



THE UNIVERSITY OF
MELBOURNE

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



HONOURS & MASTERS PROJECTS 2021

[Honours](#) and [Master of Biomedical Science](#)

Student Information Evening: 17 September 2020, 5.30pm

[Register here](#)

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LABORATORY BASED RESEARCH PROJECTS

Infection and Immunity

1. Immune mechanisms of peanut allergy remission

Food allergies are a major health burden globally, and Australia has the highest reported rates of food allergy in the world. There is currently no cure so research has focused on identifying approaches to redirect allergen-specific immune responses away from allergy towards a tolerant state, which can support clinical remission of allergy. Several therapies under investigation can induce remission, which may be transient or long lasting. The immune changes of long-lasting remission are unknown; understanding the key factors that lead to long-lasting remission will enable development of effective long-term treatments for food allergy. We have been investigating a combination treatment, Probiotic and Peanut Oral Immunotherapy (PPOIT), which has been shown to induce long-lasting remission that persists to 4 years post-treatment. By contrast, published reports of peanut oral immunotherapy (OIT) without immunological adjuvant suggest that OIT-induced remission may be short-lived, with two thirds (67%) of treatment responders losing their remission state by 12 months post treatment. The aim of this project is to use a combination of gene expression and flow cytometry approaches to understand the immune mechanisms involved in retraining the allergic response towards long-lasting remission of peanut allergy. Gene expression and flow cytometry data will be generated on immune cells before and after intervention in 1) patients who achieve remission of peanut allergy remission following PPOIT treatment 2) patients who achieve remission of peanut allergy following standard OIT 3) patients who remain allergic to peanut following placebo treatment. Findings will provide clues of key immune factors that drive 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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2. Characterising the immune response to RSV in preterm and term infants

Respiratory syncytial virus (RSV) is the most common viral pathogen associated with acute lower respiratory tract infection in children. Globally, RSV affects 33 million children and causes 60,000 in-hospital deaths in children under 5 years of age each year, with severe infection more likely to occur in preterm infants. The increased susceptibility to RSV among preterm infants is thought to be due to immaturity of the immune system. Using a cohort of preterm and term infant cord blood samples, we aim to characterise their immune response profiles by using a combination of cell culture, flow cytometry and multiplex cytokine assays. This data will provide important insights into the

immunological susceptibility to severe RSV during early life with the promise of developing more targeted approaches to protect this vulnerable group of infants.

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3. Streptococcal transmission and disease

The bacterium *Streptococcus pyogenes* (group A streptococcus, "Strep A") causes a range of mild to severe infections, from sore throat to toxic shock syndrome. Importantly, *S. pyogenes* infections can lead to serious sequelae, such as rheumatic fever and rheumatic heart disease. *S. pyogenes* can also colonise a variety of human tissues, including the upper respiratory tract and skin in healthy people. In a related bacterial species, *Streptococcus pneumoniae*, we have shown that viral co-infection can enhance bacterial virulence, by increasing bacterial density and inflammation in the host, and by driving changes in bacterial virulence gene expression. There is recent clinical epidemiologic evidence that viruses are also important in *S. pyogenes* pathogenesis, but little is known about this process. In this project, you will use murine and cell-culture models to examine the effect of viruses on *S. pyogenes* colonisation, transmission (spread to co-housed littermates) and disease, and the mechanisms involved. To achieve these aims, you will employ a range of methods such as animal and tissue handling, cell-culture, molecular approaches (such as qPCR and gene expression analyses), immunological assays and traditional microbiology. Our laboratory also has the resources and expertise to adapt flexibly depending on the findings you generate throughout the year, or to additional COVID-19 restrictions. These include access to clinical and laboratory isolates, clinical samples, and bioinformatics expertise. Your project will provide important novel data on key components of *S. pyogenes* pathogenesis, and inform a pathway towards improving strategies for preventing *S. pyogenes* infections.

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4. Understanding the importance of variation in the capsular polysaccharide of *Streptococcus pneumoniae*

Streptococcus pneumoniae (the pneumococcus) is a leading cause of morbidity and mortality worldwide. About 100 immunologically-distinct serotypes are known, defined by their unique capsular polysaccharide. Decisions around which serotypes are included in licensed vaccines have largely been based on data from high-income countries. These vaccines have subsequently been introduced into low and middle-income countries (LMICs), where limited local information on serotype prevalence and diversity is often available. Using DNA microarray, we have identified pneumococci from LMICs with significant genetic variation in the capsule locus. Some of this variation is predicted to change the capsule structure, indicating there is potential for undiscovered serotypes and/or the misidentification of existing serotypes. Your project will focus on the identification and characterisation of these variants. This includes the molecular basis of the variation and potential for mistyping, and also the relevance of such changes to the capsule on

pneumococcal pathogenesis. Key approaches to this project include: genetic manipulation of pneumococcal isolates, experiments with DNA and RNA, capsular typing of pneumococcal isolates as well as conducting functional assays in vitro. Our laboratory also has the resources and expertise to adapt flexibly depending on the findings you generate throughout the year, or to additional COVID-19 restrictions. These include access to clinical and laboratory isolates, clinical samples, and bioinformatics expertise. Your work will help uncover novel variants (and potentially new serotypes) to enable improved serological and molecular tools for their detection, which will be vital for accurately assessing vaccine impact and serotype replacement globally.

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5. Synergistic and antagonistic interplay between *Streptococcus pneumoniae* and respiratory viruses

The contribution of bacterial-viral co-infections to the onset and severity of disease is increasingly attracting interest from researchers globally. Specifically, it is well established that co-infections of *Streptococcus pneumoniae* with respiratory viruses (e.g. Influenza or Respiratory Syncytial Virus) impact the severity of acute respiratory infections. This is because viral replication creates a more hospitable environment for pathogenic bacteria of the respiratory tract to flourish, predisposing individuals to a bacterial superinfection. However, recent research has found that the interplay between pneumococci and viruses is more complex than previously anticipated. We and others have shown that some aspects of co-infection are synergistic (resulting in greater disease severity), while others are antagonistic, where the presence of one pathogen negatively impacts the other. In this project, you will elucidate the underlying microbiological and/or immunological mechanisms that govern the synergistic and antagonistic aspects of the interplay between pneumococci and respiratory viruses. Key approaches to this project include: working with in vivo models, as well as microbiological and immunological analysis of tissues from the respiratory tract and systemically. Our laboratory also has the resources and expertise to adapt flexibly depending on the findings you generate throughout the year, or to additional COVID-19 restrictions. Your work will help us understand the complexities of pneumococcal-viral co-infection, including their implications for the effectiveness of vaccines targeting these pathogens.

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6. Pathogenesis of bacterial pneumonia

Streptococcus pneumoniae (the pneumococcus) is the most common cause of community-acquired pneumonia and a leading killer of children world-wide. However, it is also commonly found as an asymptomatic coloniser of the upper respiratory tract (carriage), particularly in children. We are interested in elucidating the molecular processes by which bacterial species, including the

pneumococcus, can transition from the carriage to infection state, and identifying signals of pneumonia. Previous work in our laboratory using clinical samples collected from children in The Gambia, West Africa, hospitalised with pneumonia, has identified several pneumococcal genes that were upregulated in the lung. Recently, we have collected clinical samples from children with severe pneumonia at the Royal Children's Hospital, including those infected with pneumococcus, group A streptococcus and *Staphylococcus aureus*. Samples include pleural fluid, as well as some nose and throat swabs from these patients.

Your project aims will be to examine bacterial gene expression and genomics in samples and isolates collected from pneumonia patients at the Royal Children's Hospital, and elucidate the role of these candidate genes in causing pneumonia. To do this, you will use a variety of approaches including: measurement of gene and/or protein expression (using methods such as qRT-PCR, RNA-seq, western blotting, and ELISA), and analysing their importance through bacterial mutagenesis and functional assays.

Your project will provide exciting new data on the pathogenesis of bacterial pneumonia. Access to clinical samples such as pleural fluid provides the unique opportunity to examine bacterial gene expression during pneumonia. Our laboratory also has the resources and expertise to adapt flexibly depending on the findings you generate throughout the year, or to additional COVID-19 restrictions. These include access to clinical and laboratory isolates, clinical samples, and bioinformatics expertise.

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Cell Biology

7. Characterising extracellular matrix in bioengineered heart valves

Congenital heart disease is the most common congenital disorder in newborns. Currently, 1 in 100 babies are born with a heart defect, a major portion having heart valve abnormalities. Heart valves play a critical role in maintaining unidirectional blood flow through the chambers of the heart. The only treatment option for heart valve defects is replacement surgery with either a biological or mechanical prosthetic. While these prosthetics are routinely used in adults, there are no prosthetics that are designed specifically for children. This presents a major problem as the child outgrows the valve prosthetic and will have to undergo multiple replacement surgeries until adulthood. Bioengineering a valve has become a viable option in recent years as it eliminates the need for donor tissue and can utilise human pluripotent stem cells (PSCs) as a source of cellular material. We have developed a protocol to differentiate human PSC into heart valve cells that will be used to construct a 3-dimensional valve leaflet using state-of-the-art bioengineering approaches. In this project, we aim to characterise protein expression of the valve leaflets with techniques including immunohistochemistry and western blotting. This project will also involve human stem cell culture, protein extraction, and automated confocal imaging.

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Available as Masters Project: Yes

8. Generating gene edited tools for CRSIPRi screening

The use of stem cells to generate human tissue is now readily available. This provides the ability to understand the role of all genes in disease by interfering with their function within the stem cell-derived models. To facilitate screening to identify the outcome of gene inhibition, it will be necessary to build a stem cell line able to deliver CRISPRi technology. Building such a resource will train the student on gene editing technology and stem cell technology and provide an excellent training ground for eventual screening programs.

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9. Identifying safe harbour loci from stable gene expression

The stable expression of a selected gene is now commonly used in stem cells to change cellular fate, identify cellular state or readout response to compounds. Generating stable expression of an introduced gene requires the identification of 'safe harbours' that will support robust expression of the reporting gene. In this project, the student will generate gene edited lines to test out the appropriateness of different genetic loci to act as safe harbours. This will train the student in gene editing technology and stem cell technology, representing an ideal starting point for a subsequent Masters or PhD

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10. Examining the influence of macrophages on kidney organoid structure and connectivity

The generation of human kidney tissue from pluripotent stem cells is now feasible with protocols based upon our understanding of kidney development able to create complex kidney organoids containing nephrons, stroma and endothelial populations. What we know from studying kidney organoids is that maturation is challenged and some cellular components are absent. We have previously shown that the developing kidney contains resident macrophages and that the presence of these cells support appropriate growth. This project will examine the influence on kidney

organoid morphology and maturation of the introduction of stem cell derived macrophages during culture. The project will train the student in stem cell maintenance and differentiation as well as kidney development.

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11. Assessing the effect of congenital nephrotic syndrome mutations on podocyte calcium flux

Congenital nephrotic syndrome presents early in life and results in kidney failure and resulting severe proteinuria which can be life threatening. The genetically inherited forms of this condition most commonly result from mutation in genes expressed in the podocytes of the glomerulus. We have developed a method for generating human kidney tissue from pluripotent stem cells that represent good models of the human kidney. We have also established that we can model genetic nephrotic syndrome in this way. In characterisation of the forming glomeruli in this stem cell-derived kidney model, we have identified transient calcium flux within podocytes that may be related to the degree of podocyte cell-cell interaction. This project would seek to examine the effect of congenital nephrotic syndrome mutations on this podocyte readout as a measure of disease severity. The project would include the use of patient and genetically edited pluripotent stem cells and will train the student in stem cell maintenance and differentiation as well as kidney development and disease.

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Clinical Sciences

12. Cord Blood Stem Cell Therapy in Children at High Risk of Heart Failure

Our work seeks to reduce the high risk of heart failure and death faced by children with severe and complex heart diseases. Babies born with severely malformed heart and blood vessels that are inadequate for normal blood circulation undergo a series of complex heart operations, the first is performed on day 2 or 3 of life (Norwood procedure). Even after surgery, the heart is under great metabolic and mechanical stress as excessive demands do not allow normal heart muscle growth to sufficiently support blood circulation leading to high mortality in the first year of life. In other children with heart failure due to heart muscle damage (cardiomyopathy), surgical implantation of a ventricular assist device (VAD, mechanical pump) supports heart function, alleviating pressure and volume overload to allow potential adaptive repair, muscle growth, improved muscle function and weaning from the pump. However many still require a heart transplant or die within 2 years of diagnosis. From our previous research and that of others, cord blood stem cells (CBSC) have been found to stimulate normal heart muscle growth, increase pumping capacity, and reduce inflammation, fibrosis and metabolic stress after surgery. In order to apply this, we have designed a

safe way to directly treat the heart with CBSC during the cardiopulmonary bypass surgery that is employed in the Norwood and VAD implantation procedures. Depending on the qualifications and interests, a number of research projects are available at honours, Masters or PhD level, involving laboratory or clinical based work. Student background and research interests are ideally in one or more areas such as: physiology, immunology, haematology, genetics, biochemistry, pharmacology, surgery, veterinary medicine or medicine.

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Genetics

13. The use of stem cells and a monogenic model of asd to understand the neurobiology of autism

Autism (or autism spectrum disorder; ASD) is a neurodevelopmental disorder characterised by debilitating impairments in social communication and restricted interests and repetitive behaviours. In most cases, the cause of autism is unknown and because of this, there are no effective treatments for autism in the general population. However, a subset of individuals (15-20%), autism occurs in children with a clinically defined syndrome which arise from a single gene disorder. This is the case in children with neurofibromatosis type 1 (NF1), an autosomal dominant disorder caused by a loss-of-function mutation in the NF1 gene. Studying monogenic forms of autism are a logical entry point to systematically explore the neurobiological mechanisms of ASD. In this project, we will use NF1 as a monogenic model of ASD to understand the neurobiological mechanisms that contribute to ASD in this population. Whilst animal models have traditionally been used by researchers to understand disease mechanisms, translation from animal studies to effective human clinical trials has proven difficult, including in NF1. A potential explanation for this is the inadequacy of animal models to recapitulate the complexity of the human disease state. This project will use human preclinical models to characterise the neuronal deficits in individuals with NF1. Specifically, human stem cell-derived brain cell networks (comprising neurons and glia) will be used 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.

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14. Molecular diagnosis and gene discovery for individuals with vascular anomalies

Our understanding of the genetics of vascular anomalies (VA) is rapidly advancing, but remains incompletely understood. An inherited germline mutation may predispose to the development of VA with a somatic 'second hit' mutation required within the affected tissues to produce each lesion. The Vascular Anomaly Clinic at RCH has a large cohort of patients with a wide variety of VA, including those associated with overgrowth syndromes, such as Proteus and PIK3CA Related Overgrowth Syndrome (PROS). Most of these patients are sequencing naïve as they have been unable to access molecular testing. Since VA appear to be largely driven by mutations in genes involving cancer pathways, including the PI3K-AKT and the RAS-MEK-ERK pathways, there is the potential for the development of genomically-targeted therapies. This is a rapidly evolving field and access to genomic sequencing for individuals with VA is a high clinical priority. While analysis of germline DNA may not identify a mutation in individuals with VA, sequencing DNA from surgically resected tissue specimens often reveals the causative variant. High-depth sequencing or droplet digital PCR are key in detecting and quantifying mosaic variants in tissue specimens that may be present in only a small fraction of cells (~1-2% allele frequency). Identification of specific germline and somatic mutations may lead to specific targeted surgical or pharmacological interventions for these often devastating conditions that may be intractable to standard clinical care. Aims: 1. To perform genomic sequencing (germline and somatic) in individuals with VA, including sporadic and familial cases, to identify causative mutations. 2. To gain hands-on experience with current genomic technologies and understand their appropriate application, strengths and limitations. This project provides the opportunity to work in a multidisciplinary clinical and laboratory research team. In addition to laboratory experience, the development of project management, sample coordination and communication skills will be fostered.

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15. Investigating the molecular basis of parkinson's disease using novel genetic models

Parkinson's disease is a prevalent neurodegenerative disorder with largely unknown cause. However, recent advancements in genomic technologies have led to the identification of over 20 genes to be causative of around 10% of Parkinson's disease cases. The key neuropathological features of Parkinson's disease include a loss of dopamine producing neurons and the presence of alpha-synuclein containing protein aggregates in surviving neurons. We recently identified RAB39B as a novel gene for Parkinson's disease. RAB39B has a putative function in intracellular trafficking, and we hypothesise that it plays a role in the regulation of alpha-synuclein. The aim of this project is to characterise the function of RAB39B and investigate its role in the pathogenic mechanisms underlying Parkinson's disease. Studies will utilise newly developed induced pluripotent stem cell

models and mouse models to perform preclinical studies to characterise the disease process and identify potential therapeutic targets. The primary techniques that may be utilised in this project will include molecular and cell biology assays, stem cell culture and differentiation into neurons, mouse handling and behavioral testing.

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16. Understanding the molecular basis of canvas-a novel neurological disorder caused by an expanded repeat

DNA repeat expansion mutations cause over twenty neurogenetic disorders of major clinical significance which can present with heterogenous, overlapping clinical phenotypes. Discovery of novel expansions and diagnostic testing of known loci has proven extremely challenging due to the repeat sequences being refractory to standard molecular techniques. We recently determined that a novel intronic pentanucleotide repeat expansion on chromosome 4 causes the neurogenetic disorder termed cerebellar ataxia with neuropathy and vestibular areflexia syndrome (CANVAS). Our preliminary studies suggest the expansion is the most common genetic cause of ataxia in humans. This project will be a component of a larger study that aims to characterise the CANVAS repeat mutation using short read and long read gene Next Generation sequencing technologies. It will investigate pathogenic mechanisms underlying disease utilising molecular and cell biology techniques, including primary cell and induced pluripotent stem cell generation and characterisation. The candidate will also contribute to the gene discovery component of an ongoing trial testing the diagnostic utility of expansion repeat detection in next generation sequencing data.

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17. Development of phenotype assays using a genetically encoded fluorescent toolkit for study of human corticogenesis in vitro.

Studies into human cortical development (or corticogenesis) using human embryonic tissue have identified unique cellular processes during embryogenesis which further our understanding of how the human cortex is formed. However, primary human neuronal tissue can be difficult to source and is less amenable to genetic and cellular manipulation for experimental purposes. Therefore, researchers have turned to human embryonic stem cells (hESC's) to model human cortical development in culture. hESC's are highly expandable which allows for scaled up experimentation. It is also possible to generate transgenic lines, for example with fluorescent reporters, which greatly aid in studying aspects of corticogenesis such as proliferation, synaptic maturity, neurite morphology and activity. More recently, the ability to generate induced pluripotent stem cells (iPSC's) has allowed researchers to model genetic disorders specific to patients by reprogramming cells from patient tissue biopsies into a pluripotent state. While iPSC's are an exceptionally powerful system to model diseases, genetically encoded tools such as fluorescent reporters and biosensors need to be

introduced to each individual iPSC line, which can be labour and time intensive. Developing a panel of genetically encoded tools which can be virally transduced into iPSC's could bypass this issue and facilitate rapid assessment of various neuronal phenotypes across iPSC lines. The aim of this project is to generate, validate and optimise a panel of genetically encoded reporters and biosensors in iPSC's to aid in studying aspects of cortical development. This will involve DNA cloning of relevant fluorescent genes and biosensors into lentiviral vectors, culturing of iPSC cells, cortical differentiation and live cell confocal imaging to assess aspects of cortical development using these genetic tools.

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18. Development of novel human stem cell derived models of beta-propeller protein-associated neurodegeneration for disease modelling and drug screening

Beta-propeller Protein-Associated Neurodegeneration (BPAN) is a rare, X-linked neurological disorder characterised by intellectual disability, seizures and ataxia in early childhood. The condition progresses rapidly leading to development of Parkinsonism, dystonia and cognitive impairment in adolescence/early adulthood. Children affected by BPAN display brain iron accumulation at an early age, leading to classification of BPAN under a group of disorders known as neurodegeneration with brain iron accumulation (NBIA5). BPAN is caused by pathogenic variants in the WDR45 gene which encodes the WD repeat-containing protein 45. The protein plays an important role in autophagy, a biochemical mechanism that regulates degradation and recycling of cellular components. However, very little is known about the cellular effects of variants in WDR45 on the nervous system and how it causes BPAN. Hence, there are no drugs available that can cure or slow the progression of BPAN. In this project we will use patient-derived induced pluripotent stem cells (iPSC) to generate brain cell cultures in order study disease-specific mechanisms and test potential drug treatments. The first step will be to examine the effects of pathogenic variants on electrophysiological, biochemical and morphological properties of differentiated cells, with a focus on neurons. Drugs targeting relevant pathways (e.g. autophagy, iron metabolism, etc.) will be used to determine their effectiveness in modulating disease phenotype in the neuron.

This will help establish the validity of our culture model as a vital preclinical tool for BPAN drug screening. The prospective candidate will get the opportunity to learn a range of laboratory techniques including stem cell culturing, differentiation of stem cells into neurons, electrophysiology, immunocytochemistry, microscopy, drug screening assays, real-time qPCR and western blot analysis.

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19. Improving outcomes of metabolic disorders 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 in the most relevant cell lineages (i.e. heart and brain) by assessing the impact of these energy generation defects on cardiomyocytes and neural cells 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 iPSCs from mitochondrial disease patient fibroblasts. This project will validate selected cell lines from this panel and differentiate them to cardiomyocyte and/or neural lineages to assess the impact of the gene knockout on various aspects of mitochondrial and cellular function. Molecular and cellular characterization 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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20. Developing a functional assay to evaluate pathogenic variants in one of the most common genetic loci linked to paediatric mitochondrial disease

Each week in Australia a child is born with a disorder affecting mitochondria, our cellular power plants. Many such children die in the first years of life and most suffer from severe disease. Current genomic strategies have improved the ability to provide molecular diagnoses for these children and their families, with diagnosis rates around 50%. However, it is often difficult to determine whether a novel genetic variant is pathogenic, and diagnoses can be missed in regions of the genome that are more difficult to analyse, such as those with repetitive sequences. The ATAD3 locus is one such genomic region, consisting of three repeated genes with high homology. Since its identification as a mitochondrial disease locus in 2016, ATAD3 has emerged as one of the top 5 most common nuclear loci linked to mitochondrial disease. These diseases range from milder neurodegenerative diseases, to severe presentations with early lethality affecting the heart and/or the brain. Many of these severe presentations result from duplications and deletions in the ATAD3 locus that frequently arise due to its origin as a gene duplication event. While its precise function is unresolved, ATAD3 is

linked to mitochondrial DNA maintenance and cellular cholesterol homeostasis. All three ATAD3 genes encoded within the locus (ATAD3A, ATAD3B and ATAD3C) have ATPase domains, although it is unknown if they are all functional. This project will involve the development of a protocol for isolation of ATAD3 proteins and direct measurement of their ATPase activity, using extensive molecular biology and biochemistry techniques. This assay will then be used to evaluate ATPase activity in all three ATAD3 proteins, as well as to analyse the effect of known and novel variants on ATAD3 ATPase function to determine their contribution to pathogenicity. References: Desai, Frazier et al. (2017). *Brain*, 140:1595-1610. Frazier, Compton et al. (2020). *Med*, 1:1-25.

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21. Pluripotent stem cell models to investigate tissue specific protein interactions in the mitochondrial disease Sengers Syndrome

Mitochondria are our cellular power plants that burn sugars, fats and proteins to generate energy. They contain inner and outer membranes that enclose two aqueous compartments, the intermembrane space and the matrix. While mitochondria have their own DNA, it encodes a limited number of genes, all associated with the energy-generating mitochondrial oxidative phosphorylation system. Therefore, the vast majority of the ~1500 mitochondrial proteins are instead encoded on nuclear DNA, translated on cytosolic ribosomes and imported into the correct mitochondrial compartment using various molecular machineries that coordinate the process of mitochondrial protein trafficking. Mitochondrial diseases are genetic disorders affecting energy generation. Each week in Australia a child is born with a severe mitochondrial disorder, with many dying in the first years of life and most suffering from severe disease, often affecting their brain and/or heart. Access to patient tissues is limited, making it difficult to assess the mitochondrial and cellular pathways contributing to disease pathology. Multiple import proteins have now been associated with mitochondrial disease, including AGK (acylglycerol kinase), which functions in the mitochondrial inner membrane TIM22 import complex. Surprisingly, despite its fundamental role in mitochondrial biogenesis, patients with pathogenic AGK variants have a relatively tissue-specific presentation, characterized by cardiomyopathy and cataracts (Sengers syndrome). Human pluripotent stem cells can be differentiated into disease relevant cells such as beating cardiomyocytes, providing an opportunity to investigate this tissue specificity. This project will use our existing AGK stem cell models of mitochondrial disease to investigate this cardiac specific presentation. Cell culture and molecular biology will be combined with co-immunoprecipitation, BioID proximity labelling, and quantitative proteomic techniques to investigate AGK interacting proteins and the AGK and TIM22 complex "interactome", in undifferentiated pluripotent stem cells versus differentiated cardiomyocytes. References: AGK- Kang et al., (2017). *Mol. Cell*, 67:457-470.e5. BioID- Roux et al., (2012). *J. Cell Biol.*, 196:801-810.

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22. Into the Unknown: multi-omic analyses of inherited metabolic disorders with 'variation of uncertain significance'.

Individual "rare diseases" affect fewer than 1 in 2000 people but collectively the more than 7000 rare diseases affect more than 1 Million Australians. Many patients fail to receive optimal, timely medical care and disease management due to a delay in or lack of genetic diagnosis. Rare diseases are thus a major public health problem. Mitochondrial diseases are the most common form of inherited metabolic disorders and are currently known to comprise more than 350 distinct monogenic causes. Genomic sequencing technologies have transformed genetic diagnosis of rare diseases; however, many cases still remain unsolved. Australian Genomics is a collaboration of over 80 Australian centres seeking to translate genomic technologies into improved outcomes for rare diseases and cancer. Our Australian Genomics Mitochondrial Flagship has completed genome sequencing of a cohort of 132 patients with probable mitochondrial disease. DNA from 60 patients underwent whole genome sequencing and a molecular diagnosis was obtained in 22 patients (37%), with the remaining 38 now reflexed into research for more extensive analysis or functional validation. These unsolved cases will be investigated in this project. For some, candidate disease genes have been identified requiring functional validation. In others analysis of exons has thus far failed to prioritise candidates.

This project will use a combination of state-of-the-art wet and dry lab technologies to identify 'variation of uncertain significance' in known or candidate disease genes from existing whole genome sequencing. Transcriptomic and quantitative proteomic studies plus functional studies will be used to validate pathogenic significance. This will generate definitive diagnoses in previously unsolvable cases, aid understanding of pathogenic mechanisms and develop methods that can be applied to understanding the genetics of a wide range of other rare diseases.

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23. Rett syndrome and related neurodevelopment disorders: Novel disease gene discovery

Rett Syndrome (RTT) is a rare, severe neurodevelopmental disorder (NDD) resulting in significant physical and neurological defects. Despite being predominantly caused by pathogenic variants in the methyl-CpG-binding (MECP2) gene, between 3 to 15% of classic and atypical RTT individuals currently are genetically undiagnosed. Classic RTT individuals exhibit an apparently normal development until 6 to 18 months of age after which the developmental regression in acquired skills is noticed. Atypical RTT individuals have several features of classic RTT but do not meet all the specific diagnostic criteria. Recently, the classification of RTT has been expanded to include

individuals with clinical features overlapping RTT and other NDDs, often referred to as RTT-like individuals. There is an unmet need to provide precise genetic diagnosis for MECP2 negative RTT individuals which is further complicated due to the significant overlap in clinical features with other related NDDs. Next generation sequencing (NGS) studies are continuously identifying hidden genetic causes for RTT. In this project, we will use a range of NGS techniques including whole genome sequencing (WGS) and whole exome sequencing (WES) to identify variants in genes linked with NDDs. Variant filtering will be performed based on population frequency using the Genome Aggregation Database (gnomAD), predicted pathogenicity scores using a range of in silico tools such as MutationTaster, PolyPhen-2, SIFT, as well as examination of the quality of variants on the Integrated Genome Viewer (IGV) reads. For missense variants, in silico three dimensional structural modelling will be performed using the canonical transcript to investigate the effect of the predicted effect of amino acid change on overall protein function. Segregation of identified variants will be confirmed by Sanger sequencing using available DNA from parents. For novel variants, specific molecular functional assays will be designed to confirm the pathogenicity of the identified variant. This work has the potential to identify new genetic causes of RTT, allowing affected individuals to end a long and arduous diagnostic odyssey, restoring reproductive confidence for families, and potentially translating to specific future therapeutic options for the affected individuals.

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NON-LABORATORY BASED RESEARCH PROJECTS

Infection and Immunity

24. Sleep and its impacts in children with Primary ciliary dyskinesia (PCD)

Introduction: Primary ciliary dyskinesia (PCD) is a genetic disorder characterised by impaired mucociliary clearance due to abnormal ciliary function. Children with PCD may present with respiratory symptoms with early onset of persistent sino-pulmonary infections, and often develop bronchiectasis. Upper airway manifestations of PCD can cause obstructive sleep apnea (OSA) and recent studies in children with PCD have shown a higher rate of sleep disturbance and OSA compared to healthy children. Sleep disruption may impair daytime functioning and health-related quality of life (HRQOL) in children and OSA has been associated with a range of negative health impacts. There have been no studies evaluating sleep in Australian children with PCD and no studies examining the impact of sleep disturbance in this population. The Department of Respiratory and Sleep Medicine, RCH hosts the statewide PCD diagnostic and clinical service, and a tertiary sleep service. **Aims:** In the current population of children with PCD attending RCH:

- to determine the prevalence of OSA and subjective sleep complaints
- to investigate whether sleep disturbance is related to the presence of upper respiratory system manifestations and severity of lung disease
- to evaluate the impact of sleep disturbance on HRQOL and mood

Methods: All children with PCD attending RCH will be included. Physical examination, pulmonary function tests, and ear-nose-throat assessments will be obtained. All children and their parents will be asked to complete sleep, HRQOL and mood questionnaires and referred for overnight sleep study (PSG). The data collected will be collated and analysed by the student. **Clinical implications:** Sleep disruption may significantly impair health-related quality of life. In order to optimise the medical

management of children with PCD, it is important to understand the magnitude of sleep disorders in this population and to identify the predictors of at-risk patients in whom further evaluation may be indicated.

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25. Auto-titrating positive airway pressure (APAP) in Paediatric patients for the treatment of obstructive sleep apnoea (OSA).

Introduction: Obstructive sleep apnea (OSA) is a sleep breathing disorder associated with multiple neurobehavioral and medical problems in children. The first-line treatment of OSA in children is adenotonsillectomy however many have residual symptoms of OSA postoperatively and require continuous positive airway pressure (CPAP). CPAP therapy involves the provision of pressure via a facemask to treat upper airway obstruction. Currently the gold-standard for determining appropriate treatment pressure is a manual pressure titration by a sleep scientist during attended in-laboratory sleep study. This method of in-laboratory titration is labour intensive, costly and subject to hospital waitlists. Auto-titrating positive airway pressure (APAP) devices provide variable pressure delivery by constantly monitoring the patient's airflow using algorithms developed by each company. APAP for the treatment of OSA has been widely used in adult patients, particularly during the initiation phase of therapy, however there is a paucity of data in children. Aims: To assess the efficacy of APAP in treating OSA in children. Methods: All children with OSA requiring an in-laboratory CPAP titration study at the Royal Children's Hospital (RCH), February -July 2021 will undergo an unattended titration study using the ResMed Airsense 10 APAP device with portable sleep monitoring equipment to determine their appropriate treatment pressure. The sleep studies will be set-up and data collated and analysed by the student. The titration study will be analysed by Sleep Scientists to determine efficacy of APAP for treatment of paediatric OSA. Clinical Implications: CPAP therapy is an effective and safe treatment for OSA in children. In-laboratory titration PSG is standard to determine optimal therapeutic pressure in children with OSA treated with CPAP. The use of APAP devices as an alternative is not well studied in children however has the potential to provide therapeutic pressures in the home without the need for in-hospital titration sleep studies.

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26. Sleep quality in children with Phenylketonuria (PKU)

Introduction: Phenylketonuria (PKU) is an inborn error of metabolism that results in decreased metabolism of the amino acid phenylalanine. Infants with PKU are diagnosed by newborn screening and there is a prevalence of 1:15,000 births in Australia. Untreated PKU can lead to brain damage, seizures and intellectual disability however even early treated PKU patients may have a higher prevalence of neurocognitive and mental health deficits. In PKU, the disruption of the metabolic pathway of phenylalanine causes deficits in the neurotransmitters and sleep modulators dopamine, norepinephrine, and serotonin. Sleep disturbances, such as insomnia and excessive daytime sleepiness, are described in adults with PKU however there have been no studies evaluating sleep in children with PKU. Understanding sleep problems in children with PKU may help explain some of the pathophysiology of brain dysfunction in PKU patients. The Department of Metabolic Medicine, RCH provides diagnostic and therapeutic services to children with PKU, and their families, from Victoria and Tasmania, and the RCH has a tertiary sleep service. Aims: In the current population of children with PKU attending RCH:

- to evaluate sleep patterns and quality (objective and subjective)
- to assess the relationship between sleep and mood and health-related quality of life (HRQOL)

Methods: All children with PKU attending RCH will be included. All children and their parents will be asked to complete sleep, mood and HRQOL questionnaires. Sleep patterns will be assessed with actigraphy. The data collected will be collated and analysed by the student. Clinical implications: Sleep disruption may significantly impair health-related quality of life and exacerbate poor neurocognitive outcomes in PKU. In order to optimise the medical management of children with PKU and develop an additional treatment target, it is important to understand the magnitude of sleep disorders and their impact in this population.

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Available as Masters Project: No

Clinical Sciences

27. Psychosocial outcomes of parents of young children with anorectal malformations

Parents of children born with anorectal malformations (ARM) face unique diagnostic and management challenges, especially in the early years. This project is focused upon the application of validated questionnaires to evaluate the psychosocial outcomes of parents/carers of children with ARM aged less than seven years. This is part of a larger longitudinal study involving the Colorectal and Pelvic Reconstruction Service (Department of Paediatric Surgery) and the Department of Psychology at The Royal Children's Hospital and Murdoch Children's Research Institute.

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Available as Masters Project: Yes

28. Psychosocial outcomes of parents of young children with Hirschsprung disease

Parents of children born with Hirschsprung disease (HD) face unique diagnostic and management challenges, especially in the early years. This project is focused upon the application of validated questionnaires to evaluate the psychosocial outcomes of parents/carers of children with HD aged less than seven years. This is part of a larger longitudinal study involving the Colorectal and Pelvic Reconstruction Service (Department of Paediatric Surgery) and the Department of Psychology at The Royal Children's Hospital and Murdoch Children's Research Institute.

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Available as Masters Project: Yes

29. Using wearables to measure pain/anxiety in children with cerebral palsy

Children with cerebral palsy often experience pain and/or anxiety. Many children with cerebral palsy are not able to self-report their pain/anxiety due to cognition and/or communication impairments. In these cases parent proxy report is utilised which poses some limitations to the information collected. Innovative methods to detect pain/anxiety are needed to ensure we know the true extent of the pain and/or anxiety experienced by children with cerebral palsy.

This project will explore whether a wearable device is able to detect physiological signals that might indicate pain and/or anxiety in children with cerebral palsy. Children will wear the device for a specified period of time while other measures are collected simultaneously. Validation of the device will be through correlation with the other measures. Acceptability and feasibility of the device will also be examined. This project is ideally designed as a Masters project.

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30. The pharmacovigilance gap among pregnant women in Australia and worldwide

When a new medicine is developed through clinical trials, pregnant women are often excluded due to ethical concerns and technical difficulties. This means that very few studies address pharmacovigilance for adverse maternal and child outcomes from drugs/medicines taken by pregnant women. Those that do may relate to problems such as birth defects that can be detected in routine population data, and/or registries set up to study individual medicines of concern, so do not apply to subtle quantitative impacts such as neurodevelopmental outcomes. Focusing on evidence from population-based human studies and registries and other observational or experimental studies, this narrative systematic review will define 1) the most common and/or important prescription medications used today in pregnancy (e.g psychoanaleptics, antibiotics,

analgesics), 2) their association with potential adverse outcomes (short-term, eg birth outcomes, and long-term, eg diabetes, childhood infections, neurodevelopmental outcomes), and 3) the effect modifiers (eg duration, dose, pregnancy trimester). We expect to demonstrate gaps in knowledge about medications in pregnancy that may be having long term impacts for our children. If you are willing to learn how to undertake systematic reviews and learn about this important topic with a group of mission-driven people, this is the right opportunity for you!

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31. Mapping thalamocortical connectivity in the neonatal brain

Recent advances in Magnetic Resonance Imaging (MRI) have allowed the detailed mapping of the developing human brain from as early as 1 to 2 weeks of age. Techniques such as diffusion imaging can be used to non-invasively track long-distance connections in the neonatal brain, mapping networks that underlie the transmission of information across the cortex. Such networks develop rapidly over time and can be impacted by early life events such as preterm birth, with long-term consequences for motor, cognitive and clinical outcomes. The formation and reinforcement of connections between the thalamus and the cortex begins in mid-gestation and continues throughout infancy and childhood. Proper development of these pathways is essential for normal brain development and function. This project will use neuroimaging data acquired shortly after birth in a large cohort of neonates as part of the Developing Human Connectome Project (dHCP). The dHCP represents the world's largest neonatal neuroimaging project. Using state-of-the-art techniques, we will produce detailed maps of thalamo-cortical networks present in the neonatal brain. We will measure how degree and strength of connectivity to/from the thalamus varies across the cortex, and how this is altered following preterm birth. This is a computational project best suited to a Masters student, and will require use of command line programs as well as some coding in Bash and/or Python. Some experience in command line interface or programming will be beneficial. Further reading: Ball et al. (2013). The influence of preterm birth on the developing thalamocortical connectome. *Cortex*, Jun;49(6):1711-21 Ball et al. (2015) Thalamocortical Connectivity Predicts Cognition in Children Born Preterm. *Cerebral Cortex*. Nov; 25(11): 4310-4318.

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32. Sleep quality and fatigue in paediatric Multiple Sclerosis (MS) patients.

Introduction: Multiple sclerosis (MS) is an immune-mediated disease of the central nervous system that was once considered an adult disease. Paediatric onset MS (POMS) accounts for ~5% of all MS cases with a median age of 11-13 years. In adults and children with MS, fatigue is common (adults ~ 90%; children ~50% by parent report, 30% by child report) and is often reported to be the most

disabling symptom. Sleep disturbance is also common in adults however we hypothesise under-recognised and reported in children. Such manifestations would be expected to have considerable impact on mental health, academic performance, social interaction and development, and ultimately quality of life in POMS. There have been no studies evaluating sleep and fatigue in Australian children with MS and no studies examining the impact of sleep disturbance in POMS. The Department of Neurology, RCH hosts the statewide paediatric MS clinical service, and the RCH has a tertiary sleep service. Aims: In the current population of children with MS attending RCH:

- to determine the prevalence of fatigue and evaluate sleep quality (objective and subjective)
- to assess the relationship between fatigue and sleep quality
- to evaluate the impact of fatigue and sleep disturbance on HRQOL and mood

Methods: All children with PCD attending RCH will be included. All children and their parents will be asked to complete sleep, fatigue, HRQOL and mood questionnaires and referred for overnight sleep study (PSG). The data collected will be collated and analysed by the student. Clinical implications: Sleep disruption may significantly impair health-related quality of life and exacerbate fatigue and mental health problems in POMS. In order to optimise the medical management of children with MS, it is important to understand the magnitude of sleep disorders and their impact in this population.

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Population Health

33. Income-related inequality in asthma care: evidence from three Victorian hospitals and healthcare use data linkages

Title: Income-related inequality in asthma care: evidence from three Victorian hospitals and healthcare use data linkages Description: Asthma is the most common chronic childhood illness affecting approximately 10% of Australian children. Asthma hospitalisations are associated with serious outcomes including worse lung function, functional limitations, future admissions and increased risk of mortality. In addition, hospitalisation poses a significant burden on hospitals with asthma accounting for approximately 3% of all hospitalisations for Australian children aged 5-14 years in 2015-6. Approximately 1 in 5 children admitted to hospital for the treatment of asthma will be re-admitted within 1 year. This project has recruited patients from three Victorian hospitals with data linkage to Medicare. Data available for the project include administrative data on emergency department visits, hospital inpatient visits, GP visits, and prescribed medication use. The project will focus on evaluation of income-related inequality in asthma care. Student skills: descriptive statistics, moderate experience existing or to be gained with Stata.

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34. Improving the detection of childhood adversities

The Centre for Research Excellence (CRE) in Childhood Adversity and Mental Health is a five-year NHMRC and Beyond Blue co-funded initiative that aims to build evidence on how best to detect and respond to childhood adversity and child mental health problems in Australian children aged 0-8 years and their families. This student project will sit within the CRE. The project aims to evaluate the effectiveness of a training program for intersectoral service providers to improve the detection of adversities on knowledge and confidence. The student will contribute to the design, implementation, analysis and write up of a pre-post training survey.

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35. Prevalence and risk factors of cow's milk allergy in Melbourne infants.

Food allergy is on the rise globally, with Melbourne considered the food allergy capital of the world. Food allergy is a lifelong disease which severely affects quality of life and can cause life threatening anaphylaxis. We do not have data on current levels of cow's milk allergy in the Melbourne population. Our current cross-sectional study, called EarlyNuts, has collected this data. We recruited almost 2,000 1-year-old infants across Melbourne's council-run immunisation centres between 2018 and 2019. Cow's milk allergy prevalence has not yet been measured in the Melbourne population, so this will be the first report of milk allergy at a population level in Australia. We also have data on what age cow's milk is first being introduced to young infants and other potential risk factors for milk allergy. Your aim would be to measure prevalence of cow's milk allergy in these infants, and then analyse potential risk factors for milk allergy. You will learn about the seriousness of food allergy, as well as the use of statistical packages for data analysis and public health, while surrounded by a world-class team of researchers through the Centre of Food and Allergy Research.

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36. Early developmental profiles of hearing-impaired children

Research question What are the early developmental profiles of hearing-impaired children, and do specific early developmental indicators predict aetiological diagnoses? **Project summary** Congenital hearing loss affects 1-3 in 1000 children and is the most prevalent childhood disability diagnosed through newborn screening. Around 40% of hearing-impaired children have other medical comorbidities. Little is known about the early developmental profiles of hearing-impaired children, and whether specific developmental indicators can predict the underlying aetiological diagnosis. The Royal Children's Hospital Caring for Hearing Impaired Children (CHIC) clinic delivers coordinated medical and developmental care to hearing-impaired children. Developmental profiles, measured by the Ages and Stages questionnaire, were systematically collected for all children. This data, along with clinical data already collated from a clinical audit of over 500 children who attended the clinic, and audiological data, will be analysed. The student will learn to systematically organize and clean data, and carry out simple statistical analyses. The student will have the opportunity to experience how research can be used to answer clinical questions, and there will also be opportunity to publish their work.

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37. Parental mental health and experiences of newborn hearing screening through the Victorian Infant Hearing Screening Program (VIHSP)

Research question What are the experiences and mental health of parents whose newborns are referred for audiology assessment via the newborn hearing screening program in Victoria? **Project summary** The Victorian Infant Hearing Screening Program (VIHSP) delivers newborn hearing screening to >98% of newborns in Victoria. Newborns who do not pass the hearing screening process are referred for confirmatory audiology assessments. Families of infants who do not pass the second newborn hearing screen are referred to the VIHSP Early Support Service (ESS) for support as they progress through the hearing screening pathway. The range of support offered includes preparing for confirmatory audiology testing, understanding what hearing tests may show, arranging appointments and navigating the range of services available. VIHSP is interested in evaluating the mental health and experiences of these parents in order to offer appropriate support for these parents. **Methodology** Mixed methods study. Quantitative: parent report of anxiety via questionnaire. Qualitative: interviews with parents of newborns referred for confirmatory audiology assessments. The student will learn skills in both basic quantitative and qualitative research, including data collection, organization and cleaning, and carry out simple statistical analyses. The student will have the opportunity to publish their work and learn about implementation of a screening program.

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38. Determining outcomes for babies in special care nurseries in an integrated whole-of-population framework

Newborn babies who require specialist care account for substantial immediate and lasting burden of disease. More than 10% of newborns are admitted to special care nurseries (SCN), many experiencing lifelong adverse outcomes. Despite decades of research, deficiencies remaining in knowledge of risks and outcomes pertaining to babies. To rapidly improve care for babies, comprehensive knowledge of incidence, health/developmental outcomes, risk factors and care pathways, coupled with a uniform whole-of-population approach, is urgently needed. The 'Generation Victoria' cohort is targeting all 160,000 Victorian births over two years from early 2021. Within GenV, we are establishing a depth data collection for all newborns admitted to Victoria's 28 SCNs, covering important events during pregnancy and the postnatal admission. These unique whole-state data will complement data already available for the 5 neonatal ICUs and build a statewide evidence base for better physical, mental and developmental outcomes for these vulnerable babies. Project objective: For the expected 3000 babies admitted to Victoria's 28 SCNs in Feb-July 2021, we aim to determine the population incidence of morbidities (eg respiratory distress, hypoglycaemia, infection, jaundice, and feeding difficulties) in the neonatal period, and the characteristics of the babies who experience them. This Honours project may be stand-alone, or work in partnership with a second student examining the impact of variations in models of care. Working with the GenV and the SCN study team, the student will learn how registries are set up, assist with data extraction and develop definitions, coding and recording of morbidities and characteristics before proceeding to quantitative analyses to address the study objective.

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Available as Masters Project: Yes

39. Determining how outcomes for babies in special care nurseries vary by the models of obstetric and newborn care in an integrated whole-of-population framework

Newborn babies who require specialist care account for substantial immediate and lasting burden of disease. More than 10% of newborns are admitted to special care nurseries (SCN), many experiencing lifelong adverse outcomes. Despite decades of research, deficiencies remaining in knowledge of risks and outcomes pertaining to babies. To rapidly improve care for babies, comprehensive knowledge of incidence, health/developmental outcomes, risk factors and care pathways, coupled with a uniform whole-of-population approach, is urgently needed. The 'Generation Victoria' cohort is targeting all 160,000 Victorian births over two years from early 2021. Within GenV, we are establishing a depth data collection for all newborns admitted to Victoria's 28 SCNs, covering important events during pregnancy and the postnatal admission. These unique whole-state data will complement data already available for the 5 neonatal ICUs and build a statewide evidence base for better physical, mental and developmental outcomes for these vulnerable babies. Project objective: For the expected 3000 babies admitted to Victoria's 28 SCNs in Feb-July 2021, we aim to determine how morbidities (eg respiratory distress, hypoglycaemia, infection, jaundice, and feeding difficulties) in the neonatal period vary by the models of obstetric

and newborn care offered in those hospitals. This Honours project may be stand-alone, or work in partnership with a second student examining the incidence of these morbidities and characteristics of the babies who experience them. Working with the GenV and the SCN study team, the student will learn how registries are set up, assist with data extraction and map the models of care in each hospital, before proceeding to quantitative analyses to address the study objective.

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Available as Masters Project: Yes

40. Engaging high-value cohorts for a state-wide health research initiative

Generation Victoria (GenV) is a state-wide child and parent health research initiative. The GenV research cohort is targeting all 160,000 Victorian births over two years from early 2021, seeking to recruit both parents and newborns into the life-time study. With an initiative of this scale, communication with parents ahead of recruitment is critical to enable them to make an informed decision about participation. The recruitment of certain parent cohorts has proven challenging for previous health research projects. For example, Indigenous parents, those with a disability or from refugee backgrounds, are among the cohorts often missing from research samples. This greatly limits the benefits of research outcomes for those communities. For this reason, these cohorts are considered high-value for GenV and a targeted communication strategy is being implemented. This project aims to:

- Develop frameworks and processes to monitor and evaluate the effectiveness of communication with high-value cohorts
- Implement these processes to gather data on effectiveness and enable GenV to adapt communications as required
- Provide insights on effective engagement with high-value cohorts to inform communication planning for GenV and future research initiatives

Working with the GenV Cohort 2020s, Solutions Hub and marketing teams, the student will be contributing actively to data collection and management, and conducting quantitative and qualitative analyses to address the study objectives.

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Available as Masters Project: No

41. Statewide outcomes for babies in special care nurseries

Project description Newborn babies who require specialist care account for substantial immediate and lasting burden of disease. More than 10% of newborns are admitted to special care nurseries (SCN), many experiencing lifelong adverse outcomes. Despite decades of research, deficiencies remaining in knowledge of risks and outcomes pertaining to babies. To rapidly improve care for babies, comprehensive knowledge of incidence, health/developmental outcomes, risk factors and

care pathways, coupled with a uniform whole-of-population approach, is urgently needed. The 'Generation Victoria' cohort is targeting all 160,000 Victorian births over two years from early 2021. Within GenV, we are establishing a depth data collection for all newborns admitted to Victoria's 28 SCNs, covering important events during pregnancy and the postnatal admission. These unique whole-state data will complement data already available for the 5 neonatal ICUs and build a statewide evidence base for better physical, mental and developmental outcomes for these vulnerable babies. Project objective: For the expected 3000 babies admitted to Victoria's 28 SCNs in Feb-July 2021, we aim to determine the population incidence of morbidities (eg respiratory distress, hypoglycaemia, infection, jaundice, and feeding difficulties) in the neonatal period, and the characteristics of the babies who experience them. This Honours/Masters project may be stand-alone, or work with a second student examining the impact of variations in models of care. Working with the GenV and the SCN study team, the student will learn how registries are set up, assist with data extraction and develop definitions, coding and recording of morbidities and characteristics before proceeding to quantitative analyses to address the study objective. This opportunity enables an outstanding student to be involved in both developing a registry with a lasting legacy (with subsequent PhD and career opportunities), and in GenV (<https://genv.org.au/>), one of the world's most exciting new child health projects.

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Professor Jeanie Cheong

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Available as Masters Project: Yes

42. How statewide outcomes for babies in special care nurseries vary by models of care

Project description Newborn babies who require specialist care account for substantial immediate and lasting burden of disease. More than 10% of newborns are admitted to special care nurseries (SCN), many experiencing lifelong adverse outcomes. Despite decades of research, deficiencies remaining in knowledge of risks and outcomes pertaining to babies. To rapidly improve care for babies, comprehensive knowledge of incidence, health/developmental outcomes, risk factors and care pathways, coupled with a uniform whole-of-population approach, is urgently needed. The 'Generation Victoria' cohort is targeting all 160,000 Victorian births over two years from early 2021. Within GenV, we are establishing a depth data collection for all newborns admitted to Victoria's 28 SCNs, covering important events during pregnancy and the postnatal admission. These unique whole-state data will complement data already available for the 5 neonatal ICUs and build a statewide evidence base for better physical, mental and developmental outcomes for these vulnerable babies.

Project objective: For the expected 3000 babies admitted to Victoria's 28 SCNs in Feb-July 2021, we aim to determine how morbidities (eg respiratory distress, hypoglycaemia, infection, jaundice, and feeding difficulties) in the neonatal period vary by the models of obstetric and newborn care offered in those hospitals.

This Honours/Masters project may be stand-alone, or work with a second student examining the incidence of these morbidities and characteristics of the babies who experience them. Working with the GenV and the SCN study team, the student will learn how registries are set up, assist with data

extraction and map the models of care in each hospital, before proceeding to quantitative analyses to address the study objective. This opportunity enables an outstanding student to be involved in both developing a registry with a lasting legacy (with subsequent PhD and career opportunities), and in GenV (<https://genv.org.au/>), one of the world's most exciting new child health projects.

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Available as Masters Project: Yes

43. Prescribed antenatal and perinatal medication in Victorian birthing hospitals

When a new medicine is developed through clinical trials, pregnant women are often excluded due to ethical concerns and technical difficulties. This means that large-scale pharmacovigilance is urgently needed for adverse maternal and child outcomes from drugs/medicines taken by pregnant women. This requires population-level data on two fronts: (1) whole-population cohorts that can measure potentially subtle adverse outcomes, both short-term (eg birth outcomes) and long-term (eg diabetes, childhood infections, neurodevelopmental outcomes); and (2) complete data on medications prescribed during pregnancy, labour and the newborn period. In Australia, outpatient prescriptions are meticulously documented via the Pharmaceutical Benefits Scheme (PBS). However, medications prescribed via other routes, including hospitals, are not available at the population level. Project objective: This project will fill this critical gap, working with GenV (Generation Victoria), a new birth cohort targeting all 160,000 Victorian births and their mothers over two years from early 2021. The student will:

- Map how and where Victoria's 70 birthing hospitals prescribe and record medication data for pregnant women and newborns.
- Assist GenV in developing systems to link to these datasets, via this mapping and via hospital interviews and surveys.
- In a proof-of-principle analysis, study associations between hospital-prescribed medications and pregnancy and newborn outcomes in one metropolitan and one rural hospital for all births over a 6 month period.

This Honours/Masters project may be stand-alone, or work with a second student examining antibiotic stewardship policies and prescribing more specifically. In addition to the GenV team, it is expected they will work with experts spanning GenV's Pregnancy, Newborns, Data Linkage and Optimising Antibiotics Working Groups. This opportunity enables an outstanding student to develop skills in a public health area critical to lifelong human health (with subsequent PhD and career opportunities), and in GenV (<https://genv.org.au/>), one of the world's most exciting new child health projects.

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Available as Masters Project: Yes

44. Antibiotic stewardship and outcomes in Victorian birthing hospitals

Project description Optimising the use of antibiotics is critical to effectively treat infections, protect patients from short- and long-term harms and combat antibiotic resistance. Antibiotic stewardship programs can help clinicians improve these outcomes by improving antibiotic prescribing. The forthcoming GenV cohort (see below) provides the opportunity to model the costs and benefits of variations in antibiotic prescribing and stewardship across an entire state. However, this requires complete data on antibiotic prescribed during pregnancy, labour and the newborn period. In Australia, outpatient prescriptions are meticulously documented via the Pharmaceutical Benefits Scheme (PBS). However, medications prescribed via other routes, including hospitals, are not available at the population level. **Project objective:** This project will fill this critical gap, working with GenV (Generation Victoria), a new birth cohort targeting all 160,000 Victorian births and their mothers over two years from early 2021. The student will:

- Map antibiotic prescribing and stewardship policies for pregnant women and newborns across Victoria's 70 birthing hospitals.
- Assist GenV in developing systems to link to these datasets, via this mapping and via hospital interviews and surveys.
- In a proof-of-principle analysis, study associations of hospital antibiotic stewardship and prescribing policies with pregnancy and newborn outcomes in the 70 hospitals over GenV's first 3-6 months of operation.

This Honours/Masters project may be stand-alone, or work with a second student examining hospital prescribing more generally. In addition to the GenV team, it is expected they will work with experts spanning GenV's Pregnancy, Newborns, Data Linkage and Optimising Antibiotics Working Groups. This opportunity enables an outstanding student to develop skills in a public health area critical to lifelong human health (with subsequent PhD and career opportunities), and in GenV (<https://genv.org.au/>), one of the world's most exciting new child health projects.

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Available as Masters Project: Yes

45. Making cohort participation fairer to solve real problems for real populations: Generation Victoria (GenV)

Over the last 30 years, many childhood problems (like autism, coeliac, obesity, allergy, mental health) have worsened, with long-term consequences for ageing societies. Finding answers to these problems require very large scale, population-representative cohorts, such as the forthcoming GenV (see below). Unfortunately, those with potentially most to gain - families with social risk factors - are often left out of these population studies. Participation rates are typically lower among families who have high socioeconomic disadvantage, Indigenous or culturally diverse backgrounds, teenage parents, and parents with low literacy or disability. Because the research findings are then less applicable, they can further drive gaps in equality between the most and least disadvantaged families. Generation Victoria is Australia's most ambitious children's study, aiming to recruit all 160,000 Victorian babies born over 2 full years from early 2021 and their parents (genv.org.au). With guiding principles of Inclusion and Equity, GenV is designed to allow every eligible Victorian to participate (eg materials available in >25 languages, very low burden digital assessments). In Stage 1, the student will identify existing complete datasets (eg Australian Census) describing the eligible

population, and select the demographic characteristics to best determine GenV's representativeness. In Stage 2, they will then statistically compare the demographic characteristics of participants recruited in the first months of GenV to the eligible population, to understand the sample's population-representativeness and which groups are under-represented. In Stage 3, the student will identify barriers to participation through demographic characteristics (eg primary language) and reason-for-refusal from those who decline, and the GenV Recruitment team will use this evidence to refine their recruitment approach. In Stage 4, the student can measure the impacts on recruitment rates of under-represented groups going forward. This project will provide evidence for recruitment decisions that have an important legacy in GenV.

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Available as Masters Project: Yes

46. Newborn Obstetrics Network Australasia (NONA) - Developing a new quality registry for Fetal Growth Restriction

The NONA registry is being developed to improve the care for women (and their babies) who experience the most complex pregnancies. These women are generally managed at one of the five Maternal Fetal Medicine (MFM) Units in Victoria (Royal Women's Hospital, Mercy Hospital for Women, Monash Medical Centre, Joan Kirner Women's & Children's and Northern Hospital). The registry will identify key quality metrics to improve outcomes for women with a pregnancy complicated by one of three conditions:

(1) multiple pregnancy, (2) fetal growth restriction, and/or (3) antenatally-diagnosed congenital anomalies. The registry is being developed with the support of Monash Registries (Australia's leading registry infrastructure) and the statewide Gen V initiative led from the MCRI, providing rich additional predictive and long term data. Up to 3 Honours students will each take one of these 3 conditions and study its statewide epidemiology: its incidence, including patterns of geographic variation; its management, including adherence to guidelines and variations in local practice and guidelines across sites; and its newborn outcomes amongst the subset of participants who birth by 31st July 2021. The student/s will learn practical skills in registry development, data collection, analysis and reporting on defined quality metrics for the first year of the NONA registry. The registry is overseen by the NONA steering committee comprising MFM subspecialists from Victoria's major maternity hospitals and leading academics in paediatrics, women's health and registry science.

The Honours project/s will be based with GenV at the MCRI with placements in these hospitals. This is an exciting opportunity for outstanding students to be involved in both developing a registry with a lasting legacy for future maternal and child health (with subsequent PhD and career opportunities), and in GenV (<https://genv.org.au/>), one of the world's most exciting new parent and child projects.

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Available as Masters Project: Yes

47. Polygenic risk and congenital hearing loss: evidence from a state-wide population-based longitudinal databank

Hearing loss has a sizeable hereditary component with heritability estimates ranging from 35% to 55%. Affordable advances in high-throughput genotyping have continuously expanded the list of genetic variants that influence hearing ability. Alone, each variant may have a tiny effect, but when considered together these genetic variants can be used to generate quantitative polygenic risk scores (PRS), enabling epidemiological cohorts to study their causal and modulating roles with environmental influences. The world-first PRS for hearing has recently been computed from UK biobank genome-wide association study (GWAS) and was predictive of age-related hearing loss in adults. However, there is limited knowledge about the genetic polygenic contribution to hearing loss in children, in particular whether hearing polygenic risk scores can predict the degree and type of hearing loss in children. Objective: In a state-wide population-based longitudinal databank of over 900 children with congenital hearing loss in the state of Victoria, we aim to use available GWAS data to examine the extent to which PRS for hearing is predictive of the degree and type of hearing loss in children.

The Honours/Masters student, in collaboration with the study team, will conduct a literature review on the genetic predictors of hearing loss, understand the application of polygenic risk scores from GWAS, assist with audiogram and biosamples preparation, PRS calculation, and conduct quantitative analyses to address the study objective.

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Available as Masters Project: Yes

48. Newborn Obstetrics Network Australasia (NONA) - Developing a new quality registry for Multiple Pregnancies

The NONA registry is being developed to improve the care for women (and their babies) who experience the most complex pregnancies. These women are generally managed at one of the five Maternal Fetal Medicine (MFM) Units in Victoria (Royal Women's Hospital, Mercy Hospital for Women, Monash Medical Centre, Joan Kirner Women's & Children's and Northern Hospital). The registry will identify key quality metrics to improve outcomes for women with a pregnancy complicated by one of three conditions: (1) multiple pregnancy, (2) fetal growth restriction, and/or (3) antenatally-diagnosed congenital anomalies. The registry is being developed with the support of Monash Registries (Australia's leading registry infrastructure) and the statewide Gen V initiative led from the MCRI, providing rich additional predictive and long term data. Up to 3 Honours students will each take one of these 3 conditions and study its statewide epidemiology: its incidence,

including patterns of geographic variation; its management, including adherence to guidelines and variations in local practice and guidelines across sites; and its newborn outcomes amongst the subset of participants who birth by 31st July 2021. The student/s will learn practical skills in registry development, data collection, analysis and reporting on defined quality metrics for the first year of the NONA registry. The registry is overseen by the NONA steering committee comprising MFM subspecialists from Victoria's major maternity hospitals and leading academics in paediatrics, women's health and registry science. The Honours project/s will be based with GenV at the MCRI with placements in these hospitals. This is an exciting opportunity for outstanding students to be involved in both developing a registry with a lasting legacy for future maternal and child health (with subsequent PhD and career opportunities), and in GenV (<https://genv.org.au/>), one of the world's most exciting new parent and child projects.

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Available as Masters Project: Yes

49. Newborn Obstetrics Network Australasia (NONA) - Developing a new quality registry for Congenital anomalies

The NONA registry is being developed to improve the care for women (and their babies) who experience the most complex pregnancies. These women are generally managed at one of the five Maternal Fetal Medicine (MFM) Units in Victoria (Royal Women's Hospital, Mercy Hospital for Women, Monash Medical Centre, Joan Kirner Women's & Children's and Northern Hospital). The registry will identify key quality metrics to improve outcomes for women with a pregnancy complicated by one of three conditions: (1) multiple pregnancy, (2) fetal growth restriction, and/or (3) antenatally-diagnosed congenital anomalies. The registry is being developed with the support of Monash Registries (Australia's leading registry infrastructure) and the statewide Gen V initiative led from the MCRI, providing rich additional predictive and long term data. Up to 3 Honours students will each take one of these 3 conditions and study its statewide epidemiology: its incidence, including patterns of geographic variation; its management, including adherence to guidelines and variations in local practice and guidelines across sites; and its newborn outcomes amongst the subset of participants who birth by 31st July 2021.

The student/s will learn practical skills in registry development, data collection, analysis and reporting on defined quality metrics for the first year of the NONA registry. The registry is overseen by the NONA steering committee comprising MFM subspecialists from Victoria's major maternity hospitals and leading academics in paediatrics, women's health and registry science.

The Honours project/s will be based with GenV at the MCRI with placements in these hospitals. This is an exciting opportunity for outstanding students to be involved in both developing a registry with a lasting legacy for future maternal and child health (with subsequent PhD and career opportunities), and in GenV (<https://genv.org.au/>), one of the world's most exciting new parent and child projects.

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Available as Masters Project: Yes

50. Prescribed antenatal and perinatal medication in Victorian birthing hospitals

When a new medicine is developed through clinical trials, pregnant women are often excluded due to ethical concerns and technical difficulties. This means that large-scale pharmacovigilance is urgently needed for adverse maternal and child outcomes from drugs/medicines taken by pregnant women. This requires population-level data on two fronts: (1) whole-population cohorts that can measure potentially subtle adverse outcomes, both short-term (eg birth outcomes) and long-term (eg diabetes, childhood infections, neurodevelopmental outcomes); and (2) complete data on medications prescribed during pregnancy, labour and the newborn period. In Australia, outpatient prescriptions are meticulously documented via the Pharmaceutical Benefits Scheme (PBS). However, medications prescribed via other routes, including hospitals, are not available at the population level.

Project objective: This project will fill this critical gap, working with GenV (Generation Victoria), a new birth cohort targeting all 160,000 Victorian births and their mothers over two years from early 2021. The student will:

1. Map how and where Victoria's 70 birthing hospitals prescribe and record medication data for pregnant women and newborns.
2. Assist GenV in developing systems to link to these datasets, via this mapping and via hospital interviews and surveys.
3. In a proof-of-principle analysis, study associations between hospital-prescribed medications and pregnancy and newborn outcomes in one metropolitan and one rural hospital for all births over a 6 month period.

This Honours/Masters project may be stand-alone, or work with a second student examining antibiotic stewardship policies and prescribing more specifically. In addition to the GenV team, it is expected they will work with experts spanning GenV's Pregnancy, Newborns, Data Linkage and Optimising Antibiotics Working Groups. This opportunity enables an outstanding student to develop skills in a public health area critical to lifelong human health (with subsequent PhD and career opportunities), and in GenV (<https://genv.org.au/>), one of the world's most exciting new child health projects.

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51. Antibiotic stewardship and outcomes in Victorian birthing hospitals

Optimising the use of antibiotics is critical to effectively treat infections, protect patients from short- and long-term harms and combat antibiotic resistance. Antibiotic stewardship programs can help clinicians improve these outcomes by improving antibiotic prescribing. The forthcoming GenV cohort (see below) provides the opportunity to model the costs and benefits of variations in antibiotic prescribing and stewardship across an entire state. However, this requires complete data on antibiotic prescribed during pregnancy, labour and the newborn period. In Australia, outpatient prescriptions are meticulously documented via the Pharmaceutical Benefits Scheme (PBS). However, medications prescribed via other routes, including hospitals, are not available at the population level.

Project objective: This project will fill this critical gap, working with GenV (Generation Victoria), a new birth cohort targeting all 160,000 Victorian births and their mothers over two years from early 2021. The student will:

1. Map antibiotic prescribing and stewardship policies for pregnant women and newborns across Victoria's 70 birthing hospitals.
2. Assist GenV in developing systems to link to these datasets, via this mapping and via hospital interviews and surveys.
3. In a proof-of-principle analysis, study associations of hospital antibiotic stewardship and prescribing policies with pregnancy and newborn outcomes in the 70 hospitals over GenV's first 3-6 months of operation.

This Honours/Masters project may be stand-alone, or work with a second student examining hospital prescribing more generally. In addition to the GenV team, it is expected they will work with experts spanning GenV's Pregnancy, Newborns, Data Linkage and Optimising Antibiotics Working Groups. This opportunity enables an outstanding student to develop skills in a public health area critical to lifelong human health (with subsequent PhD and career opportunities), and in GenV (<https://genv.org.au/>), one of the world's most exciting new child health projects.

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52. Statewide outcomes for babies in special care nurseries

Newborn babies who require specialist care account for substantial immediate and lasting burden of disease. More than 10% of newborns are admitted to special care nurseries (SCN), many experiencing lifelong adverse outcomes. Despite decades of research, deficiencies remaining in knowledge of risks and outcomes pertaining to babies. To rapidly improve care for babies, comprehensive knowledge of incidence, health/developmental outcomes, risk factors and care pathways, coupled with a uniform whole-of-population approach, is urgently needed.

The 'Generation Victoria' cohort is targeting all 160,000 Victorian births over two years from early 2021. Within GenV, we are establishing a depth data collection for all newborns admitted to Victoria's 28 SCNs, covering important events during pregnancy and the postnatal admission. These unique whole-state data will complement data already available for the 5 neonatal ICUs and build a statewide evidence base for better physical, mental and developmental outcomes for these vulnerable babies.

Project objective: For the expected 3000 babies admitted to Victoria's 28 SCNs in Feb-July 2021, we aim to determine the population incidence of morbidities (eg respiratory distress, hypoglycaemia, infection, jaundice, and feeding difficulties) in the neonatal period, and the characteristics of the babies who experience them

This Honours/Masters project may be stand-alone, or work with a second student examining the impact of variations in models of care. Working with the GenV and the SCN study team, the student will learn how registries are set up, assist with data extraction and develop definitions, coding and recording of morbidities and characteristics before proceeding to quantitative analyses to address the study objective.

This opportunity enables an outstanding student to be involved in both developing a registry with a lasting legacy (with subsequent PhD and career opportunities), and in GenV (<https://genv.org.au/>), one of the world's most exciting new child health projects.

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53. How statewide outcomes for babies in special care nurseries vary by models of care

Newborn babies who require specialist care account for substantial immediate and lasting burden of disease. More than 10% of newborns are admitted to special care nurseries (SCN), many experiencing lifelong adverse outcomes. Despite decades of research, deficiencies remaining in knowledge of risks and outcomes pertaining to babies. To rapidly improve care for babies, comprehensive knowledge of incidence, health/developmental outcomes, risk factors and care pathways, coupled with a uniform whole-of-population approach, is urgently needed.

The 'Generation Victoria' cohort (<https://genv.org.au/>) is targeting all 160,000 Victorian births over two years from early 2021. Within GenV, we are establishing a depth data collection for all newborns admitted to Victoria's 28 SCNs, covering important events during pregnancy and the postnatal admission. These unique whole-state data will complement data already available for the 5 neonatal ICUs and build a statewide evidence base for better physical, mental and developmental outcomes for these vulnerable babies.

Project objective: For the expected 3000 babies admitted to Victoria's 28 SCNs in Feb-July 2021, we aim to determine how morbidities (eg respiratory distress, hypoglycaemia, infection, jaundice, and feeding difficulties) in the neonatal period vary by the models of obstetric and newborn care offered in those hospitals.

This Honours/Masters project may be stand-alone, or work with a second student examining the incidence of these morbidities and characteristics of the babies who experience them. Working with the GenV and the SCN study team, the student will learn how registries are set up, assist with data extraction and map the models of care in each hospital, before proceeding to quantitative analyses to address the study objective.

This opportunity enables an outstanding student to be involved in both developing a registry with a lasting legacy (with subsequent PhD and career opportunities), and in GenV (<https://genv.org.au/>), one of the world's most exciting new child health projects.

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54. Statewide outcomes for Victoria's most complex pregnancies

The NONA registry is being developed to improve the care for women (and their babies) who experience the most complex pregnancies. These women are generally managed at one of the five Maternal Fetal Medicine (MFM) Units in Victoria (Royal Women's Hospital, Mercy Hospital for Women, Monash Medical Centre, Joan Kirner Women's & Children's and Northern Hospital). The registry will identify key quality metrics to improve outcomes for women with a pregnancy complicated by one of three conditions: (1) multiple pregnancy, (2) fetal growth restriction, and/or (3) antenatally-diagnosed congenital anomalies. The registry is being developed with the support of Monash Registries (Australia's leading registry infrastructure) and the statewide Gen V initiative led from the MCRI, providing rich additional predictive and long term data.

Up to 3 Honours/Masters students will each take one of these 3 conditions and study its statewide epidemiology: its incidence, including patterns of geographic variation; its management, including adherence to guidelines and variations in local practice and guidelines across sites; and its newborn outcomes amongst the subset of participants who birth by 31st July 2021. The student/s will learn practical skills in registry development, data collection, analysis and reporting on defined quality metrics for the first year of the NONA registry.

The registry is overseen by the NONA steering committee comprising MFM subspecialists from Victoria's major maternity hospitals and leading academics in paediatrics, women's health and registry science. The project/s will be based with GenV at the MCRI with placements in these hospitals. This is an exciting opportunity for outstanding students to be involved in both developing a registry with a lasting legacy for future maternal and child health (with subsequent PhD and career opportunities), and in GenV (<https://genv.org.au/>), one of the world's most exciting new parent and child projects.

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55. Engaging high-value cohorts for a state-wide health research initiative

Generation Victoria (GenV) is a state-wide child and parent health research initiative. The GenV research cohort is targeting all 160,000 Victorian births over two years from early 2021, seeking to recruit both parents and newborns into the life-time study. With an initiative of this scale, communication with parents ahead of recruitment is critical to enable them to make an informed decision about participation.

The recruitment of certain parent cohorts has proven challenging for previous health research projects. For example, Indigenous parents, teenage parents, those with a disability or from refugee backgrounds, are among the cohorts often missing from research samples. This greatly limits the benefits of research outcomes for those communities. For this reason, these cohorts are considered high-value for GenV and a targeted communication strategy is being implemented.

This project aims to:

1. Develop frameworks and processes to monitor and evaluate the effectiveness of communication with high-value cohorts

2. Implement these processes to gather data on effectiveness and enable GenV to adapt communications as required
3. Provide insights on effective engagement with high-value cohorts to inform communication planning for GenV and future research initiatives

Working with the GenV Cohort 2020s, Solutions Hub and marketing teams, the student will be contributing actively to data collection and management, and conducting quantitative and qualitative analyses to address the study objectives.

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56. Making cohort participation fairer to solve real problems for real populations: Generation Victoria (GenV)

Over the last 30 years, many childhood problems (like autism, coeliac, obesity, allergy, mental health) have worsened, with long-term consequences for ageing societies. Finding answers to these problems require very large scale, population-representative cohorts, such as the forthcoming GenV (see below).

Unfortunately, those with potentially most to gain - families with social risk factors - are often left out of these population studies. Participation rates are typically lower among families who have high socioeconomic disadvantage, Indigenous or culturally diverse backgrounds, teenage parents, and parents with low literacy or disability. Because the research findings are then less applicable, they can further drive gaps in equality between the most and least disadvantaged families.

Generation Victoria is Australia's most ambitious children's study, aiming to recruit all 160,000 Victorian babies born over 2 full years from early 2021 and their parents (genv.org.au). With guiding principles of Inclusion and Equity, GenV is designed to allow every eligible Victorian to participate (eg materials available in >25 languages, very low burden digital assessments).

In Stage 1, the student will identify existing complete datasets (eg Australian Census) describing the eligible population, and select the demographic characteristics to best determine GenV's representativeness. In Stage 2, they will then statistically compare the demographic characteristics of participants recruited in the first months of GenV to the eligible population, to understand the sample's population-representativeness and which groups are under-represented. In Stage 3, the student will identify barriers to participation through demographic characteristics (eg primary language) and reason-for-refusal from those who decline, and the GenV Recruitment team will use this evidence to refine their recruitment approach. In Stage 4, the student can measure the impacts on recruitment rates of under-represented groups going forward.

This project will provide evidence for recruitment decisions that have an important legacy in GenV.

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57. A more complete picture of health and wellbeing– the inclusion of fathers in family research.

Over the last 30 years, many childhood problems (like autism, coeliac, obesity, allergy, mental health) have worsened, with long-term consequences for ageing societies. Finding answers to these problems require very large scale, population-representative cohorts, such as the forthcoming Generation Victoria (GenV).

GenV is Australia's most ambitious children's study, aiming to recruit all 160,000 Victorian babies born over 2 full years from early 2021 and their parents (genv.org.au). With guiding principles of Inclusion and Equity, GenV is designed to allow every eligible Victorian to participate (eg materials available in >25 languages, very low burden digital assessments).

Fathers play an important role in shaping their children's social, emotional and physical development. However, research to date has mostly focused on mothers and children, often neglecting the involvement of fathers. Not including fathers in research limits the representativeness of the population and in turn gives an incomplete picture of the family and its role in the health and wellbeing of children.

This project aims to:

1. Describe fathers' involvement in longitudinal cohort studies and successful strategies implemented in previous studies to recruit and retain fathers.
2. Describe recruitment rates for fathers in GenV including statistically comparing demographic information of participating and non-participating fathers.
3. Explore reasons for fathers declining participation and barriers to their participation.
4. Provide recommendations for GenV's future engagement with fathers at the recruitment and retention phases.

The project findings and recommendations will guide decisions for the refinement of study procedures and have an important legacy in GenV.

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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>

For further details see the Department of Paediatrics:
www.paediatrics.unimelb.edu.au Murdoch Childrens Honours Website: www.mcri.edu.au/students/honours-students MDHS website: <http://sc.mdhs.unimelb.edu.au/entry-requirements>

Honours Course Work

BIOM40001 Introduction to Biomedical Research – 12.5 points (February)

1. 10 x 2hr tutorials
2. Two written reports (each not exceeding 3000 words) (50% each)

PAED40002 The Biology of Human Health and Disease – 12.5 points (Year Long)

1. Literature review, - Hurdle requirement
2. Assignment 1: (Individual) coming to grips with your research project 34%
3. Assignment 2: (Group) Bioinformatics – Hurdle requirement
4. Assignment 3: (Group) using biostatistics in your Honours thesis – 33%
5. Assignment 4: (Group) Critical thinking and data analysis – 33%

Honours Research Project

Students will enrol in both the research project subjects indicated below to complete a total of 75 points for the research project by the end of their course.

PAED40001 Paediatrics Research Project – 25 points (semester 1)

PAED40005 Paediatrics Research Project – 50 points (semester 2)

The research project will be completed under the supervision of experienced senior scientific researcher/s and work within a research group at the Murdoch Childrens Research Institute. The student's original research project will be assessed by the following criteria:

1. A written report (thesis) of 10,000 – 12,000 words (80%)
2. An oral presentation on the research project (13.3%)
3. Supervisor's report on the student's overall research ability (6.7%)

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 2021, 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 Project and Contact Potential Supervisor: 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 2021 are also listed on the Murdoch Childrens Research Institute and Department of Paediatrics websites.

STEP 2: Submit an Online application: Register for the Honours Application Tracking System (Sonia) before making your application in Sonia. Lodge an online application by Saturday 31 October 2020 (Round 1), and Monday 25 January 2021(Round 2). <http://mdhs-study.unimelb.edu.au/degrees/honours/apply-now#apply-now>

STEP 3: Submit Project preference in Sonia

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.

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

Start Year Intake Round 1 offers will be issued around mid-December. Mid-Year Intake offers will be issued on a rolling basis. You must respond to your offer by the Offer Lapse Date noted in your offer letter.

If you have a change of mind about your offer, please **DO NOT** proceed ahead with accepting the offer. You **MUST** notify the Honours Admissions Team via mdhs-honours@unimelb.edu.au as early as possible. You may be considered for Round 2 if you have met the minimum entry requirements but are not made a Round 1 offer for Start Year Intake.

Start Year Intake

Round 1 Application Closing Date	Saturday 31 October 2020
Round 1 Project Preferences Submission Deadline	Friday 13 November 2020
Round 1 Application Outcomes Issued By	Wednesday 23 December 2020
Round 2 Application Closing Date	Monday 25 January 2021
Round 2 Project Preferences Submission Deadline	Monday 1 February 2021
Round 2 Application Outcomes Issued By	Monday 8 February 2021
Course Commencement Date	Monday 15 February 2021

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 website: <http://mdhs-study.unimelb.edu.au/degrees/master-of-biomedical-science/overview>

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 2020, applications close: 30 November 2020.

<https://study.unimelb.edu.au/find/courses/graduate/master-of-biomedical-science/>