caesarean rate in the induced group. This is likely to result in what has been described as an epidemic of induction. But what of the methodological shortcomings in this and other related research? This project will use routinely-collected data to replicate prior studies, and to re-analyse using methods to correct for problems in the initial studies.
Keywords
Induction, caesarean, low-risk pregnancy

Women's Health

New therapies for preeclampsia

Suitability: **Honours/PhD/Masters**
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leader: Prof Euan Wallace, Dr Kirsten Palmer, Dr Sarah Marshall, Dr Stacey Ellery
Email: *euan.wallace@monash.edu*

Description
Preeclampsia remains a major cause of maternal and perinatal mortality. No new treatments have been developed for over 50 years. Our group has been researching the origins and treatments of preeclampsia for over 20 years.

We have a major research program that includes drug discovery, ex-vivo models, animal models, clinical trials, and population and health service research. There are opportunities for science, medical, midwifery, and population health students in all aspects of our work.
Keywords
pregnancy, obstetrics, preeclampsia, hypertension, cardiovascular, laboratory, population, drugs, pharmacology, blood vessels, eclampsia, oxidative stress, endothelium, placenta

What do patients undergoing Assisted Reproductive Technologies (ART) know about their treatment

Suitability: **Honours**
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leader: Prof Ben Mol, Prof Luk Rombauts
Email: *ben.mol@monash.edu*

Description
In-vitro fertilisation (IVF) and other assisted reproductive technologies (ART) have revolutionised the treatment of infertility. This has led to increasing accessibility, particularly for high-resourced nations such as Australia. It is unknown whether couples who undergo IVF know exactly what the chances of their treatment are.

We plan to interview couples who went through IVF. We will ask whether they were informed upfront about their success changes, whether they were informed about complications, and whether they were informed about alternatives. As BMedSc student you will interview the couples and do a qualitative analysis of the interviews. We aim to interview about 50 couples.

Keywords
Obstetrics, Gynaecology, Women's Health, IVF, Assisted reproductive technology

Serum Markers in the Prediction of Complications in Pre-eclampsia

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

Description
Over the years there has been an observable trend of pre-term births – babies are being born further and further away from the 40-week mark. One of the reasons for this increasing disparity is the risk of complications arising from pre-eclampsia, leading to obstetricians tending toward the safer side, and hence initiating early caesareans.

You will be conducting a meta-analysis on the available evidence of serum biomarkers for the prediction of these complications, this will encompass an analysis of the various Randomised Clinical Trials, Case controls and prospective studies in the field. The review will be registered in PROSPERO. The research will focus on the simultaneous analysis of two variables to estimate sensitivity and specificity. You will be working closely with a PhD student and other members of the team working on original research in this field, combining your efforts and working together to achieve results.
Keywords
Obstetrics, Gynaecology, Women's Health, Pre-term birth, pre-eclampsia, biomarker, pregnancy-related complications

Women's Health

Individual patient data meta-analysis of studies on induction of labour

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

Description
Labour induction has now exceeded 20% of all births. Many different methods have been used, but prostaglandins remain a preferred method for cervical ripening and labour induction. Until now, published meta-analyses have focused on pair-wise 'head to head' comparisons. Individual Patient Data Meta-analysis (IPD-MA) can overcome these shortcomings We aim to compare, through IPD-MA, in women scheduled for induction of labour, vaginal misoprostol, oral misoprostol, Prostaglandin E2 and Foley catheter. We then will assess whether individual profiles of pregnant women can be used as treatment selection markers to identify the most effective preventive strategy for subgroups of women with a particular characteristic (nulli- versus multiparous, gestational age, BMI, reason for induction). The honours student will contact individual researchers around the world, collect data, clean data, perform analysis and report in a publication and at international conferences.

Keywords
Obstetrics, Gynaecology, Women's Health

Usefulness of clinical research in Obstetrics & Gynaecology

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

Description
Blue-sky research cannot be easily judged on the basis of practical impact, but clinical research is different and should be useful. It should make a difference for health and disease outcomes or should be undertaken with that as a realistic prospect. Ioannides showed that many studies, even in the major general medical journals, do not satisfy these features, and very few studies satisfy most or all of them. Most clinical research therefore fails to be useful not because of its findings but because of its design. In this project, we will assess the usefulness of clinical research in Women's health. We will study the problem base, context placement, information gain, pragmatism, patient centeredness, value for money, feasibility, and transparency of papers published in high ranked journals. This information could fuel an altered approach which could easily produce more clinical research that is useful, at the same or even at a massively reduced cost. Ioannidis JPA (2016) Why Most Clinical Research Is Not Useful. PLoS Med 13(6): e1002049. doi:10.1371/journal.pmed.1002049

Keywords
Obstetrics, Gynaecology, Women's Health

Women's Health

Assessing the implementation of telehealth consultations in maternity care on maternal and perinatal outcomes

Suitability: **Honours/PhD**
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leader: Dr Kirsten Palmer, A/Prof Ryan Hodges
Email: *Kirsten.palmer@monash.edu*

Description
In response to the SARS-COV-2 pandemic, many changes in the delivery of medical care changed to minimise the risk to both staff and patients through introducing physical distancing measures. One such change was the widespread implementation of telehealth for the delivery of antenatal care. Limited evidence exists regarding the use of telehealth for antenatal care. and whether it may impact pregnancy outcomes.

New model of care guidelines for the use of telehealth in maternity care, aimed for a reduction in face to face consults of up to 70%. Telehealth consults are limited by the inability to conduct physical examinations, so a number of adjunct measures were introduced to support blood pressure checks and assessment of fetal growth.

This research will assess the use of telehealth in maternity care at Monash Health, particularly the impact on face to face visit numbers, rate of pregnancy complications, such as pre-eclampsia and fetal growth restriction, as well as a composite of severe adverse maternal and perinatal outcomes.

This information will assist in informing the ongoing use of telehealth in the delivery of maternity care at Monash Health following the SARS-COV-2 pandemic.

Keywords
Telehealth; Obstetrics; Antenatal Care; Maternity

Assessing the implementation of modified gestational diabetes screening in maternity care during the SARS-COV-2 pandemic on pregnancy outcomes

Suitability: **Honours/PhD**
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leader: Dr Kirsten Palmer, Prof Ben Mol
Email: *Kirsten.palmer@monash.edu*

Description
In response to the SARS-COV-2 pandemic, many changes in the delivery of medical care changed to minimise the risk to both staff and patients through introducing physical distancing measures. Typically, all women during pregnancy will undergo an oral glucose tolerance test (OGTT) between 24-28 weeks' gestation to determine whether their pregnancy has been complicated by gestational diabetes (GDM).

However, the OGTT test requires 3 blood samples to be collected over a period of 2 hours within a pathology centre. With the introduction of physical distancing measures to minimise the risk to both staff and patients of contracting COVID-19, the screening protocol for GDM was modified to minimise the number of women undergoing an OGTT. Prior to the SARS-COV-2 pandemic OGTT screening resulted in ~13% of pregnant women being diagnosed with GDM.

This research project will assess whether the implementation of a modified GDM screening program has impacted on the rates of pregnancies diagnosed with GDM, as well as the impact on pregnancy outcomes, such as induction of labour, gestation at birth, fetal macrosomia, caesarean section rates for failure to progress, birth trauma and neonatal hypoglycaemia.

This information will assist in informing the ongoing use of a modified GDM screening program in maternity care at Monash Health following the SARS-COV-2 pandemic.

Keywords
Obstetrics; Antenatal Care; Maternity; Gestational Diabetes; Diagnosis; Screening

Women's Health

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

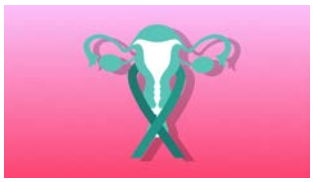
Suitability: **Honours/BMedSc**
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leader: Prof Ben Mol, Dr Wentao Li
Email: *ben.mol@monash.edu*

Description
Randomized controlled trials (RCTs) provide the most reliable information to guide clinical practice. We regrettably came across a number of RCTs concerning important clinical topics published in top rank journals having critical issues with respect to randomization, analysis, reporting, and feasibility.

In the view of the rapidly growing number of RCTs and a high proportion of RCTs yielding positive findings, it is critical to ensure the quality and data integrity of RCTs. However, little attempts have been made to systematically evaluate the quality of published RCTs.

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

Keywords
Randomised controlled trials, systematic review, data integrity, quality assessment



Quality of care for cervical and ovarian cancers in Australia

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

Description
Cervical and ovarian cancers are the most common gynaecological cancers locally and globally. Despite the large number of patients, the quality of care for these cancers has remained unexamined in Australia. Quality of care or efficiency and effectiveness of care could help minimize disease aggravation, thus improving treatment outcome as well as quality of life for patients. There have been guidelines regarding the management of gynaecological cancers to promote standardized high-quality care. To ensure that all patients receive high-quality care, it is thus imperative to evaluate the adherence of treatment centres to the recommendations outlined in these clinical guidelines.

We are going to use a registry quality dataset which recorded treatment information of all patients who underwent consultation and anti-cancer treatment in Monash Health between 2012 and 2017 to evaluate the adherence to clinical guidelines. We aim to propose a set of quality indicators based on the clinical guidelines for cervical and ovarian cancer treatment and to assess adherence to standard-of-care as an index of the quality of care in Monash Health.

This study requires a basic understanding of gynaecological cancers and evidence-based medicine. After completing this project, the student(s) is expected to have an in-depth knowledge of data analysis and the management of gynaecological cancers

Keywords
gynaecology, cervical and ovarian cancer, oncology, quality of care

Women's Health

Reporting of non-inferiority trials in reproductive medicine

Suitability: **Honours**
Location: Department of Obstetrics & Gynaecology, Level 5, Monash Medical Centre, Clayton
Project Leader: Prof Ben Mol, Dr Rui Wang
Email: *ben.mol@monash.edu*

Description
A non-inferiority trial aims to evaluate whether a new treatment is not worse than a standard treatment by more than an acceptable amount, while the new treatment has other advantages, such as greater availability, less expensive, less invasive and/or fewer side effects. Non-inferiority trials require more care on the design, analyse and report. Poor conduct and reporting could be associated with misleading conclusions, resulting in research waste and misguidance of clinical practice.

In reproductive medicine, non-inferiority trials are frequently used to assess new treatment strategies. In this project, the candidate will systematically search and critically appraise the reporting of published non-inferiority trials in reproductive medicine.

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

Exploring the role of VR in pain relief post laparoscopy

Suitability: PhD/Masters by research
Location: Department of Obstetrics and Gynaecology, Monash Medical Centre, Moorabbin Hospital.
Project Leaders: Prof Beverley Vollenhoven, Dr Vinayak Smith, A/Prof Jim Tsaltas.
Email: Vinayak.Smith@monash.edu

Project Description: Laparoscopy is a minimally invasive surgery that is commonly performed for gynaecological conditions. However, following this procedure a large percentage of patients still report severe pain despite the use of opioid analgesics. As such, adjunct therapies are necessary to bridge the gap in post-operative pain management.

Virtual reality (VR) is a technological medium that has the potential to address the current shortcomings in pain management. Through multisensorial stimulation, VR allows users to be immersed in and interact with a virtual environment. As it stands, VR has demonstrated clinical efficacy in pain reduction in various fields of medicine. However, it is yet to be proven post-operatively.

This research project will involve conducting a randomised controlled trial comparing the effect of VR as an analgesic to standard care following gynaecological laparoscopy. This study will have ethical approval prior to commencement.

Key words: Gynaecology, Laparoscopy, Post-operative pain, Virtual reality (VR), adjunct analgesia, randomised controlled trial.

Fetal & Neonatal Health: Respiratory and Cardiovascular

Transition to Life After Birth

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

Project Description: The transition to life after birth is one of the greatest physiological challenges that humans face. At birth, the airways are cleared of liquid, to allow the entry of air, which increases pulmonary blood flow and closes vascular shunts that 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

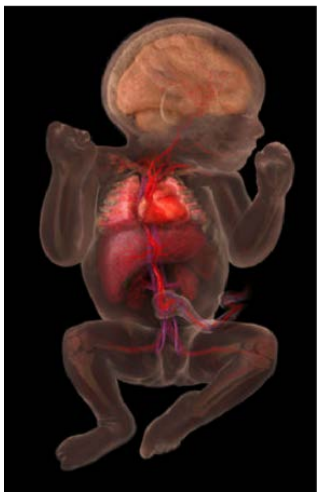
Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Stuart Hooper, Dr Erin McGillick
Email: *erin.ncgillick@hudson.org.au*

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

What role does the uterine environment have in 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: Dr Beth Allison, A/Prof Graeme Polglase, Prof Suzie Miller
Email: beth.allison@hudson.org.au
Phone: 03 8572 2488 (Dr Allison)

Project Description: Cardiovascular disease is one of the leading killers in the developed world. It is well accepted that growth restriction during gestation increases the risk of the offspring to develop cardiovascular disease as they age. Growth restriction occurs mainly through reduced placental function. The fetus adapts to the reduced placental function to maximise survival, unfortunately these adaptations impact on the development, and lifelong function of many organ systems. This project will aim to determine what impact this insult has on the cardiovascular system before and after birth, as well as in infancy. We plan to use investigate both common and novel blood pressure therapy. In this project we will be using an array of techniques including real-time PCR, histology, immunohistochemistry and image analysis.



Fetal & Neonatal Health: Respiratory and Cardiovascular

Improving breathing of preterm newborns exposed to inflammation during pregnancy

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

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

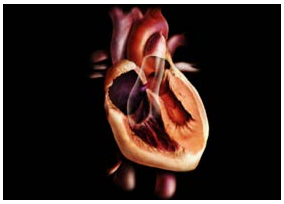
Our current research focuses on how intrauterine infection and inflammation (chorioamnionitis) affects the neural control of respiration, and whether anti-inflammatory treatments can protect these nerves and improve fetal and neonatal breathing. This project involves work with small and large animal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

Improving the transition at birth in asphyxiated infants

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

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

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



Fetal & Neonatal Health: Respiratory and Cardiovascular

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

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

Project Description: There is no appropriate algorithm for neonatal emergencies that occur in the neonatal intensive care unit (NICU). NeoResus, and other neonatal resuscitation guidelines, cover management at birth, as the newborn initiates breathing air. However, this is only relevant for the first minutes after birth and there is little data and guidance of what are the common emergencies in the NICU and how we should respond. The paediatric advanced lifesaving algorithms are not likely relevant to the hospitalised neonate, either.

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

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

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

Project Description: Is the initial assessment of premature baby accurate, specifically tone? This is an observational study using videos of very premature infants from the "Nasal versus facemask CPAP for initial respiratory support in very term infants, an RCT," to test tone as a signal for respiratory effort and spontaneous breathing.

Facemask CPAP has a high risk of failure in the delivery room because the technique is difficult and pressure to the newborn's face may cause apnea, vocal cord closure, and bradycardia.

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

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

We will create a focused 30 second, blinded clip of the baby immediately after being placed on the resuscitation table. Blinded assessors rate the baby's tone as 0, 1, or 2. Three groups of preterm infants are created and outcomes are measured: initial HR, initial SpO2, need for PPV, maximum oxygen, maximum PIP, DR intubation, surfactant, etc. This RCT was approved during stage 4 COVID restrictions and will commence September 2020. Prospective students will also help recruit and enrol patients in the RCT and be exposed to neonatal intensive care, joining rounds and teaching sessions as appropriate.

Keywords: neonatal resuscitation, apnea, respiratory drive, positive pressure ventilation (PPV), continuous positive airway pressure (CPAP), video review

Fetal & Neonatal Health: Respiratory and Cardiovascular

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

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

Project Description: This project focuses on congenital diaphragmatic hernia (CDH), a birth defect characterised by a failed closure of the diaphragm, creating a continuity between the thoracic and abdominal cavities. As a result, there is displacement of abdominal organs into the chest and this limits the space for the lungs to develop in the fetus. This leads to small lungs with abnormal airways and vessels, a condition called lung hypoplasia.

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

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

Evaluating the outcomes of undergraduate medical and biomedical student research

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

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

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

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

Fetal & Neonatal Health: Brain Injury and Neurodevelopment

Using heart rate variability to predict clinical disease in preterm babies

Suitability: Honours/PhD
Location: Level 5, Monash Medical Centre, Clayton
Project Leaders: A/Prof Flora Wong, Prof Rosemary Horne, Dr Stephanie Yiallourou
Email: *flora.wong@monash.edu*
Phone: 03 85723655 (A/Prof Wong)

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

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

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

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

Ganaxolone: A New Treatment for Neonatal Seizures

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Tamara Yawno, Prof Suzie Miller, Dr Michael Fahey
Email : *tamara.yawno@hudson.org.au, suzie.miller@monash.edu, michael.fahey@monash.edu*
Phone: 03 8572 2796 (Prof Miller)

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

Keywords: ganaxolone, neonatal seizures, brain injury, new born, brain activity.

Fetal & Neonatal Health: Brain Injury and Neurodevelopment

Improving functional deficits associated with fetal growth restriction

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Suzie Miller, Dr Amy Sutherland
Email: *suzie.miller@monash.edu*
Phone: 03 8572 2796 (Prof Miller)

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

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

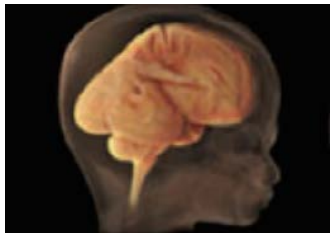
Treatments of interest include anti-oxidants, anti-inflammatory compounds, and cord blood stem cells. We will apply complimentary assessments of brain structure and function to test the efficacy of our neuroprotective treatments of interest.

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

Developing 3D brain organoids to model perinatal brain injury

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

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



Infant and Child Health

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

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

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

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

Interprofessional simulation-based education

Suitability: Honours/PhD
Location: Department of Paediatrics, Level 5 Monash Children's Hospital
Project Leaders: Dr Atul Malhotra, Dr Arunaz Kumar
Email: *atul.malhotra@hudson.org.au*

Project Description: Opportunities exist to be part of Monash Children's Simulation Centre, which is co-chaired by Dr Malhotra. Evaluation of ongoing and new interprofessional education workshops will be involved in the research.

Monash Newborn
Handled with Care

Obstructive sleep apnoea in children with Down syndrome

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

Project Description: 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

Infant and Child Health

Understanding ventilatory control in children with Prader Willi Syndrome

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

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

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

Keywords: sleep, children, paediatrics, control of breathing

Cerebral oxygenation in preterm babies in the neonatal intensive care unit

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

Description
Preterm infants are at high risk of brain injury, mainly due to low blood flow and oxygenation in the brain. With this project we aim to assess the impact of various physiological and environmental factors on brain oxygenation level in the very preterm infants undergoing intensive care. T

he various factors to be investigated include blood pressure fluctuations, cardiac output, apnoeas, oxygen desaturations, ventilation changes and blood sampling procedures. We will use Near Infrared Spectroscopy to measure cerebral oxygenation non-invasively by the cotside of preterm infants, and correlate the changes with the various factors being investigated.

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

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

Keywords
Preterm brain, brain oxygenation, infant sleep, periodic breathing, apnoea

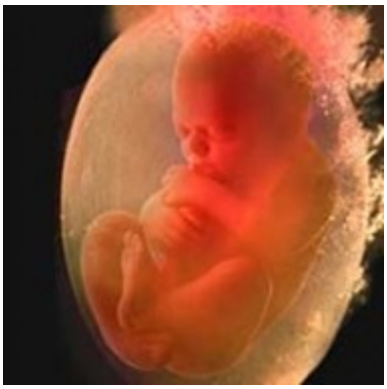
Infection, Inflammation and Immunity

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

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

Project Description: Inflammation-induced brain injury remains one of the main causes of disability after premature birth. There is no effective treatment. The pro-inflammatory cytokine interleukin 1β (IL-1β) has been implicated in inflammation – induced brain injury through activation of cerebral microglia (the brain's resident immune cell) however it remains unclear whether this association is causal.
This project is aimed at understanding the role of IL-1β in inflammation-induced brain injury in preterm fetal sheep, using an FDA approved IL-1β receptor antagonist.

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



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

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

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

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

Infection, Inflammation and Immunity

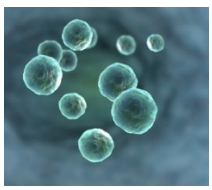
Molecular Characterisation of Regulation and Mechanism of Action of the Anti-inflammatory Cytokine Interleukin 37

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

Project Description: Direct clinical relevance: medium/low. Hands-on learning opportunities: Culture of primary human blood cells and cell lines, protein detection by ELISA, RNA detection by real-time PCR, flow cytometry, immunohistochemistry. Interleukin (IL)-37 was discovered in silico in 2000, but it remained a neglected molecule, and nothing at all was known about its function until 2010, when we described the powerful anti-inflammatory properties of this cytokine. IL-37 belongs to the IL-1 family of cytokines and imparts a strong inhibition of the production of pro-inflammatory cytokines. Interestingly, this protection from inflammatory responses is not limited to one or a few triggers, but covers a wide spectrum of inflammatory assaults - a rare property, which renders IL-37 a prime candidate for clinical use.

However, further research on the mechanism of action of this unusual cytokine is required before such steps can be taken. In this project, we will characterise several aspects of regulation and function of IL-37, in particular the mRNA and protein expression profile of IL-37 across a spectrum of cell types and the effect of IL-37 one of the key molecular regulator of inflammation, the inflammasome.

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



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

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

Project Description: 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.

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

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

Infection, Inflammation and Immunity

The Role of IL37 in the pathogenesis of inflammatory bowel disease

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

Project Description: The Role of IL37 in the pathogenesis of inflammatory bowel disease IL37 is a novel anti-inflammatory cytokine which is reduced in the circulation of patients with auto-immune diseases, including inflammatory bowel disease (1). Human peripheral blood mononuclear cells are capable of producing IL37, and in particular the T cell subset (2). Aberrant helper T cell responses play a key role in the pathogenesis of IBD (3-5). Thus, it is of paramount importance to understand the triggers for pro and anti-inflammatory cytokine production by T cell subsets of patients with inflammatory bowel disease. This project will look at characterising IL37 production in different cell subsets in the blood and lamina propria of patients with inflammatory bowel disease. Cells will be isolated from peripheral blood and colonic biopsies. Following appropriate processing or digestion and stimulation, flow cytometry will be used to characterise immune cell subsets and their capacity to produce IL37. Additionally, colonic biopsy samples will be collected and stored to create frozen sections for immunofluorescent staining. Concurrently, patient data on disease activity, medication use and response will be collected. Disease activity and response to currently available medications will be correlated with IL37 production to assess whether this cytokine plays a role not only in pathogenesis of disease, but also response to immunomodulating medications

Keywords

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

Exploration of IL-38 in inflammatory diseases

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

Project Description: Direct clinical relevance: medium. Hands-on learning opportunities: Various aspects of work with mice and patient samples, workup of tissues for various downstream applications, flow cytometry, histology, immunohistochemistry, protein detection by ELISA, RNA detection by real-time PCR. Interleukin (IL)-38 is a novel member of the IL-1 family of cytokines. The majority of IL-1 family members play important roles in inflammatory diseases – either as promoters or inhibitors of inflammation. IL-38, however, received almost no research attention until our group renamed the new IL-1 family cytokines in 2010. Thus, its function is still largely unknown. Recently, we discovered that IL-38 plays a role in systemic lupus erythematosus (SLE) – a very severe and potentially fatal autoimmune disease that mainly affects young women in their childbearing age. We found that SLE patients have elevated serum IL-38 concentrations and that IL-38 is predictive of disease severity and the development of major SLE-associated complications. Moreover, we have shown in vitro that IL-38 has anti-inflammatory properties and inhibits the production of cytokines that promote inflammation. Now, we want to investigate the function of IL-38 in vivo.

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

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

Infection, Inflammation and Immunity

Novel Anti-inflammatory Approaches for Currently Untreatable Diseases of the Preterm Baby

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

Project Description: The 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-1Ra and IL-37 by histology and flow cytometry and by analysis of selected biochemical markers.

Keywords: bronchopulmonary dysplasia, necrotizing enterocolitis, immunology, paediatrics, neonatology, translational medicine,

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

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

Project Description: The neonatal microbiome, in healthy full-term infants and in preterm infants presents with a highly dynamic nature. As such, the microbiome is extremely susceptible to external influences that can dramatically affect the short- and long-term health of the infant. In this project we set out to investigate the underlying mechanisms how the intestinal and pulmonary microbiome influences the neonatal immune system and thereby impacts disease outcome. In collaboration with Monash Children's we collect clinical data and samples from term and preterm infants. This project gives you the opportunity to closely work with clinical collaborators and also have the opportunity to gain experience in a diverse set of molecular techniques

Keywords: microbiome, immunology, intestine, lung,

Infection, Inflammation and Immunity

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

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

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

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

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

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

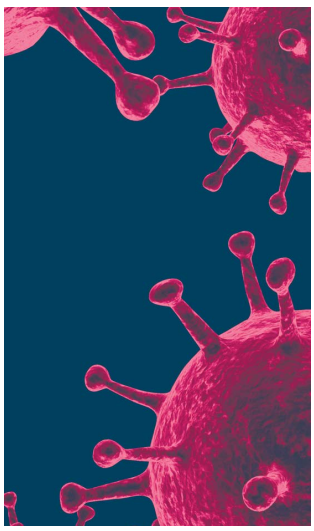
Keywords: preclinical study, inflammatory bowel disease, inflammation, immunology, interleukins, regulatory t cell, cell therapy

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

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

Project Description: Inflammation-induced brain injury remains one of the main causes of disability after birth. There is no effective treatment. Elevated levels of inflammatory proteins (cytokines) are associated with brain inflammation and impaired neurodevelopment however This project aims to improve our understanding of how cytokines disturb healthy brain development and develop new anti-cytokine therapies for inflammation-induced brain injury.

Keywords:
translational science; physiology; neuroscience; preterm birth; infection; inflammation



Cell therapy and regenerative medicine

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

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

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

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

Activating the stem cell niche

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: A/Prof Rebecca Lim, Prof Euan Wallace
Email: *rebecca.lim@monash.edu*
Phone: 03 8572 2794 (A/Prof Lim)

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

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

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

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

Cell therapy and regenerative medicine

Do Cord Blood Stem Cells Reduce Cerebrovascular Brain Injury?

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

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

Angiogenesis potential of exosomes

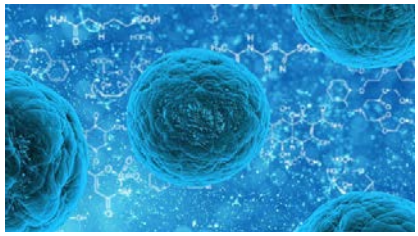
Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research, Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Mirja Krause, A/Prof Rebecca Lim
Email: *mirja.krause@hudson.org.au*
Phone: 03 8572 2874 (Dr Krause)

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

Bioengineering strategies to enhance stem cell therapeutics for vascular regeneration

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

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



Cell therapy and regenerative medicine

Novel formulations of stem cell-derived exosomes for vascular regeneration

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

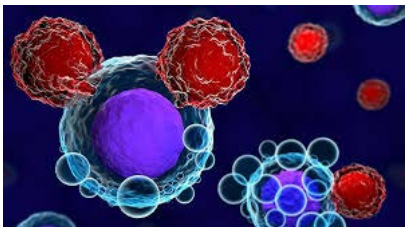
Project Description: Peripheral artery disease (PAD) affects more than 200 million people globally and the main driving forces is the ageing of the population and increase in cardiovascular risk factors, such as smoking, diabetes mellitus, and hypertension. PAD is a severe medical condition commonly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

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

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



Cell therapy and regenerative medicine

Developing a combination stem cell therapy for preterm inflammation induced brain injury

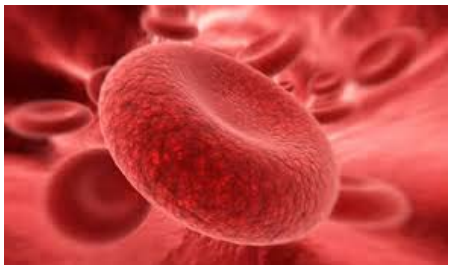
Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research, Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Dr Courtney McDonald, Prof Suzie Miller, Prof Graham Jenkin,
Email: courtney.mcdonald@monash.edu
Phone: 03 8572 2799

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

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

Suitability: Honours/PhD
Location: The Ritchie Centre, Hudson Institute of Medical Research; Level 5, Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Graham Jenkin, Dr Courtney McDonald, Dr Ashalyn Watt
Email: *graham.jenkin@monash.edu*
Phone: 0419534101 (Prof Jenkin)

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



Cell therapy and regenerative medicine

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

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

Project description: Neural stem cells (NSCs) offer great promise as a neuroprotective therapy against a range of neurological conditions, like cerebral palsy. A major challenge of NSC therapy for neurological conditions is getting the cells to the brain. Current intracerebral-delivery of NSCs is highly invasive and carries significant risks for the patient. We propose to develop a novel, non-invasive MRI-guided focused ultrasound (MRIgFUS) method for delivery of NSCs to the brain using a neonatal rodent model. MRIgFUS temporarily opens the blood brain barrier (BBB) allowing cells to directly access the brain, overcoming the need for invasive and high-risk brain or spinal administration.

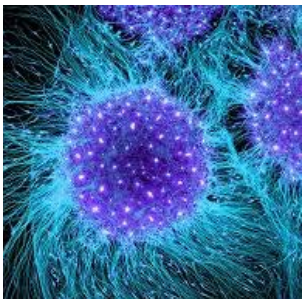
This project will (a) optimise MRIgFUS for the delivery of clinically-compatible human NSCs that minimises collateral damage to the neonatal rat brain, and (b) examine the impact of MRIgFUS-NSC transplantation on long-term outcomes (cognition, memory, motor-skills) of stroke-affected rodents. As part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

Stem Cells and Tissue Scaffolds

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

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

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



Cell therapy and regenerative medicine

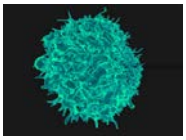
Derivation of Human Induced Pluripotent Stem Cells (iPSCs) using mRNA

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

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

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

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



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

Suitability: Honours/PhD
Location: The Ritchie Centre / Carthertics, Hudson Institute of Medical Research; Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Richard Boyd and Prof Graham Jenkin, Co-supervisors: Dr Sacha Khong, Dr Nicholas Boyd, Technical support: Kelly Cartledge
Email: *graham.jenkin@monash.edu*
Phone: 0419534101 (Prof Jenkin)

Project description: The recent revolution in bioengineering of the cellular immune system offers a promising new frontier of personalized medicine with the potential to ultimately defeat cancer. This is best exemplified by being able to "Supercharge" the anti-cancer power of the immune system by genetically engineering killer T lymphocytes with Chimeric Antigen Receptors (CARs). These CAR-T cells are yielding unprecedented clinical success in some blood cancer. Currently, CAR-T cells are generated from the patients' own blood T cells. This is very problematic because the patients will have invariably had high dose chemotherapy, which is severely toxic to the immune system, limiting both the number and quality of cells which can be transduced to express the CAR receptor.

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

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

Cell therapy and regenerative medicine

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

Suitability: Honours/PhD
Location: The Ritchie Centre / Cartherics, Hudson Institute of Medical Research; Translational Research Facility, Monash Medical Centre, Clayton
Project Leaders: Prof Richard Boyd, Prof Graham Jenkin, Co-supervisor: Dr Vera Evtimov
Email: *graham.jenkin@monash.edu*
Phone: 03 8572 2801 (Prof Jenkin)

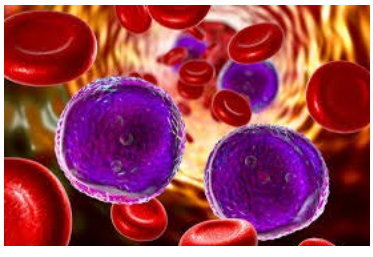
Project description: Chimeric antigen receptor (CAR-) T cells are designed to exploit the intrinsic cytotoxic function of T cells, whilst manipulating specificity by expressing a nominal antigen-specific receptor containing a cytoplasmic activation domain. CAR-T cells are providing extraordinary results in the clinic, particularly for haematological malignancies. As exciting and tantalising as this immunotherapy revolution is, there are still major hurdles to be overcome in optimising their clinical utility. This project will apply the rules that govern normal endogenous T cell function to CAR-T cells, to help their functional impact across a range of cancers and to increase their longevity after transplantation. Recent studies have shown that T cell exhaustion significantly impacts the ability for chimeric antigen receptor (CAR-) T cells to remain potent killers.

The project will utilize a variety of sophisticated technologies including the real-time impedance based xCelligence cytotoxicity and Luminex Multiplex cytokine arrays. Overall, this project will aim to characterise how T cell receptor (TCR) mediated activation and ultimately modulation of T cell exhaustion will enhance CAR-T potency in vitro and in vivo.

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

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

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

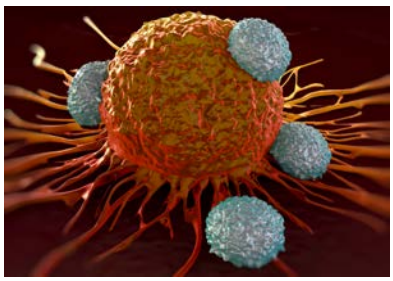


Cell therapy and regenerative medicine

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

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

Project description: Genetically modified chimeric antigen receptor T cells (CAR-T cells) represent a new revolution in anti-cancer immunotherapy. A major problem, however, is that the treatment currently relies on using the cancer patients own blood but they invariable have too few T cells available for genetic enhancement. Furthermore, prior treatment with chemotherapy substantially reduces their function. This study aims to develop a new approach to generating CAR-T cells from stem cells. T cells derived in vitro from induced human pluripotent stem cells (iPSC) offer great potential advantages in generating a self-renewing source of T cells that can be readily genetically modified for immunotherapy. The project is aiming to generate a genetically modified human stromal cell line from human Mesenchymal Stem Cells (MSC), for supporting the T cell in vitro differentiation.



Elimination of cancer stem cells using chimeric antigen receptor T cells

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

Project description: Disease relapse in CAR-T therapies of solid tumours suggests that current treatments lack the ability to eliminate the small subset of cells known as cancer initiating cells or cancer stem cells (CSCs). We propose to use the sophisticated specificity of immunotherapy to target surface membrane antigens present on the CSC, negating the current need for the cancer cell to be proliferating for killing efficacy of CAR-T therapies.

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

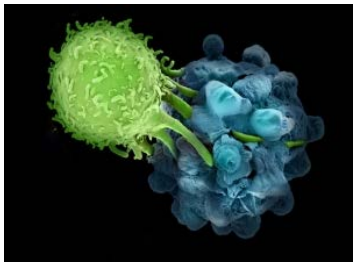
Cell therapy and regenerative medicine

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

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

Project description:
Cellular immunotherapy with chimeric antigen receptors (CARs) has provided unprecedented results in treatment of liquid cancers. However, the few FDA approved autologous based therapies have been priced around $400,000 per patient. Inherently these face major challenges to reach mass adoption. Furthermore, autologous CAR-T treatments can require ~2 months to manufacture (often time patients don't have) and produce variable (often insufficient) cell numbers as a result of poor immune systems hampered by chemotherapy. An on-demand, highly defined, universal product, which is compatible with multiple patients is required to unlock cellular immunotherapy therapy for the public.

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



Contact our supervisors

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

STEP 1: Find a project that you are interested in.

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

All the information you need to enrol is on Hudson Institute's website, or the project supervisor can help you enrol.

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

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