



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

HONOURS & MASTERS PROJECTS 2027



Honours and Master of Biomedical Science

2027 Intake Information Sessions

Wed 2 Sept, 4-5.30pm - Online and Wed 9 Sept, 5.00pm – In person

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Laboratory based

Infection, Immunity and Global Health)

1. Examination of distinct antibody responses following reduced-dose human papillomavirus vaccination

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

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Available as Masters Project: **Yes**

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2. Understanding streptococcal pathogenesis

Streptococcus pyogenes ('Strep A', group A streptococcus) is an important global pathogen. In a related bacterial species, *Streptococcus pneumoniae*, we and others 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 bacterial transcriptomics, working with in vitro and/or in vivo models such as respiratory cells from patients grown as air-liquid interface, genetic manipulation, as well as microbiological and immunological analysis of local and systemic samples. 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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Available as Masters Project: **Yes**

3. Changes in the pneumococcal population following vaccine introduction

Streptococcus pneumoniae (the pneumococcus) is a bacterial pathogen and a leading cause of morbidity and mortality worldwide. Pneumococci are classified into serotypes based on the type of capsule they produce. Although safe and effective vaccines that target a subset of these serotypes have been available for over two decades, introduction in many low- and middle-income countries (where the burden of pneumococcal disease is greatest) is frustratingly slow. Vaccine introduction also leads to profound changes in the pneumococcal population structure.

This can include a decline in vaccine-serotypes and replacement with non-vaccine-serotypes. Changes to the capsule of some strains means they are not recognized by vaccine-induced immunity (serotype switches, variants and new serotypes). However, these changes in the pneumococcal population have rarely been examined in low- and middle-income countries. In this project, you will leverage our unique set of samples from the Asia-Pacific to examine changes in the genetics of the pneumococcal population following vaccine introduction. Key approaches to this project include using genomics, bioinformatics, molecular biology, genetic manipulation of pneumococcal isolates and testing in a range of microbiological assays *in vitro*. Optional aspects include testing isolates in murine models of carriage, transmission and disease. Your research will provide new insights into how pneumococcal populations can change following vaccine introduction in high disease burden settings including Asia.

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4. Examining effects of sulforaphane on host response to human pathogens

Sulforaphane is a natural compound derived from cruciferous vegetables (e.g. broccoli) and has been shown to exhibit potent anti-inflammatory and antioxidant effects *in vitro* and *in vivo*. Our focus has been to investigate the effects of sulforaphane in the context of infectious pathogens where current treatments are limited or not available.

This project will build on our existing data showing that sulforaphane has diverse effects for common pathogens including respiratory syncytial virus (RSV), SARS-CoV-2 and non-tuberculous mycobacteria. We plan to use a variety of existing models such as human peripheral blood mononuclear cells, air-liquid interface (ALI) assays and *in vivo* mouse

models to examine the biological effects of sulforaphane. As such, the techniques that will be used include a combination of cell culture, flow cytometry, multiplex cytokine assays and PCRs.

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Available as Masters Project: **Yes**

5. Immune responses to COVID-19 booster vaccination in healthy adults

COVID-19 vaccines are highly protective against severe disease, especially when given as a booster dose. However, the magnitude and breadth of immunity over the long-term following booster vaccination has not been explored, especially to new variants. We have recently completed a randomised controlled trial in Melbourne to measure the immunogenicity of a fourth dose (second booster dose) of either mRNA or protein vaccine in healthy adults, with multiple study visits over a 30-month follow-up period. This project will examine SARS-CoV-2 immune responses using multiple immunological assays to determine differences in long-term immune protection from either vaccine. Techniques for this project include T cell assays, flow cytometry, binding antibody assays and cytokine measurements.

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Available as Masters Project: **Yes**

6. Examination of IgA responses following human papillomavirus vaccination

Human papillomavirus (HPV) is the main cause of cervical cancer. The HPV vaccine is highly potent and effective at preventing HPV infection and cervical cancer. While neutralising antibodies are considered the primary defence mechanism for HPV vaccines, the level required for protection has not been identified. Recent studies have found protection against HPV infection despite having no neutralising antibodies. Other immune markers including IgA may contribute to protection against HPV, but their role have not been characterised. This laboratory-based project will evaluate the functional role of IgA against HPV.

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Available as Masters Project: **Yes**

7. Towards better treatments for childhood lung disease

Chronic childhood lung diseases, including asthma and suppurative lung diseases such as bronchiectasis, are a major cause of morbidity worldwide, yet there remains a lack of effective biomarkers to predict disease progression and guide treatment. This project will investigate the immune and molecular mechanisms underlying childhood lung disease using respiratory and blood samples collected from well-characterised cohorts. Students will have the opportunity to apply a range of cutting-edge multi-omics approaches, including high-dimensional flow cytometry, highly multiplexed proteomics, and single-cell RNA sequencing. The project will combine laboratory work with computational data analysis to identify pathways and biomarkers associated with disease outcomes. Students will be supported by a multidisciplinary team spanning immunology, paediatric respiratory medicine, and bioinformatics, providing comprehensive training with the goal of improving outcomes for children with chronic lung disease.

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Available as Masters Project: **Yes**

8. Making antibiotic blood testing easier for children to optimise first line antibiotic use and impact on antimicrobial resistance.

Antimicrobial resistance (AMR) is a global health crisis threatening the effectiveness of antibiotics. When first-line antibiotics don't appear to be working, it is tempting to use broad-spectrum antibiotics instead, but this just increases AMR. What if the dose of the narrow-spectrum antibiotic just isn't high enough or dosing intervals are too frequent? This work has been done in adults, but the problem for children is that it is difficult to do frequent blood tests because of the pain involved and when they're little, they have very small veins. However, children tolerate having finger prick blood tests very well. This honours project aims to use a novel finger prick blood test for testing antibiotic levels in children to optimise antibiotic use.

The project involves 1) recruitment and consenting of patients in person, 2) laboratory-based work using liquid chromatography with tandem mass spectrometry as a powerful analytical technique to measure very small samples, and 3) quantification of antibiotic levels in patient samples. You will learn skills in both clinical recruitment of patients and in laboratory techniques.

This work will allow us to research how to use first-line antibiotics more effectively in children and neonates and dose-adjust childhood antibiotics individually. The impact will be to reduce development of AMR, preserving antibiotics into children's futures.

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Available as Masters Project: **No**

9. Stabilising unstable IV antibiotics so children can get home sooner.

Hospital in the home (HITH) care has been widely accepted as a safe and effective treatment option that is preferred by patients, parents and medical professionals. Portable infusers allow children to receive outpatient parenteral antibiotic therapy (OPAT) at home. However, increasing antimicrobial resistance has limited drug options available to treat serious infections caused by resistant bacteria. Some IV antibiotic treatments are effective in treating resistant infections but concerns regarding their stability, efficacy and safety when reconstituted have prevented their use in HITH. This work aims to increase the stability and improve the efficacy of antibiotics that are temperature sensitive or susceptible to degradation. This project will investigate the impact of temperature and concentration of IV antibiotic infusions, by using simple temperature control and liquid chromatography-quantitative analysis. The lab work will involve 1) establishing and validating assays, 2) measuring concentrations of antibiotics and their degradation products in the infusers, 3) testing infusers at different temperatures as well as under different carry conditions to mimic HITH care over 24 hours. 4) It may also involve patient recruitment depending on the candidate's interest in this. You will learn skills in laboratory techniques and depending on interest, in clinical recruitment of patients. If stability can be increased, this will enable patients to be treated in the home and allow greater autonomy for the patient and parent and decrease the burden on the healthcare system.

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Available as Masters Project: **No**

10. Restoring immunity across the human lifespan and in high-risk populations

Our research focuses on understanding why the same virus can lead to mild symptoms in one individual while causing severe and life-threatening disease in another. We explore the intricate interplay between viruses and our immune system, seeking to unravel the

underlying biological and molecular mechanisms dictating such various outcomes. CD8+ T cells play a critical in controlling viral infections and provide protection against severe disease outcomes by eliminating virus-infected cells. Unfortunately, we do not fully understand how virus-specific CD8+ T cell immunity develops and wanes across the human lifespan. We recently discovered that the receptors used by CD8+ T cells to recognize influenza virus infected cells change across the human lifespan, without displaying signs of exhaustion when we get older. Yet, the changes in their receptors result in reduced strength of influenza-specific immunity in the elderly. This project will use cutting-edge models and state-of-the-art techniques to investigate what is driving those age-related changes in the virus-specific T cell receptors. Specifically, this project will investigate on how the development and training of these cells in human thymus is affected by age-related changes to the human thymus tissues. The project will provide vital insights in how virus-specific CD8+ T cell immunity is generated, maintained, and lost across the human lifespan. These findings could be leverage to rationally-design treatment or vaccine strategies to restore or compensate immunity for high-risk elderly populations.

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Available as Masters Project: **Yes**

11. Whole Genome Characterization of Unusual Rotavirus Strains Using Oxford Nanopore Sequencing

Rotavirus is the leading cause of gastroenteritis in young children worldwide. Rotavirus vaccines were introduced in Australia in 2007, and high coverage has been maintained. However, rotavirus remains an important cause of gastroenteritis in young children and across the lifespan. Rotavirus is also a common cause of gastroenteritis in almost all animal species resulting in substantial viral diversity. The Australian Rotavirus Surveillance Program (ARSP) characterises rotavirus genotypes causing gastroenteritis in the Australian population. The ARSP receives rotavirus positive samples from collaborating laboratories across Australia to monitor the genotype diversity and assess the impact of vaccine on genotype distribution. Globally, the common genotype combinations identified in humans are G1P[8], G2P[4], G3P[8], G4P[8], G9P[8], G8P[8] and G12P[8]. Unusual genotypes are also detected which may be rare human variants or represent transmission of rotavirus strains from animals hosts to humans.

These strains provide important insights into host restriction of rotavirus and unusual strains have emerged to become important variants in the vaccine era; a recent example is the equine-like G3P[8] variant which is now the dominant strain nationally. These unusual strains detected in humans in recent years include G3P[3] and G3P[9] strains of canine and

feline origins, G11P[8] and G11P[25] of porcine origins and highly unusual G21P[14]. This project aims to perform comprehensive whole genome sequencing (WGS) of unusual rotavirus strains identified through ARSP surveillance data over the last decade. Specific objectives include:

1. Optimise rotavirus WGS utilizing the Oxford Nanopore Sequencing platform.
2. Conduct whole genome sequencing of unusual human isolates that represent zoonotic transmission from porcine, bovine, canine, feline and unknown host species.
3. Use phylogenetic analysis to explore the diversity, genetic relationships and transmission of these strains.

This project will combine laboratory work (PCR, library preparation and sequencing) with bioinformatics analysis. No prior experience in bioinformatics is expected.

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Available as Masters Project: **No**

12. Molecular and Immune Remodelling by Feminising Gender Affirming Hormone Therapy

Sex differences manifest in various traits, including the risk of cardiovascular, metabolic and immunological conditions. Sex hormones like estrogen and testosterone contribute to these differences, but it's often hard to separate the effects of hormones and genetics on phenotype. Despite the clear physical changes induced by gender-affirming hormone therapy (GAHT), little is known about how it affects underlying physiological and biochemical processes. This is a significant gap in health knowledge, considering that over 1.5 million individuals identify as transgender in the USA alone and GAHT represents a critical medical intervention for many to align their physical characteristics with their gender identity. In our group, we apply a systems biology approach, combining molecular and immunology techniques with next-generation sequencing and bioinformatics. In this project, you will apply these techniques to human longitudinal clinical trials of feminising GAHT and a mouse model of GAHT. Our work has shown that GAHT induces wide-spread epigenetic, transcriptional, and proteomic changes, which influence molecular pathways in immune cells and their responses to microbial compounds. How these GAHT-induced changes influence the risk and symptoms in autoimmune and other inflammatory conditions is an area of ongoing research.

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Available as Masters Project: **Yes**

13. Trained Immunity (aka Innate Immune Memory) induced by microplastics and small RNAs

Trained immunity (TRIM) describes the capacity of innate immune cells to develop nonspecific memory characteristics in response to certain exogenous exposures through metabolic and epigenetic reprogramming. This has wide-ranging implications for immunological responses in complex diseases and infections. TRIM was originally identified in human monocytes in response to microbial exposures, but has subsequently been associated with certain metabolites and danger signals, as well as being reported in other immune (macrophages, neutrophils, natural killer cells, and dendritic cells) and even nonimmune (epithelial and endothelial) cells. The underlying mechanisms that confer TRIM and inflammatory memory occur at the level of chromatin. Our team has previously characterised the mechanisms of trained immunity (Novakovic Cell 2016; Ziogas Cell 2025). In this project, you will use human primary monocytes in an in vitro Trained Immunity model to study how microplastics and small RNA ligands influence monocyte differentiation and response to microbial stimulation.

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Available as Masters Project: **Yes**

14. Defining molecular signatures of remission and persistent inflammation in juvenile idiopathic arthritis using multi-omics

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease of childhood and remains a major cause of pain and disability. Despite major advances in treatment, clinicians currently lack reliable biomarkers to identify children in true immunological remission or those at risk of future disease flare. Recent work from our group has identified distinct molecular signatures across JIA subtypes, with systemic JIA showing marked alterations in inflammatory proteins, immune cell populations and metabolites, while GlycA emerged as a promising biomarker of disease activity. This project will build on these findings by analysing samples from the CLARITY biobank and national A3BC cohort.

The student will integrate clinical data with targeted inflammatory measurements and immune cell phenotyping to identify biomarkers associated with remission, persistent inflammation and long-term outcomes. Comparisons will focus on children achieving sustained remission versus those requiring ongoing therapy or experiencing disease flare.

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Available as Masters Project: **Yes**

15. Measuring epigenetic and metabolic landscapes in human (trained) immunity at the population level

Epigenetic and metabolic programming is inherently linked to immune cell function, particularly in innate immune cells that use these mechanisms to encode trained immunity (antigen-agnostic innate immune memory). 'Trained' immune cells clear pathogens more effectively, but maladaptive programs of training contribute to the inflammation underlying many non-communicable diseases, such as cardiovascular disease. Measuring trained immunity at the population level remains an unsolved challenge, hindered by the costliness of gold-standard methodology and the lack of cross-sectional biomarkers. This innovative project addresses this key limitation by developing a novel, scalable and cost-effective method for assessing trained immunity. The student will contribute to the development of a modular spectral flow cytometry-based method for measuring an individual's trained immunity profile. The project will involve establishing a flow cytometry panel with ~25-30 markers and bioinformatic analysis of acquired data. The method will be benchmarked against well-established in vitro cell culture models of trained immunity. Once the method is established, there will be opportunities to field-test this in cohorts of childhood inflammation. This project is ideal for a student with interest in studying innate immunity through a combination of wet-lab techniques and computational analysis (in R). Previous experience in these areas would be advantageous, but full training will be provided. This research will provide a new tool for studying drivers and consequences of innate immune training across the life course. This will be broadly applicable in settings where sample volume is limited and cost-effectiveness is key, such as studies in remote areas, paediatrics, and large cohort studies.

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Available as Masters Project: **No**

16. Double Trouble: Viral-Bacterial Co-infection in Enteric Disease

Even though vaccines are available, acute gastroenteritis remains a major global health concern, with rotavirus, *Salmonella enterica* serovar Typhi (S. Typhi) and non-typhoidal *Salmonella* among the leading causes of morbidity and mortality. Together, these pathogens cause hundreds of millions of infections per year and over 300,000 deaths, primarily in children less than 5 years of age. These pathogens are typically studied independently; however, co-infections are increasingly observed in endemic areas where these pathogens circulate simultaneously. Viral infection may disrupt intestinal epithelial barrier function and alter innate immune responses, potentially increasing susceptibility to invasive bacterial infections. However, the mechanisms involved in these interactions are poorly understood. This project aims to determine how prior infection with rotavirus (or other enteric viruses) influences the invasion and pathogenicity of *Salmonella* in the intestinal epithelium. To study this:

- Human intestinal epithelial cell lines (Caco-2 and HT-29) or organoids will be used to establish relevant models for sequential viral-bacterial infection.
- Barrier integrity will be assessed using immunofluorescent staining of tight junction proteins.
- Bacterial invasion, intracellular survival and other virulence traits will be assessed using gentamicin protection assay, and analysed by colony-forming unit (CFU) enumeration
- Host immune responses will be characterised by quantitative PCR, ELISA and flow cytometry to measure cytokines output and immune signalling, while apoptosis and cytotoxicity will be evaluated using cell death markers.

Understanding how viral gastroenteritis could increase susceptibility to *Salmonella* infection has important clinical implications. The findings from this study could explain why some patients experience more severe disease during co-infection and identify biomarkers implicated in superinfection. This work will improve our understanding of enteric infection pathogenesis and aid in developing strategies for diagnosis, treatment and prevention in regions where these pathogens co-circulate.

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Available as Masters Project: **Yes**

17. Examination of IgA responses following human papillomavirus vaccination

Human papillomavirus (HPV) is the main cause of cervical cancer. The HPV vaccine is highly potent and effective at preventing HPV infection and cervical cancer. While neutralising antibodies are considered the primary defence mechanism for HPV vaccines, the level required for protection has not been identified. Recent studies have found protection against HPV infection despite having no neutralising antibodies. Other immune markers including IgA may contribute to protection against HPV, but their role have not been characterised. This project will evaluate the functional role of IgA against HPV.

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Available as Masters Project: **Yes**

18. Shaping TB Risk and Vaccine Response: The Role of Age in Mycobacterial Immunity

Tuberculosis (TB) is the leading cause of death from a single pathogen and a major global health threat, particularly in low-resource settings. Despite a vaccine being available for over 100 years, protective immunity against tuberculosis is not understood. In addition to *Mycobacterium tuberculosis* (Mtb), the bacterium that causes TB, other mycobacteria can cause devastating diseases such as leprosy and Buruli ulcer. While mycobacterial exposure is common only a small proportion of exposed individuals develop disease. Susceptibility to mycobacterial infection, disease progression, and vaccine effectiveness change across the human lifecourse. This project will collect samples from different age groups to characterise innate and adaptive immune responses to mycobacteria. A key focus will be on identifying age-specific immune profiles and understanding how immune maturation, and prior exposures shape the nature and magnitude of responses.

The student will gain experience in human immunology (immunophenotyping and functional assays), comparative analysis across age groups, and interpretation of immune function in the context of infectious disease risk.

Findings from this work will contribute to a broader understanding of immune development and ageing, and inform more effective interventions for TB and other mycobacterial diseases across the lifespan.

If you are interested in this PhD project send an email to Dr Nicole Messina (id.research@mcri.edu.au) explaining why you would like to be considered for this

opportunity and how the project fits with your experience and interests. Make sure to attach your CV and transcripts to the email. Only enquiries sent via email will be considered.

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Available as Masters Project: **Yes**

19. Improving Immunodiagnostic Tools for Tuberculosis Through Insights into Mtb Infection and Host Response

This project focuses on improving immunodiagnostic tests for *Mycobacterium tuberculosis* (Mtb) infection by investigating host immune responses that reflect an individual's ability to clear the infection without antibiotic treatment. Current immunodiagnostics for tuberculosis (TB), such as interferon-gamma release assays (IGRAs), have important limitations, particularly in distinguishing latent infection from active disease and in predicting which individuals are at highest risk of developing TB. This project aims to improve the performance and interpretability of immunodiagnostic tests for TB, with a focus on identifying immune signatures that predict susceptibility to chronic Mtb infection. Characterising these responses in clinical samples from local and international cohorts, the project will develop and validate new biomarkers for diagnosing Mtb infection and will contribute to understanding the immunopathogenesis of TB. The candidate will apply immunological and molecular techniques (e.g. cytokine profiling, epigenetic analysis) to identify markers with diagnostic and prognostic potential. The project will explore how these immune signatures vary by factors such as age, comorbidity and lifestyle (e.g. smoking). This project is well suited to a student with an interest in immunology, infectious diseases and translational research. The student will gain skills in translational immunology, assay development, and working with human samples from clinically relevant settings. The work will contribute to the development of improved diagnostic tools and a deeper understanding of TB pathogenesis, supporting efforts to detect, treat, and ultimately prevent active disease. If you are interested in this PhD project send an email to Dr Nicole Messina (id.research@mcri.edu.au) explaining why you would like to be considered for this opportunity and how the project fits with your experience and interests. Make sure to attach your CV and transcripts to the email. Only enquiries sent via email will be considered.

Dr Nicole Messina

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Available as Masters Project: **Yes**

Stem Cell Medicine

20. Inducing quiescence in induced pluripotent stem cell derived hematopoietic stem cells

The clinical translation of induced pluripotent stem cell-derived hematopoietic stem cells (iHSCs) remains a major milestone in cellular regenerative medicine. While current protocols-such as our established platform -successfully generate iHSCs, capturing the definitive functional hallmarks of bona fide primary bone marrow HSCs remains a challenge. A major bottleneck is cell cycle regulation: unlike primary bone marrow HSCs, which are in a slow-cycling quiescent state to preserve stemness, single-cell RNA sequencing (scRNA-seq) data reveals that in vitro generated iHSCs are actively cycling. This project aims to optimize culture conditions to actively induce dormancy in iHSCs and correlate this state with functional stem cell potency. Utilizing in-house generated reporter cell lines, the student will track and isolate specific cell cycle phases in real time to recreate the microenvironmental profiles captured in our scRNA-seq datasets. Crucially, the student will systematically manipulate upstream signaling pathways using targeted cocktails of small molecules, cytokines, and growth factors to alter the cycling program. By resolving how cell-cycle arrest impacts transcriptomic patterns, the student will uncover key signaling pathways essential for replicating key elements of stem cell biology in a dish. This work is critical for developing safe, durable, and translation-ready iPSC-derived cellular therapies. Depending on progress, this project offers an avenue for extension from an honours project into a comprehensive Master's study through the incorporation of in vivo mouse bone marrow transplantation and long-term engraftment assays into the project.

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Available as Masters Project: **Yes**

21. Developing bioengineered stem cell-derived alveolar models

The alveolus is continuously exposed to mechanical forces during breathing, which play important roles in regulating epithelial development, homeostasis and responses to injury. However, current in vitro lung models often fail to capture these dynamic biomechanical cues, limiting our understanding of how the physical environment influences alveolar

epithelial function. This project will combine bioengineering and stem cell biology to develop a flexible alveolar model using human induced pluripotent stem cells. The project will optimise and characterise a custom mechanically active culture platform, including the use of engineered biomaterials to modulate properties such as substrate stiffness and cyclic mechanical stretch. Stem cell differentiation, advanced imaging and molecular approaches will be used to investigate how biomechanical cues influence alveolar epithelial identity, function and responses to respiratory viral infections. This project will establish a next-generation human alveolar model to better understand mechanisms regulating lung development, repair and disease.

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22. Bioengineering a dynamic culture platform to improve the maturity of iPSC-derived valve engineered tissue

Heart valve disease is a critical health burden and growing cause of mortality worldwide. To understand disease mechanisms and develop future treatments for heart disease, we have developed a valve engineered tissue platform derived from human pluripotent stem cells. Maturation of stem cell-derived tissues is an ongoing area of research, therefore the aims of this project are to improve tissue maturation with a dynamic culture platform to mimic the mechanical environment of the valve in the body. This project will utilise human pluripotent stem cell culture, directed differentiation protocols, bioengineering techniques, 3D printing, high throughput confocal microscopy and molecular biology techniques.

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Available as Masters Project: **Yes**

23. Using stem cell-derived valve tissues for Rheumatic Heart Disease research

Rheumatic Heart Disease (RHD) is a global healthcare problem affecting >40 million people worldwide, disproportionately affecting Australia's First Nations peoples and those in low-middle income settings. RHD is an autoimmune condition where the heart valves suffer permanent damage following repeated and untreated bacterial infection with *Streptococcus pyogenes*. Studying RHD is particularly challenging because it is a human specific disease, which makes traditional animal models unsuitable for this research. We have developed a

human stem cell model of valve tissue to study RHD. This project aims to understand the role of autoantibodies in disease progression. The project will utilise human pluripotent stem cell culture, directed differentiation protocols, confocal microscopy, flow cytometry, patient serum isolation and molecular biology techniques.

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Available as Masters Project: **Yes**

24. Investigating the Role of KMT5B in Neurodevelopment and Disease Using Stem Cell-Derived Brain Organoids

Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by cognitive, motor, and sensory deficits. Despite hundreds of genes have been associated with risk for ASD, the phenotypic alterations in the developing human brain induced by ASD-risk gene mutation are not fully understood. Stem-cell-derived 3D brain organoids represents a major advance in modelling the cellular complexity of the developing human brain and offers unprecedented opportunities to investigate neurodevelopmental abnormalities associated with mutation in ASD-risk genes. The histone methyltransferase KMT5B has emerged repeatedly as top hit in studies of ASD genetic risk, and is associated with severe neurodevelopmental abnormalities, including macrocephaly, in patients. However, the biological function of KMT5B during human brain development is largely unknown.

In this project, we propose to leverage a 3D model of the developing cerebral cortex (cortical organoids) to identify ASD-specific developmental abnormalities associated with haploinsufficiency in the KMT5B gene. By taking advantage of a variety of experimental approaches, which include single-cell-omics technologies, we aim to unbiasedly discover the transcriptional, morphological, and electrophysiological changes induced by KMT5B loss of function during early cortical development, and identify the molecular mechanisms involved. This work, through the identification of the specific cell types affected, molecular processes involved, and functional features compromised, will yield novel insights into the role of KMT5B in the pathogenesis of ASD and will provide an experimental paradigm for investigating the contribution of additional genes to neurodevelopmental disorders. The prospective candidate will get the opportunity to learn a variety of laboratory techniques, including stem cell culturing, differentiation into 3D brain organoids, immunohistochemistry, microscopy, real time PCR, western blotting, in addition to a range of single-cell genomic technologies.

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Available as Masters Project: **Yes**

25. Forced Growth Factor Expression during Human Haematopoietic Development From Pluripotent Stem Cells

Human haematopoietic cells generated from induced pluripotent stem cells (iPSCs) in vitro have many applications in biotechnology and medicine. Current techniques for generating these cells require the addition of exogenous growth factors to drive differentiation towards specific lineages. This requirement is both costly and time consuming, particularly for large scale cultures systems. This project will examine the effect of enforcing expression of specific growth factors on the trajectory of haematopoietic differentiation from iPSCs. The project will explore the use of transgenic expression techniques and lipid nanoparticles as means to endogenously produce growth factors capable of directing lineage specification, expansion and differentiation. The primary objective of the project will involve in vitro differentiation experiments, with the option to perform in vivo experiments (in mice) should the former experiments show promise. Students will learn tissue culture techniques related to PSC growth and differentiation, flow cytometry, gene expression analysis (RNAseq) and fluorescence microscopy.

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Available as Masters Project: **Yes**

Clinical Sciences

26. Integrative analysis of post-transcriptional regulatory mechanisms during human iPSC-derived neuronal differentiation

The differentiation of induced pluripotent stem cells (iPSCs) into functional neurons involves extensive transcriptional and post-transcriptional remodelling that establishes neuronal identity and function. While gene expression changes during neuronal differentiation have been well characterised, the dynamic regulation of alternative splicing, poison exon inclusion, allele-specific expression and RNA editing remains poorly understood. Together, these post-transcriptional mechanisms shape neuronal development, molecular diversity and neuronal excitability. Their dysregulation is increasingly implicated in neurodevelopmental disorders and epilepsy. This project will investigate post-transcriptional regulation across a human neuronal differentiation and maturation time course comprising peripheral blood mononuclear cells (PBMCs), induced pluripotent stem cells (iPSCs), and iPSC-derived neurons representing early (D7), intermediate (D14), late (D21), and mature (D28) stages of neuronal development. Using bulk RNA sequencing datasets generated from multiple individuals, the student will characterise differential exon usage, investigate patterns of poison exon inclusion, quantify allele-specific expression, and

characterise transcriptome-wide RNA editing throughout neuronal differentiation. The resulting datasets will then be interrogated to determine whether these regulatory mechanisms represent coordinated developmental programmes across the transcriptome or preferentially affect specific biological pathways, gene families or clinically relevant genes, including ion channels and genes associated with epilepsy. The project will define the landscape of post-transcriptional regulation during human neuronal differentiation and establish an analytical framework for investigating these mechanisms in patient-derived iPSC models of neurological disease. Ultimately, this project aims to determine whether post-transcriptional analyses provide biologically and clinically meaningful information beyond conventional gene expression analyses. The findings will inform the future integration of these approaches into functional genomics workflows, molecular diagnostics and precision therapeutic strategies for epilepsy and other neurodevelopmental disorders.

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27. Mechanistic Insights into CDKL5-Associated Epilepsy Using Resected Brain Tissue and Patient-Derived Neuronal Models

CDKL5 encephalopathy is a severe early-onset epilepsy caused by mutations in the X-linked CDKL5 gene, leading to intractable seizures and profound neurodevelopmental impairment. We have already applied Xenium spatial transcriptomics to resected cortical tissue from CDKL5 patients to better understand the factors that underlie seizures in these children. In this project, the student will undertake a comprehensive analysis of these spatial datasets to identify cell-type-specific transcriptional alterations and disrupted molecular pathways. Key tasks include image-guided region segmentation, differential gene expression and pathway enrichment analyses, integration with in-house and publicly available single-cell and bulk RNA-seq resources, and validation by immunohistochemistry on additional brain regions. To validate candidate drivers of seizures, the student can leverage existing patient-derived iPSC lines differentiated into cortical neurons. Validation approaches may include qPCR, immunostaining for synaptic markers, and multielectrode array recordings to assess network activity. Pharmacological perturbations using compounds known to modulate CDKL5-linked pathways will test the functional relevance of top candidate genes. By combining spatial transcriptomics with patient-derived neuronal models, this honours/master's/PhD project aims to uncover the cellular and molecular underpinnings of CDKL5-associated epilepsy and to identify potential targets for therapeutic intervention.

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Available as Masters Project: **Yes**

28. Functional Validation of Epilepsy-Associated Variants of Uncertain Significance

IPCHiP (International Precision Child Health Partnership) is an initiative to accelerate discovery and improve outcomes in rare paediatric disease, and Gene-STEPS is its flagship programme—a rapid genetic-diagnostic pipeline for childhood epilepsies that integrates high-coverage sequencing with detailed phenotyping across four international centres. Despite these advances, many variants of uncertain significance (VUS) in epilepsy genes remain unclassified, leaving families without clear answers. In this project, the student will collaborate across our laboratory and clinical teams to identify patients harbouring high-priority VUS, then draw on our in-house multi-omic datasets to design and implement bespoke functional assays. Using cell-based models, including patient-derived induced pluripotent stem cell lines, the student will apply molecular and cellular readouts to detect variant-driven changes in gene function, protein behaviour and cellular physiology to determine VUS pathogenicity. In addition, they will evaluate targeted interventions for their ability to rescue any observed deficits. By leveraging the Gene-STEPS discovery pipeline, this project will deliver the functional evidence needed to reclassify VUS, improve diagnostic yield in epilepsy, and potentially uncover novel targets for precision therapy.

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Available as Masters Project: **Yes**

29. Solving Uncertain Epilepsy Diagnoses Using Patient-Derived Neurons

Genomic sequencing is increasingly used to diagnose children with severe epilepsy, but many receive an uncertain result because the effect of their genetic variant is unknown. We hypothesise that studying patient-derived neurons will reveal changes that cannot be predicted from DNA sequencing alone. To test this, we have developed a rapid platform that compares neurons derived from patient and control induced pluripotent stem cells using an integrated multi-omic approach. This project will apply the platform to one or more high-priority epilepsy-associated variants identified through clinical diagnostic testing. These variants require functional evidence to determine whether they are likely to cause disease. Candidate variants, clinical information and relevant genomic datasets will be selected before the project begins. This will allow the experimental and analytical approach to be tailored to how each variant is predicted to affect the gene or protein. Depending on the

selected gene, the student may also use RT-qPCR, immunofluorescence microscopy, neuronal morphology or neuronal activity assays.

The findings will be returned to the clinical diagnostic team to help classify the variant, improve diagnostic certainty and provide clearer answers for affected children and their families.

The results may also guide studies of responses to drugs used in clinical practice or identify opportunities for precision treatments, including antisense oligonucleotides. Skills developed: human cell culture, molecular biology, microscopy, multi-omic data analysis and interpretation, quantitative data analysis, genetic variant interpretation and translational research within a multidisciplinary clinical and laboratory team.

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Available as Masters Project: **Yes**

30. Mapping the Cellular Drivers of Epilepsy Using Spatial Transcriptomics

Drug-resistant epilepsy is often caused by abnormal brain tissue, but the cells and molecular pathways that generate seizures remain poorly understood. Standard sequencing measures gene activity across mixed cell populations and loses information about where cells are located within the tissue. We hypothesise that high-resolution spatial profiling will identify cell populations, tissue regions and signalling pathways that contribute to seizure generation. This project will analyse archived human brain tissue collected during epilepsy surgery. The student will integrate spatial transcriptomic and single-nucleus RNA sequencing datasets to map gene expression, identify cell types and determine how neurons, glial cells and infiltrating immune cells are organised and interact within epileptic tissue. These findings will be compared with available histopathological, genetic and clinical information to determine how specific cellular patterns relate to epilepsy-associated pathology. The project may also prioritise genes and pathways for further validation as potential therapeutic targets. It offers experience working with clinically derived human brain tissue and advanced single-cell and spatial datasets within a multidisciplinary epilepsy, pathology and bioinformatics team. Skills developed: spatial transcriptomic analysis, single-nucleus RNA sequencing, bioinformatics in R and Python, image-based cell segmentation, cell-type annotation, differential gene expression, pathway analysis, multi-omic data integration, data visualisation and translational neuroscience.

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Available as Masters Project: **Yes**

31. Improving the Diagnosis of Malformations of Cortical Development Using DNA Methylation

Malformations of cortical development are a major cause of drug-resistant epilepsy, but diagnosis can be difficult because different subtypes may look similar on imaging and histopathology. DNA methylation profiling can identify disease-specific molecular signatures and may provide additional diagnostic information beyond routine pathological assessment. We hypothesise that a methylation classifier developed for malformations of cortical development will improve molecular classification of tissue removed during epilepsy surgery. This project will use a published DNA methylation dataset together with an independent dataset generated in-house from brain tissue collected during epilepsy surgery to develop and test a molecular classifier. The student will analyse genome-wide methylation data, assess classifier performance and compare molecular classifications with histopathological, genetic and clinical findings. Cases that do not classify clearly will be examined to determine whether the model can be improved. The findings will determine whether DNA methylation profiling can be incorporated into the clinical diagnostic pathway for patients undergoing epilepsy surgery. Skills developed: DNA methylation data analysis, bioinformatics in R and Python, quality control, classification modelling, data visualisation, integration of molecular and clinical data, and translational diagnostic research.

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Available as Masters Project: **Yes**

Genomic Medicine

32. Improving outcomes of mitochondrial diseases using human stem cell models

Mitochondria are our cellular power plants that burn sugars, fats and proteins to generate energy. Each week in Australia a child is born with a severe mitochondrial disorder. Many of these children die in the first years of life and most suffer from severe disease, particularly affecting their brain and/or heart. Access to these tissues from patients is limited, making it difficult to assess the impact on mitochondrial and other pathways contributing to disease pathology.

This project will therefore use human pluripotent stem cell models of mitochondrial diseases that can be differentiated into clinically relevant cell types, such as neurons and cardiomyocytes, to investigate disease mechanisms and treatment approaches. The aims include:

1) Characterising cellular models of mitochondrial disease using human Embryonic Stem Cells (hESCs) and Induced Pluripotent Stem Cells (iPSCs) to study pathogenic pathways in

differentiated cardiomyocytes or neurons, as well as their impact on mitochondrial function and cellular physiology.

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

We have established a panel of pluripotent stem cell models representing a range of mitochondrial diseases and pathways. This project will involve validation of a selected cell model from this panel, differentiated to either cardiomyocytes or neurons to assess the impact of the gene knockout on various aspects of mitochondrial and cellular function. Molecular and cellular characterizations may include generation of correction lines, mitochondrial and cellular functional assays (e.g. ATP synthesis, fluorescence microscopy, FACS, multi-electrode arrays), quantitative proteomics, RNAseq and organoid modelling. Students will develop skills in cell culture, molecular biology and biochemistry.

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33. How does ACTN3 R577X influence postnatal muscle development?

Alpha-actinin-3 (ACTN3) is a skeletal muscle protein responsible for maintaining the integrity of the contractile apparatus in fast-glycolytic muscle fibres. A common null polymorphism (R577X) leads to complete alpha actinin 3 deficiency in ~20% of people worldwide. While this does not cause disease, the absence of alpha-actinin-3 results in significantly lower muscle mass and strength/power in elite athletes and in the general population. Using our alpha-actinin-3 knockout mouse model (Actn3 KO), we have shown that alpha actinin 3 deficiency reduces muscle mass and fast fibre size, increases oxidative metabolism and calcium handling, and heightens susceptibility to eccentric contraction damage. Recently, we found that the absence of alpha-actinin-3 also alters various pathways that regulate muscle mass, such as androgen receptor (AR) signalling. Alpha-actinin-3 deficiency results in reduced AR expression in both mouse and human muscles. Analysis of Actn3 KO mice showed that they lose more muscle mass and strength in response to androgen deprivation and gain less muscle following androgen treatment. Since androgens are important for the development and growth of skeletal muscles, we hypothesise that reduced AR signalling with alpha-actinin-3 deficiency during early muscle development shapes adult skeletal muscle phenotypes.

This project will examine the role of alpha-actinin-3 during postnatal muscle development. We have collected muscles from wildtype (WT) and Actn3 KO mice from ages P0, P7, P14, P28, 8 and 12 weeks.

These timepoints coincide with various key stages of muscle development and maturation. We will examine for morphological, metabolic and calcium handling differences between WT and Actn3 KO muscles throughout development. This project will involve laboratory-based techniques such as cryosectioning, immunohistochemistry, microscopy and western blotting to examine temporal changes in WT and Actn3 KO muscles.

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Available as Masters Project: **No**

34. Engineering Skeletal Muscle in a Dish: Using Electrical and Biochemical Cues to Tune Muscle Maturation and Fibre Type

Skeletal muscle is a remarkably adaptable tissue, capable of altering its structure and function in response to different types of stress, including exercise, disuse, and injury. In the Muscle Research lab at the Murdoch Children's Research Institute, we use innovative stem cell technologies to model skeletal muscle in vitro. This project will focus on developing and characterising 2- and 3- dimensional skeletal muscle models derived from either primary muscle cells or induced pluripotent stem cells, from healthy individuals and those with genetic muscle conditions. A key goal of the project is to explore how different electrical stimulation protocols and metabolic or hormonal cues, drive muscle maturation and the development of disease. Students will investigate whether these interventions can promote a shift toward slower, more fatigue-resistant muscle fibres (like those used in endurance sports) or faster, more powerful fibres (critical for sprint performance).

These findings have applications across the spectrum-from enhancing our understanding of genetic muscle diseases like muscular dystrophy, to modelling elite muscle performance.

The project will involve a range of techniques, including stem cell culture and differentiation, 3D tissue engineering, immunofluorescence imaging, gene and protein expression analysis, and functional assays using the Mantarray system for real-time force measurement.

This interdisciplinary project offers a unique opportunity to contribute to translational research with applications in regenerative medicine, sports science, and therapeutic development. Students will be supported by a multidisciplinary team of physiologists, stem cell biologists, and geneticists.

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Available as Masters Project: **Yes**

35. Defining the pathogenic threshold of the sca8 repeat expansion in cerebellar ataxia

The hereditary cerebellar ataxias (CA) are a clinically and genetically heterogeneous group of progressive neurodegenerative disorders, many of which are caused by short tandem repeat (STR) expansions. Despite advances in genomic testing, most individuals with a clinical diagnosis of CA lack a molecular diagnosis i.e. the cause of their condition is unknown. This is, in part, because pathogenic size thresholds for many STRs are imprecisely defined.

Spinocerebellar ataxia type 8 (SCA8) exemplifies this problem. SCA8 is an autosomal dominant ataxia caused by a CTG·CAG expansion at the ATXN8OS/ATXN8 locus. Its pathogenic threshold is currently poorly defined, so the repeat has low positive predictive value in diagnostic settings, and its allele-size distribution in affected and healthy populations remains poorly characterised.

This project will analyse the SCA8 locus in two existing cohorts highly suited to defining pathogenic thresholds in repeat expansion disorders.

The first is a clinically ascertained cohort of ~500 individuals with CA and the second is a large cohort of ~2000 healthy controls aged well beyond the typical age at onset of SCA8. Comparison of allele-frequency distributions and repeat motif composition between cohorts will be used to interrogate current pathogenic thresholds, and Kaplan-Meier analysis will model the relationship between repeat length, penetrance, and age at onset.

You will develop skills in molecular techniques (long-range and repeat-primed PCR, capillary electrophoresis), statistical analysis, variant curation, and scientific communication, within an active neurogenetics program at the research-diagnostic interface.

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Available as Masters Project: **No**

36. Characterising somatic instability of the fgf14 repeat expansion in sca27b patient-derived cerebellar organoids

Many repeat expansion disorders show somatic instability: the causative repeat continues to change in length and sequence composition in affected tissues after development, and this ongoing expansion is increasingly implicated in disease onset and progression. Whether this occurs for the FGF14 GAA repeat that causes a common spinocerebellar ataxia (SCA27B) is unknown, in part because of limited availability of the affected brain tissue (cerebellum).

Patient-derived cerebellar organoids provide a tractable, disease-relevant model of SCA27B. FGF14 is expressed highly in cerebellar Purkinje neurons, the cell type central to the disease. Cerebellar organoids generate Purkinje precursors and neurons during differentiation and development, allowing repeat behaviour to be tracked directly in the relevant cellular context over time. This project draws on an established resource: and banked for analysis.

The project will characterise the FGF14 GAA repeat in cerebellar organoids from four individuals with SCA27B (two male, two female) with paired isogenic controls, cultured across a differentiation time course. Repeat length and GAA purity will be determined to test for somatic instability relative to the isogenic control. Matched transcriptomic data will test whether instability predicts FGF14 and downstream expression changes, with an exploratory comparison of instability between male and female lines. You will develop skills in molecular techniques (long-range and repeat-primed PCR, capillary electrophoresis), multi-omic and statistical data integration, variant interpretation, and scientific communication, within an active neurogenetics program at the research-diagnostic interface.

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Available as Masters Project: **No**

37. Investigating genes involved in female infertility

Female infertility affects millions of women and couples worldwide, yet its genetic basis remains poorly understood, limiting accurate diagnosis and precision care. This project aims to investigate candidate genes associated with female infertility to better understand their roles in ovarian function and female reproductive health.

The student will gain hands-on experience in molecular biology techniques, including cloning, PCR, Western blotting, cell culture, and microscopy, while contributing to ongoing research in the laboratory. The findings will help improve our understanding of disease mechanisms and may identify novel genetic contributors to female infertility, with potential implications for future diagnosis and treatment.

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Available as Masters Project: **Yes**

38. Evaluating Novel Therapeutic Candidates for Neurofibromatosis Type 1 Using Human Stem Cell Models

Neurofibromatosis type 1 (NF1) is one of the most common genetic neurodevelopmental disorders, affecting approximately 1 in 2,700 children. Up to 80% of children with NF1 experience cognitive and behavioural difficulties, including learning disabilities, ADHD, autism spectrum disorder (ASD), and executive dysfunction. Despite their significant impact on quality of life, there are currently no treatments that address the underlying biological causes of these impairments. This Honours project will build upon recent drug discovery efforts within our laboratory that have identified several promising candidate compounds for NF1-associated neurodevelopmental disorders. The project will utilise our unique collection of NF1 patient-derived induced pluripotent stem cell (iPSC) lines and gene-corrected isogenic controls, which have already revealed deficits in neuronal development, synapse formation,

and neuronal network activity. The student will investigate whether selected candidate compounds can rescue these disease-associated abnormalities in human stem cell-derived cortical neurons and three-dimensional brain organoids. Using a range of cutting-edge techniques, including high-content imaging, immunofluorescence, molecular analyses, and functional assays, the student will assess the effects of compound treatment on neuronal growth, maturation, and function. This project offers an exciting opportunity to gain hands-on experience in stem cell biology, neuroscience, and translational research while contributing to the development of potential new therapies for children with NF1.

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Available as Masters Project: **Yes**

39. Epigenetic control of cerebellar development in basilicata-akhtar syndrome

Basilicata-Akhtar syndrome is a rare genetic disorder characterised by profound intellectual disability, speech and language impairment, and movement difficulties. It is caused by deleterious variants in MSL3, the gene which encodes a component of the Male-Specific Lethal (MSL) histone acetyltransferase complex. We and others have shown that this complex is essential for acetylation of Histone H4 at Lysine 16 (H4K16ac). Loss of MSL3 dramatically reduces H4K16ac across the genome, disrupting normal developmental gene regulation. Brain imaging of children with Basilicata-Akhtar syndrome consistently shows underdevelopment of a brain region called the cerebellum, particularly the cerebellar vermis. This midline structure within the cerebellum is essential for motor control and higher cognitive function. However, why MSL3 is required for cerebellar vermis development, and whether restoring H4K16ac could rescue this defect, remain unknown. In this project, you will use human stem cells to investigate these questions. Using MSL3 knockout stem cells, you will generate three-dimensional cerebellar organoids and compare their development with genetically matched controls. These organoids model key stages of human foetal cerebellar development, providing a unique system to study disease mechanisms.

You will determine how loss of MSL3 alters H4K16ac during in vitro cerebellar development and assess the downstream impacts this has on cerebellar growth overtime and cellular processes involved in cerebellar vermis formation. Our lab has identified molecules capable of increasing H4K16ac. Therefore, you will also test whether increasing H4K16ac can improve cerebellar development in MSL3 knockout organoids; a major step in treatment development for Basilicata-Akhtar syndrome.

This project provides skill development in stem cell modelling, advanced microscopy, molecular biology, and drug screen array techniques. Furthermore, you will benefit from a cross-disciplinary supervisor panel. Spanning both the laboratory and clinic, our team

ensures you gain a broad technical skillset alongside a deep understanding of the clinical impact of your project.

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Available as Masters Project:**No**

40. Investigating Axonal Transport Dysfunction and Therapeutic Interventions for Vision Loss in KIF1A-Associated Neurological Disorder: An iPSC-Derived Retinal Ganglion Cell Study

Background and Significance: KIF1A-Associated Neurological Disorder (KAND) is a devastating childhood dementia caused by pathogenic KIF1A variants, resulting in intellectual disability, treatment-resistant epilepsy, and progressive vision loss from optic nerve degeneration, a priority concern identified by KIF1A families and their Foundations (KIF1A.org). Our preliminary proteomics revealed reduced levels of KIF1A (a key neuronal motor protein) in KAND mouse optic nerves, suggesting impaired axonal transport drives RGC death. With no existing therapies, this study will establish the first patient-derived induced pluripotent stem cell (iPSC)-RGC model to investigate disease mechanisms and test already identified repurposed therapeutic compounds. **Research and Hypothesis:** Pathogenic KIF1A variants disrupt RGC axonal transport causing optic nerve degeneration, which can be modelled in patient iPSC-RGCs and rescued by repurposed drugs. **Aims and Objectives:**

Aim 1: Generate and characterise KAND patient iPSC-derived retinal ganglion cell models.

Objectives:

- Differentiate and validate iPSC-derived 2D RGC cultures from 3 different KAND patients harbouring distinct KIF1A variants.
- Characterise KIF1A localisation, neurite outgrowth, and survival compared to healthy control iPSC-derived RGCs.
- **Aim 2:** Identify disease mechanisms, biomarkers, and drug targets through quantitative proteomic analysis of KAND iPSC-derived RGCs.
- **Objectives:**
- Perform quantitative proteomics comparing KAND and isogenic control RGCs and identify differentially expressed proteins and dysregulated biological pathways
- Validate selected proteomic findings using orthogonal western blot assays
- Correlate proteomic signatures with specific KIF1A variants

Aim 3: Test therapeutic efficacy of pre-identified re-purposed small molecules in KAND RGC models

Objectives:

- Evaluate dose-dependent effects of 3 already identified small molecules on RGC survival, neurite outgrowth, and cellular morphology
- Determine optimal treatment concentration and duration for maximal therapeutic benefit Expected outcomes and significance:

This study will establish the first KAND iPSC-RGC mode, advancing KIF1A understanding whilst accelerating drug repurposing for vision preservation and enabling personalised, clinically-applicable therapies for affected families.

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Available as Masters Project:**Yes**

41. Precision therapy for a progressive childhood genetic brain disease

Details: We identified a new severe childhood neurological disorder where all affected children are homozygous for the exact same mutation in a well-conserved splice site of TRAPPC4 [1]. There are no treatments. We have designed and refined antisense oligonucleotides (ASOs) to modify aberrant splicing processes. Our lead ASOs increase protein levels and normalise the mis-splicing events.

To our knowledge no stem cell models exist for this disease. In the proposed studies we will achieve the following: 1: Utilise existing patient-derived stem cells and characterise neuronal phenotypes due to TRAPPC4 deficiency. 2: Undertake functional validation of lead ASOs in patient stem cell derived iPSC, neurons and potentially brain organoids.

By the end of this study, we anticipate identifying top safe ASO for future human trials.

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42. What are the consequences of CDKL5 dysregulation human neurons?

Details: The Cyclin-Dependent Kinase-like 5 (CDKL5) protein is critical for neuronal function and differentiation. CDKL5 Deficiency Disorder (CDD) is an X-linked developmental encephalopathy that results in early onset and difficult to control seizures and severe neurodevelopmental impairment, leading to lifelong disability. The CDKL5 protein is expressed in the brain, predominantly in neurons and regulates key phosphorylation events that in turn regulate cell proliferation, neuronal maturation, synaptic activity, neuronal network function and the movement of subcellular cargo in neurons.

The major aims of this proposal may encompass some of the following:

1. Contribute to our investigations on the critical role of the mammalian CDKL5 protein in human stem-cell derived neurons and brain organoids, through immunostaining, proteomics, electrophysiology and/or gene expression.
2. Increase our understanding of CDKL5 in key cellular events including maintenance and regulation of microtubule proteins, transcriptional regulators and DNA damage repair proteins.
3. This project will also interact with our drug repurposing screening program for CDKL5 and may encompass follow-up experiments validating drugs from our screening. We will identify key pathways regulated by CDKL5 and which will improve our understanding of how this kinase regulates synaptic activity in brain-like neural networks.

We use a range of disease models including 2D neuronal culture and brain organoids. This project will contribute to a comprehensive and detailed understanding of the CDKL5 kinase in neuronal cell biology.

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Available as Masters Project: **Yes**

43. Functional Characterisation of Cellular Stress Pathways in Mitochondrial Disease Models

Mitochondrial diseases are genetically and clinically complex disorders that affect a cell's ability to generate energy through oxidative phosphorylation. These diseases can affect single or multiple organ systems, in particular those with higher energy requirements such as the brain, heart and muscle, with a range of severities. Alongside energy production, mitochondria also play key roles in many other functions, including cellular signalling, metabolism, and inflammatory responses. As such, the genes linked to mitochondrial diseases range from those directly involved in the process of oxidative phosphorylation, to those with broader functions in mitochondrial homeostasis, such as in mitochondrial quality control, morphology, and metabolism. How these different genes and mechanisms converge at pathways that drive mitochondrial disease pathology and tissue specificity is unclear. Emerging evidence has linked mitochondrial dysfunction to cellular stress pathways, but comprehensive stress profiling across a range of different disease genes and pathways is lacking.

This project will leverage our unique mitochondrial disease molecular and patient resources to explore cellular stress pathways and how they impact mitochondrial function. In particular, it will focus on known and novel disease genes involved in mitochondrial quality control (e.g. proteases and chaperones) or in cellular stress pathways that lead to diseases with mitochondrial dysfunction.

The aims of the project include:

- 1) Generation and validation of human cellular models of mitochondrial disease linked to quality control and cellular stress responses.
- 2) Exploration of stress pathway activation in cell models and responses to stress stimuli.
- 3) Correlative analysis of stress pathway studies in patient cell lines and tissues.

This functional genomics project will involve a range of cell biology and molecular biology techniques including cell culture, cloning, PCR/qPCR, western blotting, FACs, microscopy, mitochondrial functional assays (e.g. ATP synthesis or bioenergetic analyses) and omics (e.g. quantitative proteomics, transcriptomic).

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Available as Masters Project: **Yes**

44. NAXD deficiency: unravelling the pathological consequences, and evaluation of therapeutic opportunities

Details: There are major gaps in our basic understanding of the inborn error of metabolism, NAXD deficiency, and no specific treatments are available. It is likely that disruption of core metabolic processes including ATP synthesis, the Krebs cycle and other pathways could be aggravated by intercurrent illnesses and challenge an already compromised energetic state. Our research team focuses on uncovering the molecular basis of undiagnosed childhood brain disorders using genomic sequencing. We have recently identified mutations in a new gene called NAXD in young children who were born healthy and developed normally until a febrile episode or common infection triggered failure of the metabolite repair system associated with NAXD. All of these children died rapidly during such an episode.

We have shown that mitochondrial energy production was severely compromised in skin cells from these children and was associated with a vast accumulation of damaged metabolites. Prior to our discovery, mutations in this gene had never been described before in humans. This work was published in *Brain* in January 2019. We will utilise a number of techniques to investigate cellular impairment including, but not limited to cell culture, mitochondrial inhibition assays, mitochondrial enzyme activities and respiration, protein expression, gene expression, metabolite extraction and analysis and proteomics. We are currently undertaking high throughput drug screening, which has identified potential lead hits to modulate the effects of NAXD deficiency.

There is scope to expand this project from an Honours to a Masters project by the inclusion of stem cell modelling for screening of potential therapeutic agents for NAXD deficiency, using patient-derived and gene-corrected iPSC for differentiation into relevant cell types for NAXD deficiency.

This research proposal will enhance our understanding of this new genetic disorder by uncovering molecular pathways perturbed by loss of gene function, and may provide an understanding of therapeutic targets to protect the brain when children with gene mutations suffer febrile illnesses that would otherwise overload the repair system.

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Available as Masters Project:**Yes**

45. Solving the Unsolved - functional approaches to enable genomic diagnosis of patients with Mitochondrial disease and 'variants of genes of uncertain significance'

Individual "rare diseases" affect fewer than 1 in 2000 people but collectively the ~10,000 rare diseases affect around 1 in 12 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 425 distinct monogenic causes.

Genomic sequencing technologies have transformed genetic diagnosis of patients suspected of Mitochondrial disease, largely replacing traditional enzyme and histochemical testing. However clinical diagnostic yields are still typically 30–50%. MitoMDT is a MRFF-funded national network for multi-omic investigation of mitochondrial diseases comprising clinicians, researchers and diagnostic scientists that aims to increase the diagnostic rate of mitochondrial disease to at least 70%. The 122 adult and paediatric patients with suspected Mitochondrial disease accepted into the MitoMDT study were assigned an individualised diagnostic pathway tailored to their prior genomic testing history and phenotype. Pathways included clinical genome sequencing, research re-analysis, and multi-omic analyses including proteomics and/or transcriptomics.

This project focuses on the cases that require further functional validation through targeted experimental testing for candidate disease genes (sometimes referred to as genes of uncertain significance or GUS) along with 'variants of uncertain significance (VUS)' in known disease genes to validate their pathogenic significance. This will identify novel genes, generate definitive diagnoses in previously unsolvable cases, aid understanding of pathogenic mechanisms and assist in achieving better health outcomes for patients with Mitochondrial Disease.

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Available as Masters Project:**No**

Non-laboratory based

Infection, Immunity and Global Health)

46. Determinants of childhood cardiovascular health

Risk for cardiovascular disease accumulates across the life course, starting early in life. Childhood cardiovascular health measures (such as blood pressure, arterial structure and stiffness) are associated with cardiovascular health later in life. There is therefore a promising but overlooked opportunity to act earlier in life to optimise cardiovascular health early in life and set children on a healthier trajectory into adulthood. Advances in this area are limited by a lack of childhood data available on early cardiovascular health measures and biological drivers of cardiovascular health. This Honours project will use recently collected data from the Barwon Infant Study (BIS), a world-class Victorian longitudinal cohort of children followed since pregnancy, to investigate environmental and molecular processes that influence cardiovascular health in mid-childhood using causal quantitative analysis methods. BIS is the only cohort worldwide to have assessed cardiovascular health measures repeatedly through childhood. Effects of exposures such as inflammation, metabolic health, and socioeconomic position on cardiovascular health will be investigated. This project is well suited to a student with interest in molecular biology, epidemiology, and/or biostatistics. This research will advance our understanding of the biological pathways involved in shaping cardiovascular health in childhood, providing important evidence to unlock potential intervention targets to reduce the risk of cardiovascular disease in adulthood. This project is based within the friendly, productive, multidisciplinary Inflammatory Origins Group at MCRI.

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Available as Masters Project:**No**

47. Who sticks with therapy? Predictors of CPAP and BiPAP adherence in a tertiary paediatric sleep and home ventilation service

Continuous and bilevel positive airway pressure (CPAP/BiPAP) are cornerstone therapies for children with obstructive sleep apnoea, nocturnal hypoventilation and neuromuscular respiratory insufficiency. Therapeutic benefit, however, depends on adequate adherence, which in paediatric populations is frequently suboptimal and highly variable. Cloud-based telemonitoring platforms (e.g. ResMed AirView) now enable objective, near real-time capture of usage, mask leak and residual respiratory events, yet evidence that telemonitoring alone improves adherence in children remains limited and inconsistent.

Benefit appears to depend on active, protocolised clinical response rather than passive availability of data.

This project will evaluate adherence to CPAP and BiPAP therapy within the complex paediatric sleep and home ventilation service at The Royal Children's Hospital (RCH), Melbourne. Using de-identified telemonitoring data and clinical records, the student will conduct a retrospective cohort analysis characterising adherence patterns across diagnostic groups, device modes and age bands, and examine clinical and demographic predictors of adherence reported in the literature, including age, sex, disease severity and developmental status. Findings will be benchmarked against published Australian and international paediatric cohorts. Data will be managed in REDCap (MCRI-hosted) and analysed in Stata, equipping the student with transferable skills in clinical data extraction, database design and biostatistical analysis, alongside direct engagement with a tertiary multidisciplinary service. The work is highly clinically relevant: it will quantify real-world adherence, identify sub-populations at risk of therapy failure, and inform service-level strategies to optimise telemonitoring workflows and follow-up. Outputs are suitable for presentation at national scientific meetings and publication. The project is non-laboratory based and suits a motivated student with an interest in paediatrics, respiratory and sleep medicine, digital health or data analysis, and can be scoped to Honours or Masters level.

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Available as Masters Project:**No**

48. Using the SnotWatch platform to understand the epidemiology and impact of respiratory viruses

The SnotWatch platform collates results of respiratory PCR tests from Victorian laboratories. There is opportunity to conduct epidemiological descriptions of tested pathogens. We have also developed an approach to describe the presentations to healthcare that are associated with peaks in virus circulation. This approach could be used to describe the association between circulating viruses and presentations for conditions such as GBS, cellulitis, myocardial infarctions and strokes.

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Stem Cell Medicine

49. CYP2C19 phenoconversion: assessment of real world impact using therapeutic drug monitoring as a clinical biomarker

Pharmacogenomics (PGx) is the study of how an individual's genetic variation influences their response to medications, providing a foundation for personalised prescribing by enabling the selection and optimisation of therapies based on a patient's genetic profile. One important consideration for the field of PGx is the phenomenon of "phenoconversion" when a patient's observed drug-metabolising phenotype differs from what would be predicted by their genetic profile alone. Although PGx testing can identify inherited variants that influence enzyme activity, environmental factors, co-administered medications, disease states, and physiological changes can alter enzyme function and lead to a mismatch between genotype and actual drug response.

CYP2C19 provides a clinically relevant example of the impact of phenoconversion on genotype-informed prescribing. CYP2C19 genotype can be used to guide therapy for medications such as voriconazole; however, a patient classified genetically as a normal metaboliser may function as a poor or rapid metaboliser if exposed to CYP2C19 inhibitors or inducers. For example, co-administration of a CYP2C19 inhibitor such as omeprazole can reduce enzyme activity and cause a normal metaboliser to exhibit a poor metaboliser phenotype, potentially increasing voriconazole concentrations.

This project aims to study voriconazole concentration in real-world paediatric oncology patients with known CYP2C19 genotypes. An assessment of whether voriconazole concentrations correspond to a patient's predicted phenotype will be performed, in addition to analysing the effects of phenoconversion on voriconazole drug levels in patients taking a concurrent proton pump inhibitor (such as omeprazole, esomeprazole or pantoprazole). Incorporating phenoconversion into clinical decision-making will improve the accuracy of prescribing recommendations by combining genetic information with current clinical factors, helping to reduce the risk of treatment failure or adverse drug reactions.

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Available as Masters Project:**No**

50. Analysis of spatial data in congenital heart diseases

Congenital heart disease affects 1 in 100 babies, while no cure currently exist, surgery in early weeks of life is usually required generating a great burden for the babies and their

families. Most of the aetiology of congenital heart disease remains unknown. Spatial gene expression patterns are critical to understand how the heart develops and what underlying genetic patterns are behind heart malformation. High-throughput spatial temporal data have been recently generated with spatial transcriptomics technologies. Capitalising on these rich datasets, we aim to build a custom analysis workflow in which the cells are profiled with precise spatial gene expression information.

The student will provide fundamental contribution to of this project, by:

- (1) analysing the spatial and single-cell RNA-seq datasets;
 - (2) cross-validating the pattern in independent datasets and
 - (3) associating observed spatial patterns with known literature in congenital heart disease.
- The outcome of this project is to discover novel genetic causes for congenital disease to improve the diagnostic and subsequent treatment of heart defects.

Skills focus: proficiency in one programming language (e.g. Matlab, R, Python), basic understanding of cell and development biology, simulation, data visualisation, bulk / single-cell RNA-sequencing analysis. Laboratory Links: <https://ramialison-lab.github.io/index.html>

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Available as Masters Project:**Yes**

51. Understanding the Lived Experience of Muscle Loss and Physical Vulnerability During Childhood Leukaemia Treatment

Children receiving treatment for acute lymphoblastic leukaemia (ALL) experience substantial declines in muscle health, physical function, and participation in everyday activities. While these physical changes are increasingly recognised, little is known about how children and their families experience these changes throughout treatment. Understanding these lived experiences is essential for designing rehabilitation strategies that are meaningful, acceptable, and responsive to family needs. This Honours project will use qualitative data collected as part of the PROTECT Study, a prospective longitudinal study investigating the impact of leukaemia treatment on muscle health and function. PROTECT follows children across four time points from diagnosis and combines measures of muscle mass (ultrasound and DXA), physical function, peripheral neuropathy, and patient-reported experiences to better understand the development of sarcopenia and physical vulnerability during treatment.

The study also includes a pilot rehabilitation arm that is evaluating the feasibility and acceptability of delivering an early rehabilitation intervention for children identified as being at risk of sarcopenia. Together, these data aim to inform future rehabilitation strategies that can be integrated into routine paediatric cancer care. The Honours student will contribute to the qualitative component of the study by conducting interviews with children and parents, transcribing interviews, and undertaking thematic analysis to explore experiences of muscle loss, physical limitations, fatigue, participation, and recovery throughout treatment.

The student will work closely with the research team to develop coding frameworks, interpret findings, and integrate results with the broader aims of the PROTECT study.

The findings will provide important insights into how children and families perceive physical changes during treatment and identify priorities for supportive care and rehabilitation. This project offers experience in qualitative health research, consumer-centred research methods, and paediatric oncology, with the opportunity to contribute to a peer-reviewed publication and inform future interventions designed to preserve muscle health and improve functional outcomes for children with cancer.

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Available as Masters Project:**No**

52. Evaluating the Validity and Clinical Utility of a Frailty Assessment Tool in Paediatric Oncology

Children receiving treatment for acute lymphoblastic leukaemia (ALL) are at risk of developing physical vulnerability due to treatment-related declines in muscle health, physical function, nutrition, and overall physiological reserve. Frailty has emerged as a useful framework for understanding these multidimensional changes; however, there are currently no validated frailty assessment tools for use in paediatric oncology. A clinically feasible tool capable of identifying children at risk of physical vulnerability could support earlier intervention and more targeted rehabilitation. This Honours project will use data collected as part of the PROTECT Study, a prospective longitudinal study investigating the impact of leukaemia treatment on muscle health and function. PROTECT follows children across four time points from diagnosis and includes assessments of muscle mass, body composition, physical function, peripheral neuropathy, patient-reported outcomes, and frailty. The study also includes a pilot rehabilitation arm evaluating the feasibility of early rehabilitation for children identified as being at risk of sarcopenia.

The project will evaluate the construct validity and clinical utility of the frailty assessment tool used within PROTECT. The student will analyse whether frailty scores reflect expected differences across clinical groups, including children with greater muscle loss, poorer physical function, higher treatment burden, or increased treatment-related toxicity. Associations between frailty and other measures of physical health will be explored to determine whether the tool accurately captures physical vulnerability. The student may also analyse qualitative interview data from clinicians to understand the acceptability, feasibility, and perceived value of incorporating frailty assessment into routine paediatric oncology practice.

This project forms part of a larger international research programme aimed at improving the identification and management of sarcopenia and frailty in children with cancer. The student will contribute to work informing an international Delphi consensus study to establish standardised definitions of paediatric cancer-related sarcopenia and frailty, and support the ongoing development of a clinically applicable assessment and management framework. The findings will help determine whether frailty screening can be feasibly integrated into routine paediatric oncology care and guide future rehabilitation pathways for children at greatest risk of physical vulnerability.

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Available as Masters Project:**No**

Clinical Sciences

53. Ethics of genetic research into gender identity: from twin studies to whole genome sequencing

This project explores the complex ethical landscape of investigating the biological underpinnings of gender identity. By exploring distinct methodologies of genetic research (i.e. twin studies, family linkage mapping, and whole genome sequencing), the student will analyse the relative risks and benefits associated with these different approaches and their potential impact on transgender and gender diverse individuals. For example, while identifying a genetic basis for gender identity may help to improve understanding and acceptance of transgender and gender diverse individuals, the identification of specific underlying genetic variants raises the spectre of eugenics.

The project is a valuable opportunity for a student to engage with high-level clinical ethics discourse, while exploring the intersections of transgender health and clinical genetics. Supervisors will include: Lynn Gillam, Ken Pang and Anja Ravine.

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Available as Masters Project:**Yes**

54. Exploring gender-affirming care for trans and gender diverse young people in primary practice

In Australia, trans and gender diverse young people are increasingly accessing gender-affirming care (e.g., gender-affirming hormones) through primary practice. Despite this, there is little known about how primary practitioners deliver this care. This project will involve surveys and qualitative interviews with primary practitioners supporting trans and gender diverse young people in Australia, to explore how they provide gender-affirming care and the barriers and facilitators to their work.

This project will give students the opportunity to be involved in data collection (e.g., through designing surveys or conducting interviews) and quantitative and qualitative data analysis, depending on their interests. This project will contribute to a larger body of work aiming to improve models of gender-affirming care for trans young people in Australia, as part of the Australian Research Consortium for Trans Youth and Children (ARCTYC).

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Available as Masters Project:**No**

55. Changing outcomes at 8 years after extremely preterm birth: The Victorian Infant Collaborative Study

Extremely preterm (EP, <28 weeks) or extremely low birth weight (ELBW, <1000 g) carries increased risk for health and developmental problems. There have been significant advances in neonatal care, but benefits are not always seen long term. The Victorian Infant Collaborative Study program of research has multiple geographic cohorts of children born EP/ELBW and contemporaneous term-born controls, i.e. in 1991-92, 1997, and 2005. The latest birth cohort born 2016-17 will have completed their 8 year assessments in late 2026. This provides the perfect opportunity to assess how a range of health and developmental outcomes have changed over eras.

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Available as Masters Project:**Yes**

56. Rotational gait disorders in children

In-toeing and out-toeing during walking are commonly observed gait deviations in children. There are multiple underlying causes of why children and adolescents walk in this way, the primary cause is attributed to structural deformity of the lower limb bones. The Gait Analysis Laboratory at the Royal Children's Hospital (RCH) routinely assesses these children and adolescents with rotational gait issues. The purpose of these assessments is to evaluate the impact of the lower limb deformity on gait, functional capacity, and participation to inform decisions regarding orthopaedic surgery. This research project will focus on a retrospective cohort of children and adolescents that were assessed for a rotational gait disorder at the RCH. The aim of the research is to: 1. Quantify surgical effect by comparing pre- and post-operative gait biomechanics, function and participation. 2. Quantify associations between structural deformities and gait biomechanics pre and post operatively 3.

Perform exploratory analysis of predictors of undergoing orthopaedic surgery (severity of deformity, symptoms, family preference, prior treatments, functional level). You will work with both the research and clinical teams from the Gait Analysis Laboratory and Orthopaedic Department. The project will involve working with a range of clinical data including, medical imaging, 3D motion capture data, surgical and patient reported outcome measures.

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Available as Masters Project:**No**

57. Forearm osteochondromas management in paediatric population

Osteochondroma is a benign endochondral bone growth that arises at the metaphysis of long bones. This condition commonly affects the forearm bones (ulna or radius) in skeletally immature, such as children and adolescents. Osteochondroma usually presents as a solitary lesion. The occurrence of two or more osteochondromas is termed multiple osteochondromas, which is a genetic disorder known as Multiple Hereditary Exostosis. Most forearm osteochondromas are managed conservatively. Surgical interventions are indicated for lesions that result in pain, progressive deformity, or functional impairment. This study aims to evaluate the clinical and radiographic outcomes in patients who have undergone surgical treatment for forearm osteochondromas. A retrospective observational study will

be conducted at the Royal Children's Hospital, Melbourne (RCH). Data will be extracted from RCH medical records. Outcomes will be measured at pre-operative and post-operative intervals during routine clinical appointments. Data on clinical presentation, surgical approach, wrist and forearm range of motion, and osseous deformity will be collected. Radiographic data will be evaluated for deformity parameters, including ulnar length, radial articular angle, carpal slip, and radial head dislocation. Data will be analysed using statistical software to compare pre- and post-treatment outcomes, applying appropriate statistical tests based on the underlying data distribution.

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Available as Masters Project:**Yes**

58. Plate migration after internal fixation of distal forearm fracture

Distal forearm fractures (distal end of the radius) are common among children and adolescents, often resulting from falls onto an outstretched hand during sports activities. Surgical management is frequently required, with internal fixation offering the most stable reduction. Internal fixation involves surgically placing metal implants such as plates and screws at the fracture site to stabilise the bone, minimise displacement, and allow proper healing. However, concerns arise in paediatric patients as growth may lead to migration of the metal plate to a more radial position, leading to plate overhang relative to bone. This can result in pain, palpable hardware, and irritation. This study aims to evaluate the clinical and radiographic outcomes in patients who have undergone plate internal fixation following distal radius fractures. A retrospective observational study will be conducted at the Royal Children's Hospital, Melbourne (RCH). Data will be extracted from RCH medical records. Presence of metalware irritation at post-operative follow-up will be recorded. Radiographs will be evaluated for plate migration. Data will be analysed using statistical software to compare pre- and post-treatment outcomes, applying appropriate statistical tests based on the underlying data distribution.

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59. Using Deep Learning to Investigate the Relationship Between Focal Areas of Signal Intensity lesions and Cognitive Impairment in Neurofibromatosis Type 1

Neurofibromatosis type 1 (NF1) is a genetic disorder affecting approximately 1/3000 births. People with NF1 can present with multiple clinical manifestations including changes to skin tissue and the growth of tumors across the spinal cord, nerves, and the brain. They also present with higher rates of attention-deficit/hyperactivity, autism spectrum, mood and anxiety disorders, which significantly impact quality of life.

Approximately 75% of people with NF1 display T2-weighted hyperintense foci on brain images, known as Focal Areas of Signal Intensity (FASI). While generally considered benign, there is uncertainty about whether FASIs impact cognitive function. Findings from this research field are inconsistent, largely due to the use of time-intensive manual, rater-dependent lesion counting, performed in small study populations. This project will improve upon this process by applying a recently developed deep learning white matter lesion segmentation pipeline to a large-scale MRI dataset from a paediatric NF1 cohort. This pipeline will generate data on FASI number, volume, size, and neuroanatomical location, which will then be linked to cognitive data.

Three aims will then be investigated:

- (1) whether FASI burden is associated with cognitive dysfunction;
- (2) whether lesion size and location predict clinical measures; and
- (3) whether there are sex-specific patterns in FASI presentation, or in the relationship between FASI and clinical outcomes.

The project is suited to a student with an interest in neuroimaging and neurodevelopmental conditions. The project does not require experience with developing deep learning/AI architectures, however it provides an opportunity to gain experience in implementing deep learning medical image analysis pipelines.

By moving beyond manual lesion assessment to a scalable imaging pipeline, this project will provide a robust characterisation of the FASI-cognition relationship in NF1. Findings have the potential to inform earlier identification of children at risk of cognitive impairment and aid in the search for more individualised prognostic counselling

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Available as Masters Project: **Yes**

60. How does disease progression affect gait in childhood-onset facioscapulohumeral muscular dystrophy (FSHD)? A longitudinal gait analysis study.

Facioscapulohumeral muscular dystrophy (FSHD) is the second most common muscular dystrophy, with earlier onset of symptoms associated with increased disease severity. Neuromuscular weakness present in childhood impacts walking. Due to the progressive but heterogeneous nature of FSHD, some children will be less affected while others may lose the ability to walk. Little is known about how gait is affected in children with FSHD and how this may correlate with muscle strength and other functional measures. This study aims to characterise gait in a small cohort of affected children and evaluate how gait parameters change over time.

This study will use functional and strength data obtained from a 2-year paediatric FSHD longitudinal outcome study and gait data from a long running natural history study of gait in children attending RCH Neuromuscular Clinic. Children are assessed walking over an electronic walkway during typical barefoot walking and while performing a six-minute-walk test (6MWT). The 6MWT is valid and reliable measure of physical endurance in children with neuromuscular disease. Other FSHD-specific severity scales and functional measures such as timed 10m walk run (10MWR), 4-stair climb (4SC) and quantitative muscle strength testing (QMT) will be correlated with spatio-temporal gait parameters.

Aim:

To investigate changes in spatio-temporal gait parameters during a typical walking and a 6MWT and correlate with FSHD severity, functional and muscle strength measures. The successful student candidate will:

- attend neuromuscular clinic and observe assessment of children with FSHD to understand the clinical picture
- conduct a literature review
- assist with data collection, cleaning and processing of gait and functional data
- conduct statistical analysis to describe the data, identify disease-specific gait characteristics during typical gait and 6MWT, assess changes in spatio-temporal data between annual evaluations and conduct correlational analyses

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Available as Masters Project: **Yes**

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

Parents of children born with anorectal malformations (ARM) face unique challenges in diagnosis and management, especially during the early years of their child's life. This project is part of an ongoing longitudinal study that commenced in 2019, aimed at evaluating the psychosocial outcomes of parents/carers of children with ARM using validated questionnaires. Students will have the opportunity to: recruit families with children diagnosed with ARM to participate in the study; administer validated questionnaires to the parents/carers; analyse data; and evaluate the psychosocial outcomes and identify potential areas of support or intervention for these families. This project will provide valuable insights into the psychosocial impact on parents/carers of children with ARM, a complex congenital condition that requires specialised care and management. By understanding their experiences and challenges, healthcare professionals can develop targeted support strategies and improve outcomes.

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Available as Masters Project:**No**

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

Parents of children born with Hirschsprung disease (HD) face unique challenges in diagnosis and management, especially during the early years of their child's life. This project is part of an ongoing longitudinal study that commenced in 2019, aimed at evaluating the psychosocial outcomes of parents/carers of children with HD using validated questionnaires. Students will have the opportunity to: recruit families with children diagnosed with HD to participate in the study; administer validated questionnaires to the parents/carers; analyse data; and evaluate the psychosocial outcomes and identify potential areas of support or intervention for these families.

This project will provide valuable insights into the psychosocial impact on parents/carers of children with HD, a complex congenital condition that requires specialised care and management. By understanding their experiences and challenges, healthcare professionals can develop targeted support strategies and improve outcomes.

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Available as Masters Project:**No**

63. Wearable vital signs monitoring in children

Wearable vital sign monitoring presents an exciting opportunity to improve child health in the context of both chronic and acute illness. However, child centred evaluation of new wearable technologies is lacking. The Joey, a novel wearable vital sign monitor developed at MCRI, is now ready for piloting in children. This project will evaluate its safety, tolerability and usability during brief supervised wear (15 minutes) along with concurrent clinical reference monitoring and extended ambulatory wear (24 hours). The study will combine quantitative assessment of device safety, signal quality and adherence with qualitative assessment of practical barriers and refinements required for paediatric deployment. The student will gain hands on experience in recruitment, consent procedures under supervision, device fitting and troubleshooting, physiological data collection and basic signal and agreement analysis, alongside qualitative data collection and thematic analysis, all supported by experience researchers and biomedical engineers. Findings will inform device optimisation and implementation strategies, and contribute to translational advances in paediatric monitoring.

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Available as Masters Project: **Yes**

64. The Self-and Others' emotion and Cognition in Adolescent Life (SOCIAL) study

Social processes, such as empathy and theory of mind, are vital for social functioning and building social competency in young people. Empathy is a social-affective process involving sharing someone's emotion. Theory of mind (ToM) on the other hand, is a social-cognitive process that involves reasoning about the thoughts or emotions of others. Both of these processes are required for successful social interactions. Impairments in these processes have been found in mental health and neurodevelopmental disorders. This project will behaviourally validate an empathy and ToM task for adolescents for ultimate use in the Magnetic Resonance Imaging (MRI) scanner.

This will result in a tool for neuroscientists to investigate these processes, how they are impacted in clinical populations, and evaluate treatments aimed to improve social processes. Depending on length of project (Masters versus PhD) and student interest/experience, this

project may involve the following: working with young people, fMRI task programming and piloting, investigation of psychophysiological or neural correlates of social processing.

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Available as Masters Project:**Yes**

65. Take C.A.Re (Concussion Assessment and Recovery Research) Team

Concussion is defined as a traumatic brain injury where an impulsive force, caused by direct blow to the head, neck or body, is transmitted to the brain, triggering a neurotransmitter and metabolic cascade, with possible axonal injury, blood flow change and inflammation affecting the brain. Concussion can result in a constellation of non-specific and heterogeneous post-concussion symptoms (PCS), including balance impairment, somatic and/or emotional symptoms, cognitive impairment, and/or sleep disturbance. For most children and adults, PCS tend to resolve spontaneously within 2 to 4-weeks post-injury, however, approximately 30% will experience persisting PCS (pPCS) for greater than 4-weeks. pPCS can interfere with participation in school, sport, social, and recreational activities, with secondary consequences on mental health and quality of life. For the 30% of children and adolescents who experience pPCS, emerging biopsychosocial conceptualisations emphasise the contribution of injury, pre-injury, psychological, social, and environmental factors to the development and maintenance of these symptoms. Our team developed a multimodal intervention, Concussion Essentials (CE), that combines targeted education and management strategies for common symptoms, with physiotherapy and psychology treatment. Student projects will involve examination of child, parent or intervention factors that contribute to recovery of pPCS.

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

This project builds on pilot data from our group, in taking the next steps to set up a longitudinal cohort of young people taking anti-epileptic drugs, with sibling controls. Participants will undergo assessments of bone density and muscle function, along with

biochemical testing and questionnaires to establish risk factors for bone health outcomes. The cohort will be followed for 3-5 yrs; the student will gain invaluable experience in setting up the cohort, establishing baseline data, undertaking analysis of these data including advanced analysis techniques such as finite element modelling.

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Available as Masters Project:**Yes**

67. Walking and Weak Feet: How does walking change over time in children with Charcot-Marie-Tooth (CMT) disease?

Charcot-Marie-Tooth (CMT) disease is a group of inherited conditions that affect the peripheral nerves. In children and teenagers with CMT, damage to these nerves can cause weakness in the feet and hands. Weakness, along with tightening of muscles and changes in foot and ankle shape, can make everyday activities more difficult. Children with CMT may experience:

- Problems with walking and balance
- Difficulty running
- Frequent trips and falls
- Reduced stamina and endurance
- Increased fatigue

There are more than 120 genetic types of CMT. Symptoms can vary greatly from one person to another, even among people with the same type of CMT. Although there is currently no cure for CMT, research studies and clinical trials are underway to develop treatments that may slow the disease or improve its symptoms.

To understand whether new treatments are effective, researchers first need to understand how CMT changes over time without treatment. The Neuromuscular Clinic at The Royal Children's Hospital (RCH) is a multidisciplinary clinic that includes neurologists, orthopaedic specialists, physiotherapists, and other allied health professionals. For more than 10 years, our physiotherapy team has been collecting information about walking patterns and physical function in children with CMT. Children in the study attend annual assessments, which include walking analysis using an electronic walkway and other clinical measures of mobility and function.

This project aims to better understand how walking ability and physical function change over time in children with CMT. Students undertaking this project will join a friendly and experienced team of neuromuscular clinicians, including doctors and physiotherapists.

Opportunities will include attending weekly paediatric neuromuscular clinics and contributing to the largest study of walking in children with neuromuscular conditions in Australia.

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Available as Masters Project:**No**

68. Co-designing a family centred paediatric blood pressure screening pathway for Generation Victoria

Paediatric hypertension is frequently overlooked despite its long term risks, and with new Australian guidelines recently released there is a timely chance to improve how childhood blood pressure (BP) screening, referral and follow-up are designed and delivered. This project will use an experience based co design approach to work with parents to develop a pragmatic, family centred BP pathway, involving 20–25 parents across one in person and two online co design workshops, supported by brief follow up interviews for rich contextual insight. The student will lead practical elements of study delivery, including participant recruitment and engagement, workshop planning and facilitation (with training and supervision), qualitative data collection and thematic analysis, and will refine communication materials and simple measures of implementation success from a family perspective. Supervision will be provided by clinicians and health services researchers experienced in paediatric care and qualitative methods, and the project offers hands on experience in co design, ethics and stakeholder engagement, qualitative analysis, and academic dissemination, suitable for students interested in health services research and improving preventive care for children. Findings will directly inform the design of GenPressure, a statewide BP screening trial in Victorian schools that is part of Generation Victoria (GenV).

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Dr Jonathan Glenning

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Available as Masters Project:**Yes**

69. Project Pump: Outcomes of an accelerated insulin pump program

Diabetes technology, in particular automated insulin delivery systems, are demonstrated to improve both clinical and psychosocial outcomes for young people living with diabetes. With the onset of a new "Project Pump" at RCH, hoping to accelerate uptake of insulin pumps amongst our cohort, we hope to assess improved clinical outcomes such as HbA1c and time in range, as well as improved satisfaction with care and quality of life.

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Available as Masters Project:**No**

70. Community and professional attitudes toward ADHD management approaches

Current guidelines recommend that people with ADHD receive a combination of medication and evidence-based psychosocial supports, with regular measurement and review of symptoms. This project aims to understand how people with ADHD, parents/caregivers, and health professionals perceive the effectiveness of various ADHD management approaches. This project will use data from a large online survey on experiences of ADHD clinical care in Australia. Findings from this project will help us understand potential barriers to care and how to improve adoption of recommended ADHD management strategies.

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Available as Masters Project:**Yes**

71 Cognitive Functioning in Children with Severe Irritability: A Matched-Control Analysis Using CANTAB Data

Severe irritability, characterised by persistent angry mood and frequent temper outbursts, is one of the most common reasons for referral to child and adolescent mental health services. Despite its prevalence and impact on social, academic, and family functioning, relatively little is known about the cognitive characteristics associated with severe irritability in childhood. Improving our understanding of cognitive functioning in this population may provide insights

into the mechanisms underlying emotional dysregulation and inform future assessment and intervention approaches.

This honours project will undertake a secondary analysis of existing data collected from two studies. The first is a completed study of children presenting with severe irritability recruited through specialist mental health services, which included comprehensive clinical assessment and cognitive testing.

The second is the ongoing COGNITION Study, an observational study of school-aged children that includes neurocognitive assessment using the Cambridge Neuropsychological Test Automated Battery (CANTAB). Participants with severe irritability will be compared with age- and sex-matched controls drawn from the COGNITION Study.

The project will examine cognitive performance across domains assessed by the CANTAB, including attention, executive functioning, and memory, to determine whether children with severe irritability show distinct cognitive profiles compared with their peers.

In addition to conducting data analysis, the honours student will have the opportunity to receive training in the administration of neurocognitive assessments used in the COGNITION Study. Through involvement in the ongoing study, the student will gain practical experience in participant assessment, research procedures, and neuropsychological data collection, providing valuable research and clinical skills development alongside the primary research project.

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Available as Masters Project: **No**

Genomic Medicine

72. Evaluating Outcome Measures of Functional Independence in Friedreich Ataxia

Friedreich ataxia (FRDA) is an autosomal recessive neurodegenerative disorder. Symptoms typically begin between the ages of 10 and 15, with the first symptoms commonly gait ataxia and impaired balance. As the disease advances, mobility and the ability to perform daily activities declines significantly. On average, individuals lose the ability to walk within 10-15 years of symptom onset, significantly affecting their quality of life and independence. Given the profound impact of FRDA on physical function, it is essential to have reliable tools to measure these changes over time. The Activities of Daily Living component of the Friedreich Ataxia Rating Scale (FA-ADL) is an outcome measure that reflects the real-world impact of ataxia on daily life. It has demonstrated sensitivity to disease progression and served as a valuable exploratory endpoint in the MOXIe (clinical trial which evaluated efficacy of

omavaloxelone in adults with FRDA. This project aims to compare the responsiveness of three outcome measures that assess independence in daily functioning: the FA-ADL, the Functional Independence Measure, and the Modified Barthel Index. Using longitudinal data from both children and adults enrolled in the studies at Murdoch Children's Research Institute (MCRI)/Monash Health, we will evaluate the internal and external responsiveness of these tools to natural disease progression. Responsiveness will also be compared to the modified Friedreich Ataxia Rating Scale, the first clinical outcome measure to be approved by the US FDA for use in clinical trials involving individuals with FRDA. Subgroup analyses will be conducted to compare progression rates across i) children vs. adults; ii) ambulant vs. non-ambulant individuals; iii) males vs. females; and iv) individuals with typical onset FRDA (onset < 20 years of age) vs. late onset FRDA. The student will join the Bruce Lefroy Centre at the MCRI, working within a multidisciplinary clinician researchers dedicated to developing sensitive and meaningful outcome measures for future clinical trials in FRDA.

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Available as Masters Project:**No**

Population Health

73. Designing integrated school-linked mental health care: An international review and stakeholder co-design study

Schools are increasingly recognised as an important setting for identifying and responding to children's emerging mental health needs. However, there is limited evidence to guide how school-linked services to support mental health should be organised, delivered and connected with health and community systems to provide equitable, sustainable and coordinated care across diverse settings. Governments are increasingly seeking practical models that can be implemented across metropolitan, regional and rural communities, yet little is known about which delivery mechanisms are most appropriate under different workforce and service contexts.

This project will comprise two complementary phases. First, an international scoping review will synthesise evidence on models for delivering school-linked mental health care, examining workforce configurations, delivery mechanisms (including embedded workforces, outreach services, hub-and-spoke models, telehealth and hybrid approaches), referral pathways, care coordination, governance arrangements and implementation strategies. Particular attention will be paid to how models have been adapted across metropolitan, regional, rural and remote settings, and the factors influencing feasibility, equity and sustainability. Second, findings from the review will inform a stakeholder consultation and co-design process involving children, families, educators, school wellbeing staff, primary care providers, allied health professionals, paediatricians and policymakers. Through focus groups

and workshops, participants will explore current system strengths and challenges, identify priorities for improving integration between schools and health services, and consider the acceptability and feasibility of alternative delivery models within the Victorian context. The project will generate an evidence-informed framework describing potential models for school-linked mental health care and recommendations for their implementation within Victoria. Outputs will include proposed workforce configurations, referral and communication pathways, shared-care arrangements, and implementation considerations to support future service development and evaluation.

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Available as Masters Project:**Yes**

74. What supports do parents report they need along the Early Hearing Detection Intervention (EHDI) pathway: Scoping review and audit of available Victorian services

The Victorian Infant Hearing Screening Program (VIHSP) is a state-wide program that screens the hearing of newborn babies in their first few weeks of life. Early detection of hearing loss and intervention including access to language and communication within the first months of life can significantly reduce the serious developmental impacts of infant hearing loss. Parents have described the Early Hearing Detection Intervention (EHDI) pathway as an anxious and uncertain time. We know that supporting parents helps to support infant and child wellbeing. This project therefore aims to better understand the supports needs parents report along each stage of the EHDI pathway, including screening, diagnostic audiology, hearing aid fitting, early intervention and cochlear implantation and what services are available to parents at these stages. This project is part of a larger piece of work that ultimately aims to co-design a tool (questionnaire) to quantify the support needs of parents along the EDHI pathway. This project will act as the foundational step and findings will inform the broad areas discussed during the co-design phase of the study.

This project will involve three stages:

Stage 1: Conduct a scoping review of the literature to gather the existing evidence about the type and timing of supports and resources parents describe they need along the EDHI pathway and describe any gaps and/or recommendations derived from the evidence. Stage 2: Audit the existing resources and services available to families along the EDHI pathway in Victoria. Stage 3: Synthesise the information gathered in Stages 1 and 2 including a gaps analysis to inform the next stage of this project.

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Available as Masters Project:**Yes**

75. Social determinants and health outcomes of homelessness from childhood to adulthood

Child and adolescent homelessness is appreciated as a significant problem but the causes and consequences, including health outcomes (social, psychological, and physical), remain understudied.

The proposed project will utilise data from population-based cohort studies of child and adolescent development to examine: (a) key modifiable social determinants of homelessness in childhood and adolescence and the earliest timing of interventions to either improve or reduce these determinants, and/or (b) the impacts of early life homelessness on health outcomes across the life course.

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Available as Masters Project: **Yes**

76. The GenV Early School Wave pilot study

Join Australia's largest-ever child and parent cohort - Generation Victoria (GenV) - and help shape its landmark Early School Wave in 2028–29. This initiative will assess 50,000+ children across Victoria to tackle rising mental and physical health challenges.

This project can support one to two students and is part of a broader team developing GenV's school-based measurement protocol across key health domains. The student(s) will work with senior GenV researchers and experts to design and test assessment measures that can be taken to scale with 6-7 year olds. Students will select from a shortlist of projects about language, physical, motor and mental health assessments. They will test their approach in different priority groups of children, and report on feasibility and acceptability data for their measure in the different groups.

This project has a high focus on inclusive and accessible research practices. Students will gain valuable experience in research design, data collection with children with and without different developmental conditions, and the practicalities of large-scale health measurement. This is a unique opportunity to pursue your interests, be part of something bigger and contribute to real-world change in children's health and wellbeing.

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Available as Masters Project: **Yes**

77. Deaf role models: exploring the when, how and who from the perspective of parents of young deaf children.

The vast majority of children born deaf or hard of hearing (DHH) have parents who themselves are not DHH. Consequently, many deaf children do not have ready access to a family member or other role model who understand from lived experience what it means to be deaf. Exposure to deaf role models reduces the stigma of deafness and helps children and their families see deafness as a valued part of who they are, rather than a limitation. Seeing successful, confident deaf adults can foster pride, acceptance, and a sense of belonging. Deaf mentors can also facilitate exposure to communication, culture and language.

Currently, there is no systematic way in which families who have a young deaf child can access a deaf role model in Victoria.

The project will involve a literature review, and collection of qualitative and quantitative data via focus groups, interviews and/or surveys. Participants will be adults with lived experience of parenting a deaf child, including those whose child was recently identified and those where identification occurred a number of years ago. We will seek parents' views on when and how deaf role models should be integrated into the Early Hearing Detection and Intervention (EHDI) pathway, and what the important characteristics are for a deaf role model.

The results will have real-world implications, with recommendations regarding what a deaf role model service should look like for young deaf children and their families.

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78. Does delayed diagnosis of chronic paediatric medical conditions lead to crisis driven care?

Delayed diagnosis of chronic conditions can have significant consequences for the patient in terms of morbidity and sometimes mortality, so timely detection of evolving chronic disease is important. Chronic paediatric medical conditions which are frequently seen in sub-specialist care may be rare to a given general practitioner or practice. Where subspecialist work may centre on a suite of less than 10 conditions, 85% of a GP workload is represented by more than 160 conditions the bulk of which relates to adults. Therefore, keeping uncommon chronic paediatric conditions front of mind is not practical or feasible in a busy clinical setting and may in turn lead to delays in the diagnostic pathway.

This study will examine the rates of presentations in children with evolving chronic disease at two tertiary emergency departments in Victoria to assess whether diagnostic delays are

associated with these crisis presentations and to identify opportunities to target interventions aiming to ensure earlier diagnosis in the primary care setting.

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Available as Masters Project:**No**

79. Sustainability as a construct in paediatric healthcare research

The implications of climate change on our health are well established with clear links between changes in our environment and an increased risk of several chronic conditions whose origins lie in childhood. However, sustainability as a domain of paediatric research is in its infancy.

This project will combine two elements; a scoping review of the literature relating to climate change or sustainability initiatives in the paediatric research setting and a qualitative study of paediatric researchers to identify barriers and facilitators of inclusion of sustainability as a component of paediatric healthcare research.

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