The University of Melbourne, Department of Paediatrics and Murdoch Childrens Research Institute
Faculty of Medicine, Dentistry & Health Sciences

HONOURS & MASTERS PROJECTS 2023
Honours and Master of Biomedical Science
Virtual Student Information Evening
Tuesday 30 August, 5.00pm onwards
Register here
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**Population Health**

- Maternal COVID19 infection and infant hearing screening outcomes: A retrospective audit of data from the Victorian Infant Hearing Screening Program (VIHSP)
- Understanding teens with hearing loss in Victoria
- Determining the top research priorities for child hearing loss
- ASQ-STEPS Learning Progressions

**UNIVERSITY OF MELBOURNE HONOURS ENTRY REQUIREMENTS**

**HOW TO APPLY - MDHS HONOURS**

**UNIVERSITY OF MELBOURNE MASTER OF BIOMEDICAL SCIENCE**
**Laboratory based**

**Infection and Immunity**

1. **Understanding pneumococcal pathogenesis**
Streptococcus pneumoniae (the pneumococcus) is the most common cause of community-acquired pneumonia and a leading killer of children worldwide. However, it is also commonly found as an asymptomatic coloniser of the upper respiratory tract (carriage). Pneumococcal carriage is an important reservoir for transmission and a precursor to disease. In this project, you will identify novel genes and characterise their role in pneumococcal carriage and/or disease. Key approaches to this project include: bacterial transcriptomics, genetic manipulation of pneumococcal isolates, working with in vitro and/or in vivo models such respiratory cells from patients grown as air-liquid interface, as well as microbiological and immunological analysis of local and systemic samples. Your research will provide new insights into how pneumococci colonise and cause disease.

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Is this project offered for Masters? **Yes**

2. **Microbial changes following pneumococcal conjugate vaccination**
Pneumococci are a major global pathogen. Pneumococcal conjugate vaccines (PCVs) protect against a subset of pneumococcal serotypes. Introduction of PCVs result in major changes to pneumococcal epidemiology and to the microbiota more broadly. In this project, you will examine nasopharyngeal samples and isolates collected from children from vaccine studies in low-income settings from the Asia-Pacific region. You will apply traditional and molecular microbiology approaches including culture and serotyping, qPCR, DNA microarray, whole-genome sequencing and antimicrobial resistance testing. Your results will inform vaccine strategies world-wide.

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Is this project offered for Masters? **Yes**

3. **Novel Functional Assays for Strep A Vaccine Efficacy Assessment**
Strep A is one of the leading causes of infection related death worldwide, yet there is currently no vaccine available. The aim of this project is to investigate the functional properties of antibodies binding to different candidate Strep A vaccine antigens, to identify mechanisms of protective immune responses and advance development of a correlate of protection. The project will use antigen-microsphere complexes to establish functional serology assays to profile the Fc-effector functions of Strep A antigen specific antibodies. This includes polyclonal avidity, FcR binding, an antibody dependent cellular phagocytosis (ADCP) assay with monocyte and/or neutrophil cell lines (THP-1/HL-60), antibody dependent complement deposition (ADCD) and antibody dependent cytokine/chemokine secretion (ADCS) assay using the CEM-NKr CCR5+ T-lymphoblast cell line. This will determine which functional antibody responses are essential for vaccine-induced protective immunity. Results will be compared to clinical outcomes to drive development of an immunological correlate of protection.

**Professor Andrew Steer**
**Dr Hannah Frost**
Is this project offered for Masters? Yes

4. **Epigenetic reprogramming of immune cells in response to cross-sex hormone therapy**

**Introduction**  
Transgender people, whose gender identity is markedly and persistently incongruent with their biological sex, almost always experience gender dysphoria. Characterised by severe distress and discomfort, and the feeling of ‘having been born in the wrong body’, gender dysphoria compels transgender individuals to seek cross-sex hormone treatment. While there is clear sexual dimorphism (differences between sexes) in immune function and response to infection, it is not known how hormone therapy influences these at the functional or molecular level. In this project we will study immune cells from individuals that underwent cross-sex hormone therapy to answer these questions.

A key aim is to understand what proportion of sexual-dimorphism is due to genetics and how much is due to sex hormones alone.

**The Project**

Two clinical trials of cross-sex therapy were completed, for which we have biological samples:

1. Whole blood genome-wide DNA methylation data is available for 12 individuals who underwent female-to-male hormone treatment and 12 underwent male-to-female hormone treatment (baseline, 6 months and 12 months after treatment). These data need to be analysed using bioinformatics tools.

2. Live frozen peripheral blood mononuclear cells are available at baseline and 6 months after cross-sex estrogen hormone treatment in male-to-female transition (n = 70). These live frozen cells will be used for immune-phenotyping, epigenetic (DNA methylation, histone modifications) and transcriptomic profiling of specific innate (monocytes) and adaptive (naïve T and B) cell types. This will evaluate the changes in immune function during sex hormone administration.

**Methods involved**  
**Molecular Biology:** RNA/DNA extraction, chromatin preparation and pulldown, sequencing library preparation.  
**Cellular Immunology:** Cell sorting and analysis of immune-phenotyping data. Cell culture to elicit inflammatory responses in immune cells.  
**Bioinformatics:** R and linux to analyse DNA methylation, ChIP-seq and RNA-seq data (no prior knowledge of coding is required).

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Is this project offered for Masters? Yes
How do monocytes remember? Application of multi-tag sequencing to study Trained Immunity

We all know that the adaptive immune system develops memory following specific antigen exposure, but is the same true for the innate immune system? An emerging field of research tells us exactly this, with epigenetic remodelling as the underlying mechanism. Innate immune cells, such as monocytes and macrophages, form this non-specific memory in response to a variety of exogenous signals. Exposure induced epigenetic remodelling governs their future response to a range of pathogens. This process can be modelled in vitro, using both yeast and bacterial antigens and metabolites (Novakovic et al. Cell 2016), metabolites (Bekkering et al. Cell 2018), vaccines (Bannister et al. Science Advances 2022) and a range of other stimuli. During pregnancy, both maternal and foetal monocytes show attenuated pro-inflammatory responses correlated with pregnancy-associated hormones. Additionally, foetal monocytes are exposed to a range of environmental factors. We hypothesise that monocytes remodel their chromatin in response to early life environments, which explains their altered function during pregnancy. To test this hypothesis, we will isolate pure monocytes from human blood, and treat them with various stimuli in vitro. After treatment we will measure cytokine release, RNA expression and epigenetic (histone modification) changes. This project is appropriate for students with an interest in molecular biology and immunology and will utilise monocyte isolation and culture, ELISA, multi-tag sequencing, DNA and RNA extraction and real-time PCR, and bioinformatic analysis of genomic data.

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Is this project offered for Masters? Yes

Molecular remodelling of endothelial cells in response to specific lymphocytes and other signals.

The vascular endothelium is a highly specialized barrier that plays a key role in the regulated migration of leukocyte cells out of the circulation and into peripheral tissues as part of the systemic immune response. In atherosclerosis, this barrier function is impaired leading to uncontrolled leukocyte accumulation and systemic inflammation. Recent data have shown that cells of the innate immune system, such as monocytes and macrophages, have capacity to develop a non-specific memory in response to inflammatory signals. Termed ‘innate immune memory’, it is increasingly clear that this is not restricted to cells of the hematopoietic lineage. We have recently demonstrated that endothelial cells of different origins have the capacity to establish innate immune memory following an initial stimulus (viral or bacterial). Further, we have mapped the molecular and cellular ‘reprogramming’ involved in this process, that enables an enhanced response to an unrelated second stimulus. It is important to note that cells do not act in isolation, and we now aim to explore the impact of a range of human plasma and lymphocyte (white blood cells) protein stimuli on endothelial memory. This project will involve culturing vascular endothelial cells with plasma from individuals of variable health outcomes (diabetes, obesity, allergic and autoimmune conditions) and endothelial-lymphocyte co-culture experiments. We couple these with state-of-the-art transcriptome and epigenetic profiling. Techniques include cell culture, DNA/RNA extraction, a range of epigenetic approaches, RNA sequencing (RNA-seq) and bioinformatic analysis. This project will reveal novel insights into the role of circulating lymphocytes and other factors in modulating
endothelial molecular function, a key determinant in a range of adverse health outcomes, including atherosclerosis and cardiovascular disease.

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Is this project offered for Masters? Yes

7. **High Dimensional Immune and Epigenetic Profiling of Children with Juvenile Idiopathic Arthritis (JIA)**

Autoimmune Disease is a condition arising from an abnormal immune response to a functioning body part. There are about 80 Autoimmune Diseases, which affect 5-10% of the population of the Western world. Around 70% of those affected are female, owing to a combination of genetic and hormonal factors. Juvenile idiopathic arthritis (JIA) is an autoimmune rheumatic disease that is one of the leading causes of childhood disability and affects around 6000 Australian children. It typically causes joint pain and inflammation in the hands, knees, ankles, elbows and/or wrists. But, it may affect other body parts too. We hypothesise that blood cells (e.g. T cells, monocytes and B cells) from JIA patients will show different responses to activation, will circulate in different numbers and have a distinct molecular profile compared to control children. To test this, You will apply immunology and molecular genomic sequencing techniques to circulating blood cells from JIA patients and matched controls. Our CLARITY (Childhood Arthritis Risk factor Identification Study) JIA biobank has grown to be one of the largest, most biospecimen- and information-dense collections in the world. We will combine samples from this cohort with state-of-the-art transcriptome and epigenetic profiling. Techniques include cell culture, cell sorting, high dimensional flow cytometry, DNA/RNA extraction, a range of epigenetic approaches, RNA sequencing (RNA-seq) and bioinformatic analysis.

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Is this project offered for Masters? Yes

8. **Immune mechanisms of peanut allergy remission**

Food allergies are a major health burden globally, Australia having the highest reported rates. There is currently no cure so management relies on allergen avoidance, causing severely reduced quality of life and rarely death. A treatment that can induce remission of allergy is needed. Understanding immune mechanisms supporting clinical remission of allergy, and long-term persistence of remission will facilitate development of novel treatments. Several therapies under investigation can induce remission, however remission may be transient or long-lasting. We have shown that a combination treatment, Probiotic and Peanut Oral Immunotherapy (PPOIT), induces long-lasting remission persisting to 4 years post-treatment; whereas remission following peanut oral immunotherapy (OIT) without an adjuvant appears short-lived, with two thirds (67%) of treatment responders losing remission by 12-months post-treatment. We have completed a large (n=201) Phase 2b randomised trial comparing PPOIT vs OIT vs Placebo with patients followed to 12-months post-treatment,
allowing identification of transient (lost) vs persistent remission. Biosamples collected before, during and after treatment are available for analysis. This project aims to characterise shifts in cytokine production that occur during the transition from allergy to remission, and patterns associated with transient vs persistent remission. Findings will contribute to understanding the immune mechanisms involved in retraining the allergic response towards remission, as well as remission that persists or is lost. Cytokine levels in cell culture supernatants will be measured by multiplex assay before and after treatment in 1) patients who achieved remission of peanut allergy following PPOIT treatment, 2) patients who achieved remission of peanut allergy following standard OIT, 3) patients who remain allergic to peanut following placebo treatment. Findings will help to identify key immune factors driving lasting remission of allergy compared to remission that is lost over time, which may in turn lead to development of more effective long-term treatments for food allergy.

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Is this project offered for Masters? **No**

**9. Beyond the clinical outcomes of the BRACE randomised controlled trial**

Interested in being part of the largest BCG vaccine trial of its kind worldwide? The BRACE trial is our international RCT of nearly 7000 healthcare workers across 34 sites in five countries. This trial is working to determine if BCG vaccination reduces the impact of COVID-19 and other respiratory diseases. In addition to data on symptoms during respiratory illness including COVID-19, participants provided information on COVID-19 risk factors, vaccinations and vaccine reactions, as well as blood samples for assessment of immune responses. Using data collected from participants in the BRACE trial and existing immunological data we have a range of projects available investigating the interplay between COVID-19 symptoms, risk factors, vaccine responses and vaccine reactions. In addition, we have several projects involving immunological analysis of samples from the BRACE trial to investigate the how BCG changes the immune system and the associations between immune markers and clinical outcomes (e.g. COVID-19 risk and vaccine reactions). The Infectious Diseases Laboratory is located at the Murdoch Children’s Research Institute, part of the Melbourne Children’s Campus, which also includes the Royal Children’s Hospital and the University of Melbourne.

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Is this project offered for Masters? **Yes**

**10. Systems serology analysis of single dose HPV vaccination in Mongolia**

A single dose of human papillomavirus (HPV) vaccine appears to be as efficacious against HPV infection, the prerequisite of cervical cancer, as two or three doses, despite inducing lower antibody titers. Neutralizing antibodies are thought to be the primary mediator of protection, but the threshold for protection is unknown. Antibody functions beyond neutralization have not been
explored for HPV vaccines. This project aims to examine antibody profiles (isotypes, subclasses) and features (Fc receptors) in the serum of girls vaccinated with a single dose of HPV vaccine in Mongolia. This study will involve multiplex fluorescent assays to several HPV types as well as methods for production and validation of HPV pseudovirus.

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Is this project offered for Masters? Yes

11. Examining the role of low affinity Fc receptor binding following HPV vaccination
The antibody response to microbial infection is diverse. The functional repertoire of an antibody is dictated by a combination of the Fab region, which determines antigen specificity, and the Fc region, which binds Fc receptors (FcR) found on immune cells throughout the body. Crosslinking of FcRs on effector cells allows a range of protective immune responses apart from neutralization to be directed against pathogens. Fc-mediated antibody effector functions have been shown to be essential for multiple infectious pathogens including malaria, Ebola, HIV and SARS-CoV-2. Similarly, Fc-mediated effector functions might also be able to prevent HPV infection through a variety of effector mechanisms. There are a number of Fc receptors which have both high and low affinity for antibody and both may be important in preventing infection. High affinity Fc receptors have been studied in more detail than low affinity Fc receptors despite the fact that low affinity Fc receptors are known to be important in modulating adaptive immune responses. This project will measure low affinity Fc receptor responses in the context of single dose HPV vaccination using our clinical cohorts to provide a greater understanding of the mechanisms of action.

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Is this project offered for Masters? Yes

12. Effect of booster vaccination on the immune response to serotype 1 bacteria
Serotype 1 pneumococcal bacteria is a highly virulent strain causing serious invasive pneumococcal diseases such as meningitis and sepsis. Current vaccines contain serotype 1 but the protective immunity that these vaccines produce largely depends on the vaccine schedule used. The WHO recommends three doses of pneumococcal conjugate vaccine (PCV) to be given to infants either as three primary doses with no booster (so called 3+0 schedule) or as two primary doses plus a booster (so called 2+1 schedule). Evidence to date suggests that the administration of a booster dose provide much more functional immunity to serotype 1 compared with if no booster is given. The reason(s) for this are poorly understood. Using samples collected from our randomised controlled trials in Vietnam, we are interested in examining serotype 1 immunity in more detail using a combination of approaches including IgG binding assays, opsonophagocytic assays and Fc receptor binding assays. This project will measure serotype 1 immunity following different vaccine schedules to understand the role of booster vaccination for this important serotype.

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Is this project offered for Masters? Yes
13. Immunogenicity of second dose COVID-19 booster vaccination in Melbourne

COVID-19 vaccines are highly protective against severe disease, especially when given as a booster dose. Recently, ATAGI has recommended that all adults >30 years of age receive a second COVID-19 booster dose to maintain protection against the new Omicron subvariants. Our lab has been funded to undertake a randomised controlled trial in Melbourne to measure the immunogenicity of a second dose COVID-19 vaccine in adults, with multiple study visits over a 6 month follow-up period. Measurement of vaccine immunity will be done using a combination of antibody (IgG, neutralising antibodies) and cellular assays (T cells, cytokines). This project will measure COVID-19 vaccine responses in vaccinated adults including ELISA, cell culture, cytokine assays and flow cytometry as required.

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Is this project offered for Masters? Yes

14. Molecular epidemiology of RSV in Mongolia from 2015-2020

Worldwide, respiratory syncytial virus (RSV) is the leading pathogen causing lower respiratory tract infections (LRTIs) in children under two years of age. There is limited data about RSV molecular epidemiology in Mongolia. We have conducted a LRTI surveillance study in Ulaanbaatar, Mongolia from April 2015 to June 2021. RSV was screened in children under 2 years of age enrolled in the surveillance project. This proposed project aims to describe the viral molecular characteristics of circulating RSV strains during the surveillance period. Understanding RSV genotypes circulating in Mongolia is critical information for an effective development of RSV vaccine.

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Is this project offered for Masters? Yes

15. New drug discovery pipeline for the cystic fibrosis superbug, Mycobacteroides abscessus

M. abscessus is responsible for causing a wide clinical spectrum of disease in the complex microenvironment of the CF airways. Current treatment regimens span months and involve cocktails of 3-5 different parenteral antibiotics with wide-ranging toxicities. The presence of M. abscessus also excludes patients from life-saving lung transplants in certain healthcare systems. Thus, there is an enhanced focus on M. abscessus infections in the context of the CF lung by clinicians and researchers alike. Our unique drug discovery pipeline combines physiologically relevant stem cell-based infection modelling with high throughput drug screening to identify new treatment options for this CF superbug. This project will include extensive validation of identified compounds in pre-clinical models of infection including cell-based assays, mouse infection model and biofilm assays.

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Is this project offered for Masters? **No**

16. **nti-inflammatory effects of sulforaphane**

Sulforaphane is a dietary compound with a diverse range of biological effects, including anti-oxidant, anti-inflammatory and chemoprevention. The biological effects of sulforaphane against infectious pathogens are less well understood, although some effects have been described for specific bacteria and viruses. Identification of novel anti-viral compounds with activity against SARS-CoV-2 is a priority research area. This project will involve undertaking some in vitro assays to assess the anti-inflammatory effects of sulforaphane against SARS-CoV-2. A combination of flow cytometry and cytokine assays will be performed.

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Is this project offered for Masters? **Yes**

17. **Analysis of cord blood immune profiles in preterm and term infants**

Preterm infants have increased susceptibility to viral and bacterial infectious diseases in comparison to term infants. The reason for this is not well understood but is thought to be due to delayed immune system development in preterm infants. Understanding early life immune responses in preterm infants is important in the development of novel vaccines or therapeutics in the prevention and/or treatment of infectious diseases. This project aims to define differences in cord blood immune responses to RSV between preterm and term infants from Vietnam using a range of immunological techniques including cell culture, flow cytometry and cytokine assays.

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Is this project offered for Masters? **Yes**

**Cell Biology**

18. **Using iPSC derived skeletal muscle cultures to study muscle disease**

Using iPSC derived skeletal muscle cultures to study muscle disease

This project aims to use skeletal muscle derived from induced pluripotent stem cells (iPSCs) collected from patients with rare inherited muscle disorders, like Duchenne muscular dystrophy (DMD) and Nemaline myopathy. The protocols needed to complete this work have been developed in our laboratory and we are now using these methods to study muscle grown in a dish in both 2 and 3 dimensional models. Cell culture-based models of muscle diseases will greatly enhance our ability to assess disease and develop novel therapeutic approaches to treat these debilitating conditions. The projects will use stem cells from patients with various muscle diseases including Nemaline myopathy, Collagen VI myopathy and mitochondrial disease. We will teach you all that is required to grown skeletal muscles from iPSCs and how to phenotype the relevant condition in vitro. The skills you will learn include aseptic tissue culture techniques as well as laboratory-based methods such as, immunocytochemistry, flow cytometry, western blotting and quantitative real-time PCR (RT-qPCR).
19. Controlling nephron patterning and segmentation in kidney organoids
The directed differentiation of human pluripotent stem cells into nephron-containing human kidney tissue provides a major opportunity to generate engineered kidney tissue for renal replacement. However, nephron function is completely reliant upon patterning and segmentation with distinct responses to morphogen gradients between the proximal and distal ends of the nephrons. An ability to provide a gradient of growth factor signalling across patterning tissue is a major opportunity to align nephrons in a particular fashion. This project will use reporter lines that can indicate the level of growth factor signalling in an individual cell to investigate how nephron patterning can be instructed or enhanced in vitro to improve the structures that are derived. The project will draw on methods in stem cell differentiation, bioengineering and computational image analysis.

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Is this project offered for Masters? Yes

20. Do mast cells play a role in type 1 diabetes?
Type 1 diabetes is an autoimmune disorder that results in destruction of the pancreatic beta cells, leading to blood glucose dysregulation. Mast cells have been implicated in other autoimmune disorders, such as rheumatoid arthritis and multiple sclerosis. We hypothesise that mast cells may also play a role in type 1 diabetes. We will test this hypothesis by examining a potential role for mast cells in antigen presentation and other T-cell interactions using mast cells differentiated from pluripotent stem cells derived from type 1 diabetic donors. This project will involve analysis of single-cell transcriptomics, cell culture, directed differentiation of human pluripotent stem cells and flow cytometry.

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Is this project offered for Masters? Yes

21. Expanding pancreatic progenitor cells for treatment of type 1 diabetes
Pluripotent stem cells (PSCs) are a promising alternative to cadaver-derived islets, potentially providing an unlimited supply of insulin-producing beta cells for transplantation therapies to treat type 1 diabetes. Numerous protocols that promote the differentiation of PSCs towards a beta cell fate have been published and generally aim to recapitulate signalling processes that occur during embryogenesis. However, there is one noticeable discord between in vivo pancreatic development and in vitro pancreatic differentiation - the absence of a clearly defined progenitor expansion stage
in vitro differentiations. In the embryo, prior to pancreatic specification, the gut tube undergoes significant expansion as the embryonic axis extends. Following this, the pancreatic progenitor compartment rapidly proliferates, undergoing branching morphogenesis, prior to endocrine differentiation, delamination and islet formation. The goal of this project will be to identify factors that can expand human PSC-derived pancreatic progenitor pools, thus allowing for efficient generation of large numbers of human PSC-derived endocrine cells for subsequent use in transplantation therapies. This project will involve cell culture, directed differentiation of human pluripotent stem cells and flow cytometry.

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Is this project offered for Masters? Yes

**22. Creating a novel iPSC-derived model of the human alveolus**

The alveolar compartment of the lung includes structural cells, like type 1 and 2 alveolar epithelial cells, and immune cells, like macrophages. These alveolar epithelial cells and macrophages are in constant communication, and together orchestrate innate immune responses to inhaled noxious stimuli. This project will develop a novel human alveolar platform using induced-pluripotent stem cell (iPSC). Using established directed differentiation protocols iPSC-derived alveolar epithelial cells and iPSC-derived macrophages will be derived. This project will then determine optimal conditions to co-culture these cell types together. Moreover, this project will functionally characterize this model using techniques such as immunofluorescence, and RNAseq of co-cultured cells (compared with pre-co-culture). In addition, this project will validate innate immune responses in this model. This novel human alveolar platform will be vital in future research studying respiratory diseases and identifying novel therapeutic targets.

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Is this project offered for Masters? Yes

**23. Establishing a human iPSC-model of RSV infection**

Respiratory syncytial virus (RSV) infection is the most common cause of bronchiolitis and pneumonia in infants. Severe and/or frequent RSV infections are often followed by episodes of wheezing and subsequent diagnosis of asthma. While the response of the upper airway to RSV infection is well characterized, how the distal regions of the lung respond to RSV (where bronchiolitis and pneumonia occur) has been less studied in humans. Moreover, there is currently no vaccine against RSV and therefore there exists a major gap in understanding viral pathogenesis in the human lung to identify novel therapeutic avenues. This project will use novel induced-pluripotent stem cell (iPSC)-derived lung epithelial cell platforms to address this knowledge gap. This project will establish for the first time an RSV-infection model of iPSC-derived lung epithelial cells and characterize the cellular response to infection. This will include determining viral load (e.g., viral shedding, immunofluorescence staining for virus), and elucidating the host's innate response to infection (e.g., cytokine arrays, single-cell RNA-seq) to identify novel therapeutic targets to accelerate RSV clearance in the distal lung.

**Professor Ed Stanley**

**Dr Rhiannon Werder**
24. Investigating human lung development using iPSC-based models
Twin studies and genome-wide association studies suggest that genetics strongly influence lung function. Low lung function in adulthood is likely affected by suboptimal development during early life and is associated with a later diagnosis of chronic respiratory diseases. However, it is unclear how genes associated with lung development influence human lung development. This project will use induced-pluripotent stem cell (iPSC) models of human lung epithelial development. The project will use cutting-edge CRISPR interference (CRISPRi) and CRISPR activation (CRISPRa) iPSC tools (Werder et al, 2022 Sci Adv) to interrogate lung development gene function. To understand lung development gene function, a number of assays will be performed, including measurements of lung epithelial cell function, global transcriptomic and proteomic changes, and response to injury.

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Is this project offered for Masters? Yes

25. Role of glia maturation factor beta (GMFb) and the actin cytoskeleton in neuronal differentiation during development and in the childhood cancer neuroblastoma

Neuroblastoma is the most common solid tumour of childhood excluding brain tumours. Children with this malignancy can present with disseminated disease. Of interest, infants with neuroblastoma occasionally demonstrate spontaneous disease regression, especially those without MYCN amplification, but the mechanism to explain this phenomenon is poorly understood. Glia maturation factor beta (GMFb) was initially considered as an exogenous growth factor. However, in silico modelling and subsequent in vitro studies demonstrate that GMFb is a member of the actin depolymerizing family and is a cofilin homologue. Transient overexpression of GMFb leads to significant neurite outgrowth in neuroblastoma cells and may promote tumour differentiation in vitro. Moreover, GMFb is a phosphoprotein. Preliminary data shows GMFb is expressed in the tumour stroma around undifferentiated tumour cells and in differentiated ganglioneuroblastoma cells. The student will perform GMFb gain and loss of function studies in neuroblastoma cell lines in vitro using CRISPR gene editing methods, including spinning disc confocal microscopy, assessment of actin cytoskeleton dynamics, and invasion, migration and colony forming assays. Identification of upstream cell signalling pathways that phosphorylate GMFb during development will potentiate the development of novel therapeutics for this complex and often fatal childhood cancer.

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Is this project offered for Masters? Yes
26. Gene regulation in the developing retina and the childhood eye cancer retinoblastoma

Retinoblastoma is the most common eye cancer of infancy and childhood; these tumours are considered to be developmental in origin. The seven cell types of the retina all derive from a pool of retinal progenitor cells (RPC). The distalless (DLX) family of evolutionarily-conserved homeobox genes encode transcription factors expressed in the developing and mature retina as well as the majority of retinoblastoma tumours examined to date. The DLX transcription factors are necessary for retinal ganglion cells (RGC) development, in part due to direct regulation of other transcription factors that are either activated or repressed during eye development. The student will undertake RNAseq and ChIPseq studies in the developing mouse retina to identify DLX2 gene regulatory networks, validate in transgenic mouse models available in the laboratory and assess expression of these DLX2 targets in retinoblastoma. The student will learn key methods in molecular, cell and developmental biology, including primary cell culture and advanced microscopy skills. The student should preferably have an undergraduate background in cell, developmental and/or molecular biology.

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Is this project offered for Masters? Yes

Clinical Sciences

27. Adjunct Cord Blood Cell Therapy for Paediatric Heart Failure

A high risk of heart failure complications and death is faced by children with severe congenital heart disease such as hypoplastic left heart syndrome (HLHS), and by children with dilated cardiomyopathy or severe myocarditis requiring ventricular assist device implantation and support. HLHS requires extensive complex surgical reorganisation of the neonatal heart, however metabolic supply-demand insufficiencies limit postoperative recovery at a time when neonatal myocardial growth and increased myocardial performance is required. For cardiomyopathy patients, workload-dependent energy demand, pressure and volume load in excess of capacity drives progressive worsening of myocardial dysfunction, cardiac remodelling and heart failure. Their survival requires mechanical assist device implantation to permit ventricular unloading and increased cardiac output. In both patient cohorts cardiopulmonary bypass surgery is a first step in initiating respective treatments. Despite advances in surgical intervention, further advances are required to target myocardial remodelling directly at a cellular level. Our work examines how cord blood immune and stem cells influence adaptive processes involved in muscle growth and metabolism, inflammation and fibrosis by promoting growth and limiting adverse myocardial remodelling in the paediatric heart at risk of failure. Recently, we demonstrated a new method of delivering cord blood stem cells to the heart using an experimental animal model of paediatric cardiopulmonary bypass surgery and have completed a preliminary safety trial in neonates with HLHS. Project opportunities may involve studies of immune cell metabolism, paracrine cell-cell interactions between cord blood cells and heart cells in models of inflammation, fibrosis and angiogenesis. More than one project is available according to student qualifications and interests.
28. **Exploring the liquid proteome of a preterm model**

Due to their central role in biological function, proteins control the mechanisms which lead to disease states. This makes them ideal for both biomarker discovery and development of novel diagnostic tests of disease. Blood tests are commonly accepted for the diagnosis of disease states, however in a preterm baby the amount of blood available for testing may be limited. This project will explore the use of alternative biosample sources such as lung fluid or urine for the diagnosis of preterm lung injury. In this project the student will use mass spectrometry to detect proteins from a variety of sample types and use integrative biostatistics to better understand the connection between tissue and liquid biosamples.

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Is this project offered for Masters? **Yes**

29. **HEART TO HEART: Assessing the cardiac impact of mechanical ventilation at birth.**

The most dramatic changes which occur in the circulation during the life of an individual are those that occur as a baby takes its first breath. 70% of all preterm infants within the Neonatal Intensive Care unit (NICU) are unable to breathe at birth and therefore require assisted respiratory support such as via mechanical ventilation. However very few studies have explored the coordinated response of the heart and lung to initiation of ventilation via a mechanical ventilator. In this project the student will use a range of techniques, including echo data analysis and proteomics to assess the impact of early post-birth mechanical ventilation on heart imaging and protein expression within the left and right heart ventricle.

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Is this project offered for Masters? **Yes**

**Genetics**

30. **KIF1A-Associated Neurological Disorders: Generating tools for gene-editing based therapy.**

Microtubules are essential structures in neurons that transport cargo from one part of the neuron to another to maintain proper structure and function of the brain. The Kinesin family member 1A
(KIF1A) is a neuron-specific microtubule plus end-directed motor protein that is involved in ATP-dependent fast anterograde transport of specific synaptic vesicle precursors such as Brain Derived Neurotrophic Factor to the tips of neurons. In children, defective trafficking by dysfunctional KIF1A due to mutations in the KIF1A gene triggers a devastating spectrum of rare progressive brain disorders collectively referred to as KIF1A-Associated Neurological Disorders (KAND).

The symptoms appear at birth or early childhood and have variable severity including death within 5 years of life. There is no cure or treatment for this condition and there is an enormous unmet therapeutic need to alleviate cellular impairments caused by pathogenic mutations in the KIF1A molecular motor. Gene therapy is a technique that enables the modification of a person's genes to treat or cure a disease. Recombinant Adeno-Associated Virus (AAVs) are bioengineered tools used to transport modified genetic material (cDNA) safely into tissues and cells of patients with genetic conditions. While AAVs are safe and do not integrate into the genome, their utility is limited in that they can only hold 4.4Kb of genetic material. In this project we wish to explore the potential utility of a gene therapy-based approach as a treatment for KAND. Due to the large size of the KIF1A cDNA (~5.3kb; >AAV size limit), it is critical to develop a KIF1A mini-gene containing only relevant functional domains required for the biological function of KIF1A.

This project will involve the development of a number of KIF1A mini-gene constructs and testing their function in a COS-7 cell based model.

Hypothesis: Mini constructs of KIF1A can transport KIF1A-specific cargo(s) along cellular microtubules.

Aim 1: To develop a series of KIF1A mini-genes using standard cloning methods.

Aim 2: To validate the KIF1A mini-gene in-vitro using transient COS-7 cells-based model. The project on offer includes various cell and molecular based techniques such as cloning, PCR, Sanger sequencing, agarose gel electrophoresis, transfections, immunocytochemistry, microscopy, immunoblotting, biochemical and other functional assays. This project will provide future opportunities to design and test AAV based therapeutics in patient-derived neurons and organoids.

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Is this project offered for Masters? No

31. Discovering novel genes and pathways to ataxia

Ataxia is the term for a group of neurological diseases that affect movement and coordination, impacting ~1:15,000 individuals. While there is considerable evidence that gene mutations cause ataxia, currently only ~30% of affected individuals receive a genetic diagnosis. A focus of our research is to identify novel genes that cause ataxia. We have recently identified a novel genetic cause of ataxia, caused by a pathogenic repeat expansion. This is when a segment of repetitive DNA, termed a short tandem repeat, is significantly expanded in size compared to the general population. This project will utilise modern genomic technologies, including exome and genome sequencing and transcriptomics to characterise the size and structure of this novel repeat expansion. Subsequently,
the expansion will be characterised in patient-derived cells to study disease-specific mechanisms and identify potential therapeutic treatments.

The successful candidate will get the opportunity to learn a range of laboratory techniques including generating and analysing Next Generation Sequence data, cell culture, immunocytochemistry, microscopy, real-time qPCR and western blot analysis. In addition, they will work closely with clinicians and bioinformaticians within a large multidisciplinary team.

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Is this project offered for Masters? Yes

**32. A high throughput drug screen to identify candidate targets for the treatment of Neurofibromatosis Type 1.**

NF1 is a single-gene disorder caused by a loss-of-function mutation in the NF1 gene resulting in a reduction of the protein neurofibromin. Cognitive deficits occur in approximately 80% of children with the genetic syndrome, neurofibromatosis type 1 (NF1), making them the greatest cause of disability for individuals with this lifelong genetic condition. These manifest as academic failure due to learning disabilities (70%), attention deficit-hyperactivity disorder (ADHD; 40%) and a significantly increased risk for autism spectrum disorder (ASD; 25%). Current therapies, whether medication or behavioural interventions, are often ineffective because they use ‘trial and error’ approaches targeting symptoms, rather than the cause. Therefore is an urgent need to discover new therapeutics for the impairing neurodevelopmental symptoms experienced by children with NF1. This drug screening project aims to identify compounds that may modulate neurofibromin expression using patient derived stem cell lines. Cells will be differentiated into neuronal cells and then used to perform a high throughput drug screen. Functional readouts from the screen will include assessment of neurofibromin steady state levels as well as structural readouts including neurite development, length and number of neurons in the cultures. Once candidate compounds have been identified, validation assays will be performed in NF1-patient derived stem cell models to determine whether the compound treatment/s can ameliorate neuronal deficits. Extensive functional analyses will be performed including the assessment of neuron growth and maturation (using immunofluorescence assays), neuron function (using multi electrode arrays and calcium imaging) as well as biochemical assays such western blotting, real time PCR and ELISAs to determine biological changes in our patient lines versus control lines.

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Is this project offered for Masters? Yes
33. Understanding the neurobiology of autism in NF1 using patient derived stem cell models

Neurofibromatosis Type 1 (NF1) is an inherited neurological syndrome, with a prevalence of 1:3000 that affects major organs including the brain, spinal cord, peripheral nerves and skin. Approximately 80% of children with NF1 suffer lifelong cognitive deficits. We and others have shown that NF1 mutations confer additional risk for common neurodevelopmental disorders (NDD) including autism spectrum disorder. There are currently no evidence-based treatments for the NDDs in NF1. Research to date is based on mouse models which are limited in modelling higher cognitive functions and have not led to any useful targeted therapies. Increased understanding of how NF1 mutations affect brain development in a human setting will allow for the advancement of therapeutic strategies that rescue neurodevelopmental deficits and will significantly improve the quality of life of individuals with NF1.

This project will investigate how and why 80% of children with the genetic syndrome NF1 develop neurodevelopmental disorders. To answer this, we will use our established unique NF1 patient-derived stem cell models to characterise the neuronal deficits in individuals with NF1. Specifically, human stem cell-derived brain cell networks will be generated to examine the effects of NF1 mutations on neuronal development, determine how well they connect together in networks and whether they are able to function efficiently. Various drugs targeting specific pathways important in NF1 will also be used in the stem cell derived neuronal networks to determine whether they can reverse the biological abnormality in these cells. Some of the techniques that will be used in this project include stem cell culturing, differentiation of stem cells into brain cells, confocal microscopy, network activity assays, drug screening techniques, real time PCR and western blot analysis. This project will help us understand the molecular mechanisms underpinning neurodevelopmental deficits associated with NF1 and identify effective treatments for the neurodevelopmental aspects of NF1.

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Is this project offered for Masters? Yes

34. Improved modelling of human cortical development using multi-lineage transcription factor induced stem cell differentiation

Studies into human cortical development (or corticogenesis) have identified unique cellular processes during embryogenesis which further our understanding of how the human cortex is formed. During corticogenesis, excitatory neurons expand and mature from local neural precursor cells, whilst inhibitory interneurons migrate into the developing cortex from ventral structures. In the third trimester, a neuron-to-glia switch occurs where neural precursors in the cortex begin to generate astrocytes - the support cells within the brain necessary proper brain function. Researcher’s have attempted to model cortical development in culture using human embryonic stem cells (hESC's) which they differentiate using extra-cellular mitogens and inhibitors to promote neural differentiation. To date, mitogen-based cortical differentiation protocols have improved both in reproducibility and complexity. However, long-term differentiation (6+ months) is required to obtain astrocyte development and ventrally-derived inhibitory neurons are underrepresented, making it difficult to assess mature aspects of cortical function in a reasonable timeframe. Rapid
neuronal differentiation techniques have allowed the generation of mature neurons within 4 weeks of differentiation. Although useful, they only contain a single cell-type and lack the multi-cellular complexity of the human brain.

We have recently developed three transgenic hESC lines with inducible knock-in cassettes expressing excitatory neuron, inhibitory interneuron and astrocyte specific transcription factors respectively which rapidly generate all 3 cell types when induced. The aims of this project are to characterise the fidelity of these lines at accurately generating 3 cortical cell types and whether co-culturing of these three cell-types influences the maturity and complexity of neuronal networks and connections over-time. The co-culture methods creates a more complex, physiologically relevant in vitro model that mimics cortical development more closely to gain a better understanding of the developing human brain.

This project will involve molecular biology techniques including rtPCR, protein quantification, hESC culturing, immunofluorescence, calcium imaging and multielectrode arrays to address the project aims.

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Is this project offered for Masters? *Yes*

### 35. How does ACTN3 deficiency influence the long-term response to anabolic steroids in muscle?

Alpha-Actinin-3 (ACTN3) is a major structural component of skeletal muscle. 1 in 5 people worldwide are completely deficient in alpha-actinin-3 due to homozygous inheritance of a common null polymorphism (R577X) in ACTN3 (ACTN3 577XX). While this does not cause disease, alpha-actinin-3 deficiency results in significantly lower muscle mass, reduced muscle strength/power generation but enhanced endurance performance capacity in elite athletes and in the general population. To date, there is no Olympic level sprint athlete who carry the ACTN3 577XX genotype. We have generated a knockout mouse (Actn3 KO) to model human alpha-actinin-3 deficiency.

Using this model, we have shown that alpha-actinin-3 deficiency decreases muscle mass and fast-twitch muscle cell size, shifts muscle glucose metabolism towards slower, oxidative phosphorylation and increased response to exercise training - all of which explains the changes in muscle function in ACTN3 577XX humans. Recently, we found that alpha-actinin-3 deficiency also reduces expression of androgen receptor (AR) and downstream AR signalling in skeletal muscle. Interestingly, acute treatment of Actn3 KO mice with the androgenic anabolic steroid (AAS) dihydrotestosterone (DHT) showed that alpha-actinin-3 deficiency diminishes the muscle growth response to AAS doping. It is thought that there is also a long-term effect with AAS doping. It is postulated that skeletal muscle has a cellular memory in which hypertrophy is 'remembered' through the retention of newly recruited myonuclei long after steroid exposure, and this is reactivated upon exercise training. This has implications for anti-doping policy making in elite sports, as it suggests that someone who "dopes" once with AAS may acquire a life-long physical advantage.

This project will examine the effect of alpha-actinin-3 deficiency on the long-term effects of acute steroid exposure. Silastic tubing containing solid DHT (or empty tubing) will be implanted in WT and Actn3 KO mice for 6 weeks, then removed. Three weeks after implant removal, mice will then
undergo resistance training for 8 weeks by weighted ladder climbing. Mice will then be evaluated for increases in muscle force generation and muscles harvested for analysis. This project will involve animal handling and laboratory-based techniques such as immunohistochemistry, western blotting and muscle physiology.

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Is this project offered for Masters? Yes

36. Improving outcomes of mitochondrial diseases using human stem cell models
Mitochondria are our cellular power plants that burn sugars, fats and proteins to generate energy. Each week in Australia a child is born with a severe mitochondrial disorder. Many of these children die in the first years of life and most suffer from severe disease, particularly affecting their brain and/or heart. Access to these tissues from patients is limited, making it difficult to assess the impact on mitochondrial and other pathways contributing to disease pathology. This project involves the characterization of human pluripotent stem cell models of mitochondrial energy generation disorders that can be differentiated into clinically relevant cell types.

The aims include:

1) Developing cellular models of mitochondrial disease using human Embryonic Stem Cells (hESCs) and human Induced Pluripotent Stem Cells (iPSCs) to study phenotypic rescue of novel defects, pathogenicity and treatment approaches.

2) Characterize pathogenic pathways by assessing the impact of these energy generation defects on cardiomyocytes generated from hESCs or iPSCs, as well as their impact on mitochondrial function and cellular physiology.

3) Define the impact of targeted therapeutic strategies in these models on the cellular proteome and other markers of cellular homeostasis.

We have established a mitochondrial disease panel of hESCs using CRISPR/Cas9 mediated gene disruption, and iPCs from mitochondrial disease patient fibroblasts. This project will validate selected cell lines from this panel and differentiate them to cardiomyocytes to assess the impact of the gene knockout on various aspects of mitochondrial and cellular function. Molecular and cellular characterizations may include generation of correction lines, mitochondrial and cellular functional assays (e.g. ATP synthesis, fluorescence microscopy, FACS, multi-electrode arrays), quantitative proteomics and RNAseq. Students will develop skills in cell culture, molecular biology and biochemistry.

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Is this project offered for Masters? Yes
37. Genetic Diagnosis of Children with Vascular Anomalies for a Therapeutic Clinical Drug Trial

Young people with differences of sex development / intersex conditions may have differences in the genital appearance resulting in potential genital examinations for ongoing assessment and some may require genital surgery. The impact of these examinations and their preference for what age their surgery is undertaken is a current topic of debate. This will be a qualitative exploration with co-design input to try and understand the preferences of young people who have been exposed to either genital examinations and/or genital surgery as part of their clinical care.

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Is this project offered for Masters? Yes

Non-laboratory based

Infection and Immunity

38. Identifying a diagnostic test for food allergy that can replace the food challenge

Food allergies are a major health burden globally, and Australia has the highest reported rates. Currently, the oral food challenge (OFC) remains the gold standard test to detect presence or absence of food allergy and the only test to detect response to food immunotherapy (sustained unresponsiveness, also referred to as remission of allergy). While allergen-specific IgE (sIgE) can support the diagnosis of food allergy, these tests have high sensitivity but poor specificity, so can confirm allergy diagnosis at high concentrations or with positive clinical history, yet perform poorly as screening diagnostic tests and as tests for allergy resolution. Despite significant research effort, advances toward identifying an affordable, safe and simple alternative to the OFC has been severely limited by the absence of well phenotyped longitudinal studies that measure both immune biomarkers (skin prick test, serum sIgE) and challenge-confirmed food allergy outcomes at multiple time points. Our suite of internationally unique studies at the Murdoch Children’s Research Institute overcomes this obstacle. We have developed a novel modelling approach that can accurately detect (test for) and predict (forecast) a child’s allergy status following peanut oral immunotherapy treatment. Further work is now required to validate this approach and to establish similar predictive models for detecting and predicting response to egg and milk oral immunotherapy. Additionally, this approach will be applied to develop accurate models that diagnose food allergy at first presentation (untreated patients) and predict the likelihood of future resolution of food allergy. This project is an exciting opportunity for a student with a biostatistics background to work with us in further testing and developing this algorithm for detecting response to food immunotherapy and diagnosis of food allergy.

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Is this project offered for Masters? Yes
39. Off-target effects of BCG vaccination on allergic and infectious disease in adults

Interested in being part of the largest BCG vaccine trial of its kind worldwide? In addition to protecting against its target disease, tuberculosis, the Bacillus Calmette-Guérin (BCG) has beneficial off-target ('heterologous' or 'non-specific') effects on human health. This includes reducing all cause infant mortality, likely by protecting against non-mycobacterial infectious diseases. Studies also suggest the BCG vaccination protects against allergic disease in children. The BRACE trial is our international RCT of in nearly 7000 healthcare workers across 34 sites in five countries. This trial is working to determine if BCG vaccination reduces the impact of COVID-19 and other respiratory diseases.

In addition to data on respiratory illness, data was collected on other non-respiratory infections, and allergic and autoimmune disease. Using data collected from participants in the BRACE trial you will investigate the clinical off-target effects of BCG on non-respiratory infections, allergic and autoimmune disease in adults. Moreover, you will identify factors which influence the off-target effects of BCG. In this project you will have the opportunity to combine clinical findings with existing immunological data from the BRACE trial. The findings of this project will provide important insights into the off-target effects of BCG vaccination in adults and the factors that influence these responses. The Infectious Diseases Laboratory is located at the Murdoch Children's Research Institute, part of the Melbourne Children's Campus, which also includes the Royal Children's Hospital and the University of Melbourne.

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Is this project offered for Masters? Yes

40. Donor human milk for infants of mothers with gestational diabetes

More than 40 000 infants are born to mothers with gestational diabetes (GDM) in Australia each year. In addition to other morbidities, these infants are at high risk of developing hypoglycaemia, which is associated with adverse neurodevelopmental outcomes. Infants of mothers with GDM often require admission to neonatal intensive care, and frequent blood tests for glucose monitoring. Most infants cannot access sufficient maternal breast milk in the first 24-48 hours of life to maintain normoglycemia. These infants are highly likely to require supplemental nutrition, with the majority receiving in-hospital cow's milk formula supplementation. Cow's milk formula increased long term risks of cow's milk allergy and metabolic disorders (obesity, hypertension). There is emerging evidence that donor human milk may help infants of mothers with GDM, as short-term supplementation to maintain normoglycemia, ensuring an exclusively human milk diet and acting as a bridge to breastfeeding until the infant can access sufficient maternal milk.

This project will involve collection of baseline data about in-hospital feeding practices for infants of mothers with gestational diabetes at the Royal Women's Hospital and Frances Perry House (co-located private maternity hospital) over a 3-month period. You will also be asked to assist in development of an electronic parent survey examining perceptions of donor human milk (benefits and risks) for term born infants. The data collected in this study will be suitable for publication, and
will also assist in development of a randomised controlled trial of donor human milk for infants of mothers with GDM.

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Is this project offered for Masters? Yes

41. Enhanced virtual home sleep studies in Duchenne Muscular Dystrophy patients
Children with Duchenne Muscular Dystrophy (DMD) require sleep studies to diagnose sleep disordered breathing however many patients struggle to sleep in a hospital environment and the waitlists for in hospital ("in-laboratory") studies is lengthy. The aim of this study is to assess whether our enhanced virtual home sleep studies are feasible in a cohort of children with DMD. The current gold standard sleep diagnostic test remains in-laboratory attended polysomnography (PSG) - known as level 1 PSG. PSG's have multi-channel monitoring with video, audio, and are attended by a trained sleep scientist. They are expensive and hard to access (long waiting times), hence associated with delays in treatment which may increase health burden to the child. Our service offers level 2 home PSG via Hospital-in-the-home, however these studies are unattended, limited channel, lack video/audio and carbon dioxide monitoring and hence have limited ability to diagnose hypoventilation which is important in children with neuromuscular disease eg DMD. They are not currently recommended by the American Academy of Sleep Medicine due to insufficient evidence, however we recently published details of our level 2 service at RCH challenging this idea. To address limitations of current level 2 home PSGs, we have developed novel equipment capable of level 2 PSG acquisition with the addition of transcutaneous CO2, camera and audio monitoring bringing it up to level 1 capability. In addition, the new set-up includes capability to connect to hospital servers and allow virtual monitoring. This new optimised virtual home PSG process has been piloted on 5 patients with successful data acquisition from the patient’s home. Thus, the new home equipment meets the gold standard diagnostic capability of level 1 PSG in hospital. Children with DMD need regular access to polysomnography as part of routine care, particularly in the teenage years where they are more prone to hypoventilation in the context of their declining lung function. This study evaluates a new novel system for home sleep studies with benefits to the patients, families and hospital sleep service.

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Is this project offered for Masters? No

42. Wearable devices for the monitoring of sleep and sleep disordered breathing in children
The aim of this study is to assess the feasibility of wireless, wearable electronic skin sensors to measure sleep and sleep disordered breathing in a paediatric population alongside the gold standard
diagnostic sleep test. Polysomnography (PSG) is the current gold standard for the assessment of sleep and sleep disordered breathing. A PSG setup at the RCH involves application of 32 sensors to the patient, connected to a digital amplifier at the bedside via a series of long wires. This setup is often not tolerated by a subset of our patients, e.g. children with sensory issues, developmental delay and severe anxiety. Recent advancements in microelectronics and fabrication techniques have introduced a new avenue for the collection of relevant physiological data in this patient population - wireless wearable devices. Two such devices now have TGA approval, the Somfit and the Sunrise. Somfit is a wireless wearable device applied with a single sticker on the forehead and measures electroencephalography (EEG), electrooculography (EOG) and oxygen saturation (SpO2). These variables are used in the analysis of sleep versus wake, different stages of sleep and arousal from sleep. Sunrise is a wireless, wearable device applied with a single sticker to the chin and measures mandibular movements as a surrogate for upper airway movements and respiratory effort and is used to generate an estimate of respiratory disturbance index. This index is a marker of sleep disordered breathing. We propose that these sensors will improve our capability to collect usable sleep data in our patient population, and would provide us a viable alternative in patients where a full PSG setup cannot be applied. We are confident this will substantially improve our diagnostic yield by reducing signal loss and study failure, and thus enhance our ability to provide care and improve clinical outcomes in all children with sleep disorders.

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Is this project offered for Masters? No

43. Sleep quality in children and adolescents with Cystic Fibrosis in hospital versus Hospital in the Home (HITH)

Children and adolescents with Cystic Fibrosis have more sleep disturbance than healthy children. Poor sleep quality has a negative effect on immune function and pain tolerance, both critical to recovery from illness. Additionally, sleep disturbance during hospital admission may negatively impact on the coping skills of children and their co-sleeping caregivers. Whilst sleep is fundamental to a child’s health, previous studies have shown that children have shorter sleep duration and more sleep disturbance in hospital than at home. To date no studies have investigated sleep quality in children and adolescents with CF in the inpatient setting. This study will compare their sleep quality whilst an inpatient in hospital and at home. The aims of this study are to evaluate objective and subjective measures of sleep quality in children and adolescents with Cystic Fibrosis (CF) during hospital admissions and Hospital in the Home (HITH) admissions. Also, to assess perspectives (child, caregiver, nurse, doctor) on the most frequent disruptors of sleep during inpatient admissions. Objective measures of sleep patterns and quality include actigraphy (a wrist-worn device that quantifies sleep using a movement algorithm) together with a sleep diary. Subjective measures of sleep patterns and quality include standardised questionnaires and a medical record review from each admission. We hypothesise that children with CF admitted to hospital are exposed to factors which reduce the duration and quality of their sleep in addition to the sleep disruption associated with a disease exacerbation. These extrinsic factors are potentially modifiable through behaviour change and reconfiguration of the clinical environment. The results of this study will inform the design of an intervention study that targets modifiable, child-centred alterations to night-time ward
culture, focusing on measurable child and parental outcomes. This quality improvement project has the potential to improve sleep quality for all children and parents during hospitalisation at both the RCH.

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Is this project offered for Masters? No

Cell Biology

44. Benchmarking, mining and visualisation of spatial transcriptomics datasets for congenital diseases

The formation of the human body relies on the deployment of the right genes at the right time and place during embryo development. Any perturbations will lead to anatomical malformations and will eventually result with the baby being born with congenital defects. Genes interact in complex spatial 3D environments in cells and tissues, and the timing and location of these interactions play a critical role in embryo formation. This project leverages on the novel spatial transcriptomics technologies to identify components of the developmental gene regulatory networks (GRNs) at spatial resolution. The project will involve benchmarking of emerging tools for spatial transcriptomics data analysis, mining spatial transcriptomics data in the context of childhood disease and developing visualisation tools in immersive environments. The candidate is expected to have strong bioinformatics, computational, statistical, mathematical training or equivalent, with a strong interest in biological processes and will be based at the Murdoch Children's Research Institute.

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Is this project offered for Masters? Yes

Clinical Sciences

45. Changing respiratory admissions for children with neurodisability across the pandemic

Children with neurodisability, for example cerebral palsy, are at increased risk of serious respiratory infection due to a number of factors related to their neuromuscular status, and have a high burden of repeated and lengthy hospitalisations. There is growing evidence of the decrease in respiratory infections during periods of social restrictions employed to reduce Covid-19 transmission across the population. However, since children with NI have different causes to their respiratory risk compared to the broader population, it is hard to know how relevant population data is. This study aims to investigate patterns in hospitalisation for lower respiratory tract infections among children with neurodisability relative to Covid era - three periods will be investigated, prior to Covid (<2020), during periods of Covid social restrictions (2020-2021), and in a period of Covid exposure without restrictions (2022). Patient and hospitalisation data will be collected from the electronic medical record and categorised by number of admissions, length of stay, reasons for admissions, clinical markers and pathogen if known. Additionally, a survey will be used to examine patient and family factors that might influence respiratory risk across these periods. Among other factors, the survey
will explore whether families practiced measures over and above government restrictions to reduce Covid-19 risk and whether their children with neurodisability attended school when able.

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Is this project offered for Masters? Yes

46. Children born with a congenital anorectal malformation: patient and parent outcomes
Children born with an anorectal malformation (ARM; inappropriate placement of the anus and rectum) require surgery to establish a normal anus and rectum. Despite significant surgical advances, these children face unique diagnostic and management challenges. Parents and families of children with an ARM are also significantly impacted. This study will recruit families of children who have previously undergone surgery for ARM and are currently managed at The Royal Children's Hospital (Melbourne). Families will complete a survey (via telephone) to explore parent wellbeing (anxiety and depression), parent quality of life, and parent experience of illness. Patient/child quality of life will also be explored via validated measures. This is part of a larger longitudinal study involving the Colorectal and Pelvic Reconstruction Service (Department of Paediatric Surgery) at The Royal Children's Hospital and Murdoch Children's Research Institute.

Associate Professor Sebastian King  
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Is this project offered for Masters? Yes

47. Children born with Hirschspung disease: patient and parent outcomes
Children born with Hirschsprung disease (HD; a condition that prevents the last part of the rectum from relaxing) require an operation to establish normal function. Despite significant surgical advances, these children face unique diagnostic and management challenges. Parents and families of children with HD are also significantly impacted. This study will recruit families of children who have previously undergone surgery for HD and are currently managed at The Royal Children's Hospital (Melbourne). Families will complete a survey (via telephone) to explore parent wellbeing (anxiety and depression), parent quality of life, and parent experience of illness. Patient/child quality of life will also be explored via validated measures. This is part of a larger longitudinal study involving the Colorectal and Pelvic Reconstruction Service (Department of Paediatric Surgery) at The Royal Children's Hospital and Murdoch Children's Research Institute.

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Is this project offered for Masters? Yes
48. Improving accuracy of blood pressure measurement in children

Blood pressure is an important vital sign that is relied upon by clinicians to care for children in many hospital and non-hospital settings and with a variety of conditions, including congenital heart disease, chronic kidney disease, and paediatric hypertension. However, there is limited data available regarding the accuracy of non-invasive cuff blood pressure measurement in children. Automated cuff devices may be inaccurate for a number of reasons: 1) they often use proprietary algorithms (based on the 'oscillometric method') that were developed for adults, 2) they are not validated in children, and/or 3) the reference standard used for validation is also a cuff-based method (the 'auscultatory method') that involves inherent errors that are not well characterised. The overarching goal of this project is to better characterise, and ultimately improve, the accuracy of non-invasive blood pressure measurement in children. The student will recruit 35 children from the Royal Children's Hospital Paediatric Intensive Care Unit, who are undergoing planned surgery for congenital heart disease or spinal problems. During their post-operative recovery, recordings of cuff blood pressure (using the oscillometric and auscultatory methods) will be acquired during simultaneous measurement of the 'gold-standard' invasive method via a radial arterial catheter. This data will enable us to characterise the accuracy of current methods, as well as the development of new paediatric-specific algorithms that could be incorporated into future devices. The project would best suit a student with some background/interest in medical technology or biomedical engineering, and who would like to gain experience in clinical research.

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Is this project offered for Masters? Yes

49. Mitral Valve in Patients with Aortic Arch Hypoplasia

Evaluate the consequences of the mitral valve anatomy of long term outcomes of patients with hypoplastic aortic arch.

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Dr Remi Kowalski  
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Is this project offered for Masters? No

50. The effect of anti-epileptic drugs on bone health

This project builds on pilot data from our group, in taking the next steps to set up a longitudinal cohort of young people taking AEDs with sibling controls. Subjects will undergo assessments of bone density and muscle function, along with biochemical testing and questionnaires to establish risk factors for bone health outcomes. The cohort will be followed for 3-5 yrs but a higher degree student will gain invaluable experience in setting up the cohort, establishing baseline data, undertaking analysis of these data including advanced analysis techniques such as finite element modelling.

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Prof Mark Mackay  
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51. Informing the Psychological Care of Children and their Families in the Colorectal and Pelvic Reconstruction Service (CPRS)

The Colorectal and Pelvic Reconstruction Service (CPRS) was established in 2019. It is a multidisciplinary service that aims to deliver comprehensive clinical care to children and families with complex colorectal and pelvic conditions such as Anorectal Malformations (ARM), Hirschsprung Disease (HD) and Chronic Constipation (CC). Compared to other congenital disorders, there is very little research available on what the impact of diagnosis, hospitalisation (including surgery) and illness in families of children aged 0-12 years with HD and ARM. This is despite the number of surgeries and medical treatments that children have, including their social adjustment to their condition. There are often chronic significant psychosocial challenges that children experience with a colorectal condition. This study aims to conduct semi-structured interviews with parents of children aged 0-12 years old to explore the perceived psychological impact of illness, hospitalisation and surgery on the child and family.

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Is this project offered for Masters? Yes

52. A qualitative study of young peoples with differences of sex development/ intersex conditions and their attitudes towards genital examinations and genital surgery

Young people with differences of sex development / intersex conditions may have differences in the genital appearance resulting in potential genital examinations for ongoing assessment and some may require genital surgery. The impact of these examinations and their preference for what age their surgery is undertaken is a current topic of debate. This will be a qualitative exploration with co-design input to try and understand the preferences of young people who have been exposed to either genital examinations and/or genital surgery as part of their clinical care.

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Is this project offered for Masters? Yes

53. Is there a role for Mechanical Power in neonatal respiratory disease

Respiratory failure is the most common reason why an infant needs care in intensive care. Supporting the diseased neonatal lung comes with the risk of causing injury that can persist into adulthood. In adult ICU it is now understood that the pressure (mechanical power) placed on the lung is a major cause of lung injury. It is unknown if mechanical power influences neonatal lung
injury. In this clinical project students will work in The Royal Children’s Hospital NICU to measure the lungs of babies needing respiratory support to determine whether mechanical power is different in babies with and without acute lung disease. Students will learn how to measure lung physiology in babies.

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Is this project offered for Masters? Yes

54. Social media and decision-making in the neonatal intensive care unit  
Social media has influenced the way in which parents engage with the healthcare system and receive health information. This project will explore how social media influences parental decision-making for critically unwell babies with rare diseases using novel qualitative methodology. The student will have the opportunity to learn qualitative methodologies including thematic analysis, ethical enquiry and gain exposure to activities of the Children’s Bioethics Centre and the neonatal intensive care unit. The student will be supported by a team of neonatal intensivists and clinical ethicists with the opportunity to develop a paper and present at conferences.

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Is this project offered for Masters? Yes

Population Health

55. Maternal COVID19 infection and infant hearing screening outcomes: A retrospective audit of data from the Victorian Infant Hearing Screening Program (VIHSP)  
The Victorian Infant Hearing Screening Program (VIHSP) is a state-wide program that screens the hearing of newborn babies in their first few weeks of life. Early detection of a hearing impairment and remediation within the first months of life can significantly reduce the serious developmental impacts of infant hearing loss. Newborn Hearing Screening (NHS) programmes provide a unique opportunity to investigate a potential relationship between maternal infection and neonatal hearing loss. There is a known association between certain maternal viral infections and hearing loss in neonates. The aim of this project is to conduct a retrospective audit of VIHSP data looking at the relationship between maternal COVID infection and infant hearing screening outcomes?

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Is this project offered for Masters? Yes
56. Understanding teens with hearing loss in Victoria
The last 20 years have seen significant changes to methods of detection, intervention and services available to deaf and hard of hearing children. Universal newborn hearing screening, early intervention and cochlear implantation have revolutionised the opportunities for deaf and hard of hearing children, but their language, learning and wellbeing still lag behind their hearing peers. This project will sit within VicCHILD (The Victorian Childhood Hearing Longitudinal Databank) which has almost 1200 participants with hearing loss aged 0 to 19 years and holds a wealth of survey data, direct assessment data and linked data on participants.

This project will involve searching the literature and designing the appropriate measures to collect outcomes from approximately 80 young people aged between 15 and 19 in the VicCHILD databank. Areas of research focus could include quality of life, mental health, social skills, language skills, academic attainment, life pathways.

Past research in children with hearing loss has focused on younger age groups, and the VicCHILD databank presents a unique opportunity to investigate outcomes of deaf and hard of hearing teens.

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Is this project offered for Masters? Yes

57. Determining the top research priorities for child hearing loss
The Victorian Childhood Hearing Longitudinal Databank (VicCHILD) is a statewide registry for Victorian deaf and hard of hearing children, with the aim of finding ways to optimise outcomes for these children. Since 2012, it has almost 1200 participants with hearing loss aged 0 to 19 years, and holds a wealth of survey, direct assessment and linked data on participants at baseline, 2 years, 5-7 years and 9-12 years. VicCHILD is now interested in putting focus on analysing its data to answer research questions that matter most to families of deaf and hard of hearing children. In 2022, we are completing focus groups with VicCHILD participant parents to gain an overall understanding of what their top research priorities may be. This project will use the results (themes) generated from these focus groups to design a short survey to be delivered to VicCHILD participant families to rank the themes, then complete focus groups/interviews with hearing health stakeholders (clinicians / audiologists / early intervention services) to determine the top research questions that can be answered through VicCHILD.

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Is this project offered for Masters? No

58. ASQ-STEPS Learning Progressions
Learning and development assessments are commonly used in early childhood to identify children’s developmental skills and progress. These assessments are typically designed for use by clinicians
with health-based qualifications, such as Allied Health Practitioners, and result in quantitative scores which must be interpreted. These scores are not easily applied by educators in early education settings in a meaningful way. To make results relevant for educators we need to develop qualitative descriptions of the scales that underpin the assessments. These descriptions, also known as learning progressions (LP), illustrate the breadth of skills within a measure and the typical sequence of progression observed. They provide explicit guidance and a common language for educators to support them to 1) target their practice at the appropriate developmental level for the child; and 2) describe and monitor developmental progress. In Australia, a project to create a culturally appropriate, psychometric assessment for Aboriginal and Torres Strait Islander children is underway. The ASQ-Steps for Measuring Aboriginal and Torres Strait Islander child development (ASQ-STEPS) is a developmental outcome measure which provides information about children’s developmental progress. The results of the ASQ-STEPS are quantitative, and require additional translation to inform educational practice. This study will work with ASQ data to develop Learning Progressions for ASQ-STEPS domains.

The project will include:

1. Reviewing the relevant literature - Learning Progressions and use of assessments in early years;
2. Exploration of the alignment of the ASQ domain/s with early childhood learning and development frameworks;
3. Analysis of existing ASQ data to develop draft ASQ-STEPS Learning Progressions for use in the Aboriginal and Torres Strait Islander context; and
4. Creation of practice examples illustrating how the ASQ-STEPS Learning Progressions would be used to map evidence-based teaching practices to different levels of developmental progression within the domain/s.

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Is this project offered for Masters? **Yes**

**UNIVERSITY OF MELBOURNE HONOURS ENTRY REQUIREMENTS**

To be eligible to enter the Bachelor of Biomedicine (Degree with Honours) or the Bachelor of Science (Degree with Honours), applicants must satisfy both:

- the Faculty of Medicine, Dentistry and Health Sciences (MDHS) or Faculty of Science entry requirements.
- and the requirements of the department offering the Honours program.

Please note demonstrated eligibility does not guarantee a place in the Honours program. All successful applicants will also need to be selected for admission by the Department. The University of Melbourne handbook contains detailed information.
about the subjects available and entry requirements for departments offering Honours. [https://handbook.unimelb.edu.au](https://handbook.unimelb.edu.au)

For further details please visit;

Department of Paediatrics: [www.paediatrics.unimelb.edu.au](http://www.paediatrics.unimelb.edu.au)

MCRI: [https://www.mcri.edu.au/students/honours-students](https://www.mcri.edu.au/students/honours-students)

MDHS: [http://sc.mdhs.unimelb.edu.au/entry-requirements](http://sc.mdhs.unimelb.edu.au/entry-requirements)

**HOW TO APPLY - MDHS HONOURS**

**Course Codes:**

Bachelor of Biomedicine (Honours) – **BH-BMED**

Bachelor of Science (Honours) – **BH-SCI**

RCH Academic Centre Enrolling Unit is: **Department of Paediatrics**

If you wish to be considered for Honours in 2023, and you would like to undertake your project and coursework with the Murdoch Childrens Research Institute, Royal Children’s Hospital, Academic Centre, Faculty of Medicine and Dentistry Sciences with the enrolling unit being Department of Paediatrics, you will need to carry out a FOUR STEP PROCESS.

**STEP 1: Look for Projects and Contact Potential Supervisor (Note: 2023 Start Year Intake projects will be available in Sonia by mid-August.)** You will need to decide which Supervisor(s) and Project(s) that you wish to apply for. To do this, contact potential supervisors listed in this Handbook, you should speak to them and organise a meeting to discuss the project further. Projects available for 2023 are also listed on the Murdoch Childrens Research Institute and Department of Paediatrics websites.

**STEP 2: Submit Online Application:** Register for the Honours Application Tracking System (SONIA) before making your application in SONIA. Lodge an online application by Monday 31 October 2022 (Round 1), and Friday 20 January 2023(Round 2).


**STEP 3: Submit Project preference in Sonia:** For Round 1 applicants, once you have submitted an online course application and met the minimum entry requirements, you will receive an email within 3 working days with your personal login to access the Honours Project Preference System – Sonia. Please follow the instructions to set up your login and submit your project preferences. If you have applied for Round 2, you will be contacted in early January about project preference submission in Sonia. You
may select up to 4 project preferences in Round 1 or 3 project preferences in Round 2 and mid-year. You MUST contact the relevant supervisor(s) and reach an agreement before selecting their projects. You can log into Sonia to change your preferences any time by the preference submission closing dates.

**STEP 4: Respond to Your Offer:** Round one offers for entry into 2023 will be issued around mid-December 2022. Students must accept their offer by the Offer Lapse Date notes in their offer letter. Students who meet the minimum entry requirements but are not made a Round 1 offer may be considered for Round 2 under specific circumstances, but that is not guaranteed.

**UNIVERSITY OF MELBOURNE MASTER OF BIOMEDICAL SCIENCE**

The Master of Biomedical Science is a coursework program (Course code MC-BMEDSC) offered through the Department of Paediatrics. This program offers graduates a pathway into research or other science-based careers and can lead on to PhD studies. Students may consider undertaking a Masters as an alternative to the Honours Program.

Students undertake a major research project and discipline-specific coursework subjects offered by MDHS. A range of professional development subjects are offered to complement and enhance the research undertaken and to progress students’ career opportunities.

MDHS:  

**MASTERS RESEARCH PROJECT**

The Master of Biomedical Science is a two-year full-time course (four years part time) and mid-year entry is available. Students must complete 200 credit points comprising:

- Discipline-specific subjects (50 credit points)
- Professional skills subjects (25 credit points)
- Research subject (125 credit points)

The research subject is completed as a project under the supervision of experienced senior scientific researcher/s within a research group at the Murdoch Childrens Research Institute.

To organise the research project, students must speak to the prospective supervisor/s listed in this Handbook for projects marked as available for Masters. Students should meet with the supervisor/s to discuss the project further. Projects available for 2020
are also listed on the Murdoch Childrens Research Institute and Department of Paediatrics websites.

For commencement in semester one 2023

**Applications closing dates**
Semester 1 (February) entry - 30 November
Semester 2 (July) entry - 31 May

**Late application closing dates**
Semester 1 (February) entry - 15 January
Semester 2 (July) entry - 15 June

*late applications may be accepted based on the availability of places. Only timely applications will be considered for Commonwealth Supported Places (CSP).

http://futurestudents.unimelb.edu.au/admissions/applications/grad-dom