The University of Melbourne, Department of Paediatrics and Murdoch Childrens Research Institute

Faculty of Medicine, Dentistry & Health Sciences

HONOURS & MASTERS PROJECTS 2022

Honours and Master of Biomedical Science

Student Information Evening: 8 September 2021, 5.00pm

Register here

Contents

Laboratory based research

Infection and Immunity

1. Immune mechanisms of peanut allergy remission

Food allergies are a major health burden globally, Australia having the highest reported rates. There is currently no cure so management relies on allergen avoidance, causing severely reduced quality of life and rarely death. A treatment that can induce remission of allergy is needed. Understanding immune mechanisms supporting clinical remission of allergy, and long-term persistence of remission will facilitate development of novel treatments.

Several therapies under investigation can induce remission, however remission may be transient or long-lasting. We have shown that a combination treatment, Probiotic and Peanut Oral Immunotherapy (PPOIT), induces long-lasting remission persisting to 4 years post-treatment; whereas remission following peanut oral immunotherapy (OIT) without an adjuvant appears short-lived, with two thirds (67%) of treatment responders losing remission by 12-months post-treatment. We have completed a large (n=201) Phase 2b randomised trial comparing PPOIT vs OIT vs Placebo with patients followed to 12-months post-treatment, allowing identification of transient (lost) vs persistent remission. Biosamples collected before, during and after treatment are available for analysis. This project aims to characterise shifts in cytokine production that occur during the transition from allergy to remission, and patterns associated with transient vs persistent remission. Findings will contribute to understanding the immune mechanisms involved in retraining the allergic response towards remission, as well as remission that persists or is lost. Cytokine levels in cell culture supernatants will be measured by multiplex assay before and after treatment in 1) patients who achieved remission of peanut allergy following PPOIT treatment, 2) patients who achieved remission of peanut allergy following standard OIT, 3) patients who remain allergic to peanut following placebo treatment. Findings will help to identify key immune factors driving lasting remission of allergy compared to remission that is lost over time, which may in turn lead to development of more effective long-term treatments for food allergy.

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Available as Masters Projects: Yes

2. Understanding pneumococcal pathogenesis

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

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3. Interplay between Streptococcus pneumoniae and respiratory viruses

In this project, you will elucidate the underlying microbiological and/or immunological mechanisms that govern the synergistic and antagonistic relationships between pneumococci and respiratory viruses. Key approaches to this project include: working with in vitro and/or in vivo models to understand the effect of coinfection on the host and microbes, including microbiological and immunological analysis of local and systemic samples. Your project will provide novel insights into bacterial-viral interactions.

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4. Microbial changes following pneumococcal conjugate vaccination

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

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5. Anti-inflammatory effects of sulforaphane

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

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

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

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7. How do monocytes remember? Characterisation of the early life exposures that induce Innate Immune Memory.

We all know that the adaptive immune system develops memory following specific antigen exposure, but is the same true for the innate immune system? An emerging field of research tells us exactly this, with epigenetic remodelling as the underlying mechanism. Innate immune cells, such as monocytes and macrophages, form this non-specific memory in response to a variety of exogenous signals. Exposure-induced epigenetic remodelling governs their future response to a range of pathogens. This process can be modelled in vitro, using both yeast and bacterial antigens and metabolites (Novakovic et al. Cell 2016), metabolites (Bekkering et al. Cell 2018), vaccines (Arts at el. Cell Host Microbe 2018) and a range of other stimuli.

During pregnancy, both maternal and foetal monocytes show attenuated pro-inflammatory responses correlated with pregnancy-associated hormones. Additionally, foetal monocytes are exposed to a range of environmental factors. We hypothesise that monocytes remodel their chromatin in response to early life environments, which explains their altered function during pregnancy. To test this hypothesis, we will isolate pure monocytes from human blood, and treat them with various stimuli in vitro. After treatment we will measure cytokine release, RNA expression and epigenetic (histone modification) changes. This project is appropriate for students with an interest in molecular biology and immunology and will utilise monocyte isolation and culture, ELISA, chromatin immune-precipitation (ChIP), DNA and RNA extraction and real-time PCR.

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

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

Two clinical trials of cross-sex therapy were completed, for which we have biological samples: 1. Whole blood genome-wide DNA methylation data is available for 12 individuals who underwent female-to-male hormone treatment and 12 underwent male-to-female hormone treatment (baseline, 6 months and 12 months after treatment). These data need to be analysed using bioinformatics tools. 2. Live frozen peripheral blood mononuclear cells are available at baseline and 6 months after cross-sex estrogen hormone treatment in male-to-female transition (n = 30). These live frozen cells will be used for immune-phenotyping, epigenetic (DNA methylation, histone modifications) and transcriptomic profiling of specific innate (monocytes) and adaptive (naïve T and B) cell types. This will evaluate the changes in immune function during sex hormone administration.

Methods involved Molecular Biology: RNA/DNA extraction, chromatin preparation and pulldown, sequencing library preparation.

Cellular Immunology: Cell sorting and analysis of immune-phenotyping data. Cell culture to elicit inflammatory responses in immune cells.

Bioinformatics: R and linux to analyse DNA methylation, ChIP-seq and RNA-seq data (no prior knowledge of coding is required).

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Genetics

9. Modelling cortical development with human stem cells to ellucidate the role of epigenetic regulators in neuronal maturation and activity

Studies into human cortical development (or corticogenesis) have identified unique cellular processes during embryogenesis which further our understanding of how the human cortex is formed. However, primary human neuronal tissue can be difficult to source and is less amenable to genetic and cellular manipulation for experimental purposes. Therefore, researchers have turned to human embryonic stem cells (hESC's) to model human cortical development in culture. hESC's are highly expandable which allows for scaled up experimentation and established cortical differentiation protocols mimic key cellular hallmarks of corticogenesis such as neural stem cell proliferation, synaptic maturity, neurite morphology and activity. More recently, the ability to generate gene knockouts with CRISPR/Cas9 technology has allowed researchers to scrutinise the role of specific genes in the development of their tissue of interest. Our interest is focused on a subset of epigenetic regulators - proteins which modify histones and DNA to regulate transcription of underlying genes - and how these genes regulate aspects of neurodevelopment. A growing body of genetic evidence has identified a large number of epigenetic regulator genes to be associated with neurodevelopmental disorders resulting in intellectual disability, suggesting that neurodevelopment is highly susceptible to epigenetic changes as neurons develop and mature. How these genes affect neuron-specific functions at the cellular level is largely unexplored. The aim of this Honours project is to generate a CRISPR/Cas9-mediated knockout of an epigenetic regulator gene associated with intellectual disability and characterise its role in corticogenesis using a stem cell-based model of cortical development. This will involve designing and cloning of CRISPR/Cas9 constructs, clonal generation of knockout stem cell lines, live-cell imaging of stem cell-derived neurons using virally delivered fluorescent reporters and calcium indicators to assess cell proliferation, synaptogenesis, maturation, neurite extension and activity, and biochemical assays to assess changes in histone modifications during neuronal development in the knockout neurons.

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

NF1 is a single-gene disorder caused by a loss-of-function mutation in the NF1 gene resulting in a reduction of the protein neurofibromin. Cognitive deficits occur in approximately 80% of children with the genetic syndrome, neurofibromatosis type 1 (NF1), making them the greatest cause of disability for individuals with this lifelong genetic condition. These manifest as academic failure due to learning disabilities (70%), attention deficit-hyperactivity disorder (ADHD; 40%) and a significantly increased risk for autism spectrum disorder (ASD; 25%).

Current therapies, whether medication or behavioural interventions, are often ineffective because they use 'trial and error' approaches targeting symptoms, rather than the cause. Therefore is an urgent need to discover new therapeutics for the impairing neurodevelopmental symptoms experienced by children with NF1.

This drug screening project aims to identify compounds that may modulate neurofibromin expression using patient derived stem cell lines.. Cells will be differentiated into neuronal cells and then used to perform a high throughput drug screen. Functional readouts from the screen will include assessment of neurofibromin steadystate levels as well as structural readouts including neurite development, length and number of neurons in the cultures. Once candidate compounds have been identified, validation assays will be performed in NF1-patient derived stem cell models to determine whether the compound treatment/s can ameliorate neuronal deficits. Extensive functional analyses will be performed including the assessment of neuron growth and maturation (using immunofluorescence assays), neuron function (using multi electrode arrays and calcium imaging) as well as biochemical assays such western blotting, real time PCR and ELISAs to determine biological changes in our patient lines versus control lines.

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Available as Masters Projects: Yes

11. Understanding the neurobiology of autism in nf1 using patient derived stem cell models

Autism (or autism spectrum disorder; ASD) is a neurodevelopmental disorder characterised by debilitating impairments in social communication and restricted interests and repetitive behaviours. In most cases, the cause of autism is unknown and because of this, there are no effective treatments for autism in the general population. However, a subset of individuals (15-20%), autism occurs in children with a clinically defined syndrome which arise from a single gene disorder. This is the case in children with neurofibromatosis type 1 (NF1), an autosomal dominant disorder caused by a loss-of-function mutation in the NF1 gene. Studying a monogenic disorder with a high prevalence of autism will allow a more targeted and deeper understanding of the neurobiological mechanisms of ASD in NF1.

Whilst animal models have traditionally been used by researchers to understand disease mechanisms, translation from animal studies to effective human clinical trials has proven difficult, including in NF1. A potential explanation for this is the inadequacy of animal models to recapitulate the complexity of the human disease state.

This project will investigate how and why 25% of children with the genetic syndrome NF1 develop neurodevelopmental disorders such as autism. This project will use patient derived stem cell models to characterise the neuronal deficits in individuals with NF1. Specifically, human stem cell-derived brain cell networks (comprising neurons and glia) will be generated to examine the effects of NF1 mutations on neuronal development, determine how well they connect together in networks and whether they are able to function efficiently. Various drugs targeting specific pathways important in NF1 will also be used in the stem cell derived neuronal networks to determine whether they can reverse the biological abnormality in these cells. Some of the techniques that will be used in this project include stem cell culturing, differentiation of stem cells into brain cells, confocal microscopy, network activity assays, drug screening techniques, real time PCR and western blot analysis.

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12. Developing a functional assay to evaluate pathogenic variants in one of the most common genetic loci linked to paediatric mitochondrial disease

Each week in Australia a child is born with a disorder affecting mitochondria, our cellular power plants. Many such children die in the first years of life and most suffer from severe disease. Current genomic strategies have improved the ability to provide molecular diagnoses for these children and their families, with diagnosis rates around 50%. However, it is often difficult to determine whether a novel genetic variant is pathogenic, and diagnoses can be missed in regions of the genome that are more difficult to analyse, such as those with repetitive sequences.

The ATAD3 locus is one such genomic region, consisting of three repeated genes with high homology. Since its identification as a mitochondrial disease locus in 2016, ATAD3 has emerged as one of the top 5 most common nuclear loci linked to mitochondrial disease. These diseases range from milder neurodegenerative diseases, to severe presentations with early lethality affecting the heart and/or the brain. Many of these severe presentations result from duplications and deletions in the ATAD3 locus that frequently arise due to its origin as a gene duplication event. While its precise function is unresolved, ATAD3 is linked to mitochondrial DNA maintenance and cellular cholesterol homeostasis. All three ATAD3 genes encoded within the locus (ATAD3A, ATAD3B and ATAD3C) have ATPase domains, although it is unknown if they are all functional.

This project will involve the development of a protocol for isolation of ATAD3 proteins and direct measurement of their ATPase activity, using extensive molecular biology and biochemistry techniques. This assay will then be used to evaluate ATPase activity in all three ATAD3 proteins, as well as to analyse the effect of known and novel variants on ATAD3 ATPase function to determine their contribution to pathogenicity.

References: Desai, Frazier et al. (2017). Brain, 140:1595-1610. Frazier, Compton et al. (2020). Med, 1:1-25.

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

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 mitochondrial 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 may identify targets to modulate 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. Please note that this is primarily a laboratory-based project and there are only limited opportunities for remote work.

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Available as Masters Projects: Yes

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

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.

This project will contribute to our investigations on the critical role of the mammalian CDKL5 protein in neurons. CDKL5 is a kinase that regulates key phosphorylation events on many proteins. Some recently identified targets of CDKL5 in neuronal cells include microtubule proteins, however only a few targets have been discovered, leaving many potential targets yet to be identified. The phosphorylational regulation of microtubules is very important as it will affect neuronal maturation, synaptic activity, and neuronal network function and the movement of subcellular cargo in neurons. This project will validate potential new targets regulated by CDKL5. These targets will be validated using complementary in vitro techniques.

We will validate potential CDKL5 targets using a combination of standard biochemical and molecular biology techniques including, but not limited to cell culture, qPCR, SDS-PAGE immunoblotting, phospho-specific western blotting, cloning, co-immunoprecipitation, immunofluorescence and enzyme assays. 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. This project will for the first time provide a comprehensive and detailed understanding of the CDKL5 kinase in neuronal cell biology. Our project will provide future opportunities for drug design and therapeutics targeting kinase activity.

Please note that this is primarily a laboratory-based project and there are only limited opportunities for remote work.

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15. Novel Transcriptomic Signatures in Peripheral Tissues and Brain Predictive of Behaviour in PWS

Prader-Willi syndrome (PWS) is a complex neurodevelopmental disorder arising from a deletion or duplication of the 15q11-q13 imprinted region, affecting the regulation of genes essential for normal neurodevelopment. The clinical features of PWS in childhood include intellectual disability, and behavioural challenges including autistic features and hyperphagia. However, there is significant variability in symptoms which is not well understood, particularly between deletion and non-deletion subtypes. Better understanding the relationships between the biology underlying these differences is important for improved stratification of patients and for the development of targeted early treatments.

We have recruited and assessed 35 individuals with PWS. Extensive behavioural and parent-reported medical history data, as well as bio-specimens including DNA, RNA and protein lysates have been collected from various tissue types for most participants. We have also processed post-mortem brain tissues from 16 individuals with PWS and 30 neurotypical controls. We then characterise changes at DNA copy number, methylation, RNA and protein levels between tissues of these individuals to help us better understand biological pathways involved in pathology of deletion and non-deletion sub-types of PWS.

This project will expand on this work to examine relationships between expression of key genes in different peripheral and brain tissues within the 15q11-q13 imprinted region (e.g., UBE3A, MAGEL2, NIPA, NDN), and will relate these to formal clinical assessments. Ten new participants will be recruited and assessed. Molecular analyses for the new PWS participants and RNA from 10 post-mortem PWS brain tissues will be performed as part of this study. These data will be combined with the existing dataset to provide a more comprehensive understanding of the mechanisms underlying clinical features between different sub-types of PWS. The student will gain experience in laboratory work, interpreting genetic and clinical data, biostatistics, and working with children and families affected by PWS.

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16.Genetic Diagnosis of Children with Vascular Anomalies for a Therapeutic Clinical Drug Trial

Our understanding of the genetics of vascular anomalies is rapidly advancing but remains incompletely understood. An inherited germline gene variant may lead to a predisposition to developing vascular anomalies, with a 'second hit' somatic variant occurring within affected tissues. In other sporadic cases, a somatic variant alone arising in the affected tissue at low frequency during early development may be sufficient to cause the vascular anomaly. Analysis of DNA from blood may not identify a causative variant in individuals with vascular anomalies, however sequencing DNA from affected tissue may yield a genetic diagnosis. Patients in whom appropriate variants are identified will be eligible for our new 5-year MRFF-funded Rare Cancers Rare Diseases Unmet Needs (RCRDUN) Clinical Trial of targeted therapies for vascular anomalies commencing in 2022. Aims: 1. To perform high depth gene panel or exome sequencing, or sensitive droplet digital PCR in individuals from families with multiple affected individuals, sporadic cases, or those with atypical clinical presentations, to identify causative mutations in known and novel genes. 2. To gain hands-on experience with current genomic technologies and understand application, strengths and limitations of these technologies. 3. To understand the pathway from the clinic, through laboratory processes, to molecular diagnosis, culminating in clinical trial of targeted drug therapies for patients with severe disease intractable to standard care.
Methodology: 1. Recruitment of families with multiple affected individuals (~15 families) and sporadic cases without family history (~30 individuals) 2. Application of current genomic testing technologies to these families and individuals using paired DNA samples extracted from lymphocytes and from affected tissue. This project provides the opportunity to work in an established multidisciplinary clinical and laboratory research team with clinical trial expertise. In addition to clinical

experience and laboratory techniques, the development of project management, sample coordination and communication skills will be fostered.

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Available as Masters Projects: Yes

Clinical Sciences

17. SPILLOVER: What is the impact of preterm respiratory support outside of the lung?

70% of all preterm infants within the Neonatal Intensive Care unit (NICU) require assisted respiratory support. However whilst life-saving, even brief periods of support when applied to the immature lung may not only initiate lung injury, but may also result in extra-pulmonary organ dysfunction. In this project the student will use a range of techniques, including histology, proteomics and integrative biostatistics, to assess the impact of different ventilation strategies on protein expression within the liver, small intestine and lung.

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Available as Masters Projects: Yes

18. The tree of life: Mapping changes in the trachea, bronchus and alveolus during ventilation of the preterm lung

The majority of studies to date have focussed on the impact of mechanical ventilation on the gas exchange units of the lung (alveolus) with large bodies of evidence demonstrating that even brief periods of support when applied to the immature lung can initiate lung injury. What is not clear is how mechanical ventilation parameters such as flow, pressure and tidal volume, influence the morphometry and function of other respiratory tissues such as the trachea and bronchus. In this project the student will use a range of techniques, including histology, proteomics and integrative biostatistics, to assess the impact of different ventilation strategies on protein expression within the trachea, bronchus and lung.

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Cell Biology

19. Generating gene edited tools for CRISPRi screening

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

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20. Identifying safe harbour loci from stable gene expression

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

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Available as Masters Projects: Yes

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

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

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22. Generating a patient-specific model for focal segmental glomerulosclerosis due to a de novo mutation in TRIM8

Focal segmental glomerulosclerosis (FSGS) is a kidney disease that can be caused by genetic mutations affecting podocyte biology. Kidney organoids are mini-kidney tissues in a dish that can be differentiated from patient-derived induced pluripotent stem cells as a model of that patients disease. Our laboratory has demonstrated the utility of this approach in the study of genetic glomerular diseases. The aim of this project is to study the effect of genetic variants in TRIM8 using iPSC derived from a local patient presenting with FSGS and comorbid epilepsy (a known association). TRIM8 plays a role in ubiquitination, which marks proteins for degradation within the cell. We plan to study the effect of mutant TRIM8 protein on fundamental slit diaphragm proteins and podocyte biology using kidney organoids derived from this patient's cells. The student with gain skills in culturing induced pluripotent stem cells, directed differentiation to kidney organoids, immunofluorescent staining and confocal microscopy. For the willing and capable student, there could be opportunities to extend this project into a Masters or Doctorate degree.

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Available as Masters Projects: Yes

23. Evaluating the generation of morphogen gradients for patterning of stem cell derived tissues

The directed differentiation of human pluripotent stem cells into nephron-containing human kidney tissue provides a major opportunity to generate engineered kidney tissue for renal replacement. However, nephron function is completely reliant upon patterning and segmentation with distinct responses to morphogen gradients between the proximal and distal ends of the nephrons. An ability to provide a gradient of growth factor signalling across patterning tissue is a major opportunity to align nephrons in a particular fashion. This project will use reporter lines that can indicate the level of growth factor signalling in an individual cell to investigate how nephron patterning can be instructed or enhanced in vitro to improve the structures that are derived. The project will draw on methods in stem cell differentiation, bioengineering and computational image analysis.

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Available as Masters Projects: Yes

24. Characterising molecular and mechanical properties of bioengineered heart valve tissues

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

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Available as Masters Projects: Yes

25. Gene regulation in the developing retina and the childhood eye cancer retinoblastoma

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

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Available as Masters Projects: Yes

26. How does ACTN3 deficiency influence the short and long term response to anabolic steroids in muscle?

Alpha-actinin-3 (ACTN3) is a major structural component of skeletal muscle. 1 in 5 people worldwide are completely deficient in alpha-actinin-3 due to homozygous inheritance of a common null polymorphism (R577X) in ACTN3 (ACTN3 577XX). While this does not cause disease, the alpha-actinin-3 deficiency results in significantly lower muscle mass and strength/power in elite athletes and in the general population. We have generated a knockout mouse (Actn3 KO) to model human alpha-actinin-3 deficiency. Using this model, we have shown that alpha-actinin-3 deficiency alters muscle mass, fast fibre size, muscle metabolism, calcium handling, and increases muscle susceptibility to eccentric contraction induced damage - all of which explains the altered muscle function in ACTN3 577XX humans. Recently, we found that alpha-actinin-3 deficiency alters the pathways that regulate muscle mass. Actn3 KO mice showed reduced expression of androgen receptor in skeletal muscle and also reduced downstream androgen receptor signalling. Actn3 KO mice also showed reduced muscle hypertrophy in response to acute treatment with dihydrotestosterone (DHT) compared to WT mice, suggesting that alpha-actinin-3 deficiency diminishes the hypertrophic response to anabolic steroids.

This project will examine the mechanism behind the diminished response to DHT with alpha-actinin-3 deficiency as well as the long term effects of acute steroid exposure. Skeletal muscle is thought to have a cellular memory in which hypertrophy is 'remembered' through the retention of newly recruited myonuclei long after steroid exposure and onset of muscle atrophy. Silastic tubing containing solid DHT (or empty tubing) will be implanted in WT and Actn3 KO mice for 6 weeks, then removed, and mice will

be assessed at 3 and 11 weeks following implant removal. This project will involve animal handling and laboratory-based techniques such as immunohistochemistry, western blotting and muscle physiology.

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Available as Masters Projects: No

27. Linking enteric nervous system development to Hirschsprung Disease in children

The developing gastrointestinal tract (GIT) is accompanied by development of the enteric nervous system (ENS) along the proximal-distal axis. When GIT development is impaired through disorders of neuronal migration, cell signalling, etc., then a range of GIT motility disorders can result. One of the most severe disorders is Hirschsprung Disease (HD) which can sometimes manifest as complete intestinal obstruction in the newborn infant requiring emergency surgery. More than 30% of patients with HD have loss-of-function mutations in the RET proto-oncogene or in other members of the RET signalling pathway (Sergi C et al, Pediatric Research 2017). Until recently, the transcriptional regulation of RET expression during ENS development has been under-explored. The Eisenstat laboratory studies the distalless (DLX) family of homeobox transcription factors. The Dlx1/Dlx2 double knockout mouse dies shortly after birth with several congenital anomalies of the brain, retina and craniofacial structures. They also have a distended abdomen with a phenotype of intestinal pseudo-obstruction closely resembling human HD. Moreover, DLX2 binds directly to the Ret gene promoter in vivo and regulates its expression in a proximal-distal fashion during ENS development. The student will assist to complete the ENS phenotyping of the Dlx1/Dlx2 double knockout mouse as well as assess expression of DLX2, PGP9.5, RET and Calbindin in patient samples assessed for a diagnosis of HD obtained through collaborating Paediatric anatomic pathologists and surgeons.

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Available as Masters Projects: Yes

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

The vascular endothelium is a highly specialized barrier that plays a key role in the regulated migration of leukocyte cells out of the circulation and into peripheral tissues as part of the systemic immune response. In atherosclerosis, this barrier function is impaired leading to uncontrolled leukocyte accumulation and systemic inflammation.

Recent data have shown that cells of the innate immune system, such as monocytes and macrophages, have capacity to develop a non-specific memory in response to inflammatory signals. Termed 'innate immune memory', it is increasingly clear that this is not restricted to cells of the hematopoietic lineage. We have recently demonstrated that endothelial cells of different origins have the capacity to establish innate immune memory following an initial stimulus (viral or bacterial). Further, we have mapped the molecular 'reprogramming' involved in this process, that enables an enhanced response to an unrelated second stimulus. It is important to note that cells do not act in isolation, and we now aim to explore the impact of a range of human plasma and lymphocyte (white blood cells) protein stimuli on endothelial memory.

This project will involve culturing vascular endothelial cells with plasma from individuals of variable health outcomes (diabetes, obesity, allergic and autoimmune conditions) and endothelial-lymphocyte co-culture experiments. We couple these with state-of-the-art transcriptome and epigenetic profiling. Techniques include cell culture, DNA/RNA extraction, a range of epigenetic approaches, RNA sequencing (RNA-seq) and bioinformatic analysis.

This project will reveal novel insights into the role of circulating lymphocytes and other factors in modulating endothelial molecular function, a key determinant in a range of adverse health outcomes, including atherosclerosis and cardiovascular disease.

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Available as Masters Projects: Yes

29. How does early-life epigenetic variation relate to infant metabolic profile?

In utero, the developing embryo/foetus is sensitive to a range of environmental exposures with the potential to impact growth and development. These include maternal anthropometry, metabolic profile and health during pregnancy, each with the potential to shape infant metabolism and health after birth. Techniques such as nuclear magnetic resonance (NMR) allow the simultaneous measurement of a large number of metabolites (metabolome) in both maternal and offspring circulations. While specific metabolites have been linked to a range of diseases in adults, little is known about the factors that shape metabolomic profile in early life.

We hypothesis that altered infant epigenetic profile, particularly DNA methylation at key genes, plays a role in mediating the relationship between early life exposures and childhood metabolic health. To investigate this, we will test the relationship between a range of maternal and pregnancy measures (including maternal metabolome), offspring DNA methylation profile at birth, and offspring phenotype and metabolome in infancy. We will also assess the potential contribution of DNA methylation to infant growth, as well as how genetic variation might influence these relationships.

This project is appropriate for students with an interest in understanding the link between pregnancy and childhood health, with a focus on molecular measures and biostatistics.

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Available as Masters Projects: Yes

30. The same but different: Transcriptional responses to inflammatory stimuli in phenotypically discordant monozygotic twins

The term 'epigenetics' literally means 'above DNA' and refers to the study of molecular interactions that influence chromosome structure and gene activity. We can think of epigenetic marks as signals that determine whether a stretch of DNA is 'open for business' and accessible for regulatory factors or 'closed' and therefore inaccessible. A key property of many epigenetic marks is that they not only indicate the state of the cell at a set point in time, but can also carry 'memories' of past exposures, with the potential influence cellular responses to future stimuli. Therefore, the epigenome (the complete epigenetic profile of a cell) contains information about the 'past, present, and future' of a cell or tissue. Understanding the relative roles of genetic and environmental influence to epigenetic variation is important in many aspects of human health, particularly the immune system.

Inflammation is a key outcome of the immune response to exogenous 'foreign' stimuli and is also a feature of excessive weight in children and adults. This project will examine the transcriptional response of purified blood monocytes to inflammatory stimuli in vitro in twins discordant for weight from birth to 6 years of age. As monozygotic twins are genetically identical, any differences in response will be directly attributable to cumulative environmental exposures, allowing the relative contribution of genes and environment to this important aspect of immune cell function to be directly assessed. The project will be laboratory-based and will involve will stimulating peripheral blood monocular cells and purified monocytes, profiling cytokine release and transcriptional response via single-cell RNAseq and bulk RNAseq. It is anticipated that the results will form the basis of a future publication.

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Available as Masters Projects: Yes

31. Assessing the relationship between circulating Vitamin D, genetic variation and bone density in an Australian cohort of 11-12yr old children and their parents

The role of vitamin D [calcitriol -1,25(OH)D and 25(OH)D] in bone health remains unclear, particularly early in life. Twin-based and family studies have reported a large genetic component to 25(OH)D concentrations. However, heritability estimates vary widely (20- 80%) and the estimated genetic contribution base on common SNPs is only 7.5% in mid-life adults [2]. Little corresponding data is available for calcitriol.

Utilising already generated data from the finely curated LSAC Child Health Checkpoint study in Australia this project will; (i) assess the relationship between childhood and parental measures of vitamin D, (ii) estimate the SNP-based genetic contribution to vitamin D measures, and (iii) assess the relationship between vitamin D and pQCT measures of BMD in children and adults .

This project will yield valuable insights into the interplay between vitamin D levels, genetic variation and bone mineral density in a large population-based study of children (n>2500) and their parents. It will suit students with an interest in childhood health and/or biostatistics.

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Available as Masters Projects: Yes

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

Autoimmune Disease is a condition arising from an abnormal immune response to a functioning body part. There are about 80 Autoimmune Diseases, which affect 5-10% of the population of the Western world. Around 70% of those affected are female, owing to a combination of genetic and hormonal factors.

Juvenile idiopathic arthritis (JIA) is an autoimmune rheumatic disease that is one of the leading causes of childhood disability, affecting around 6000 Australian children. It typically causes joint pain and inflammation in the hands, knees, ankles, elbows and/or wrists. Despite its relatively high incidence, the molecular and cellular changes associated with JIA remain poorly understood.

We hypothesise that blood cells (e.g. T cells, monocytes and B cells) from JIA patients will show differences in cellular proportions, responses to activation in culture, and have a distinct molecular profiles relative to controls. We will test this in the current project by applying state-of-the-art immunology and molecular genomic sequencing techniques to circulating blood cells from JIA patients and matched controls as part of our CLARITY (Childhood Arthritis Risk factor Identification Study)

biobank which is one of the largest, most biospecimen- and information-dense collections in the world. Techniques to be used in this project include cell culture, cell sorting, high dimensional flow cytometry, DNA/RNA extraction, a range of epigenetic approaches, RNA sequencing (RNA-seq) and bioinformatic analysis.

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Available as Masters Projects: Yes

33. Using iPSC derived skeletal muscle cultures to study muscle disease

This project aims to use skeletal muscle derived from induced pluripotent stem cells (iPSCs) collected from patients with rare inherited muscle disorders, like Duchenne muscular dystrophy (DMD) and Nemaline myopathy.

The protocols needed to complete this work have been developed in our laboratory and we are now using these methods to study muscle grown in a dish in both 2 and 3 dimensional models.

Cell culture-based models of muscle diseases will greatly enhance our ability to assess disease and develop novel therapeutic approaches to treat these debilitating conditions.

The projects will use stem cells from patients with various muscle diseases including Nemaline myopathy, Collagen VI myopathy and mitochondrial disease.

We will teach you all that is required to grown skeletal muscles from iPSCs and how to phenotype the relevant condition in vitro.

The skills you will learn include aseptic tissue culture techniques as well as laboratory-based methods such as, immunocytochemistry, flow cytometry, western blotting and quantitative real-time PCR (RT-qPCR).

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Available as Masters Projects: Yes

34. Unacceptable toxicities in Paediatric Cancer Survivors - the trade off of cure

Five-year survival rates have surpassed 90% for childhood Acute lymphoblastic leukaemia survivors (ALL), but survivors are frequently burdened by severe permanent health sequelae. Recently 15 international ALL study groups launched an initiative to construct a measure (designated Quality Survival (QS)) to quantify the occurrence of unacceptable toxicities (published Lancet Haematology July 2021). This project seeks to document the 21 QS conditions within an established cohort of patients treated at The Royal Children's Hospital and Monash Medical Centre, Melbourne. The reporting of the QS conditions within the established cohort will document for the first time these new measures within an Australian Cohort.

Once the QS conditions are documented within the cohort, a pharmacogenomic analysis will be performed to identify novel variants predisposing to these unacceptable toxicities. Pharmacogenomic analysis will be performed for toxicities where a functional model is available to validate findings (i.e. pluripotent stem cell derived cardiomyocytes). Ultimately, once variants are established and validated, these could be used to screen the patient population for their risk for unacceptable toxicities.

This project will be lead by a supportive team of supervisors with extensive clinical and basic science experience and an established track record both in the field of interest, and in supervision of Honours, Masters and PhD students. The project is a collaboration between The Royal Children's Hospital Children's Cancer Centre and the Cell Biology Theme within Murdoch Children's Research Institute. Funding is already established for the body of work, as is HREC approval. The project is suitable for a Masters student, with the option of extension to a PhD dependent on progress.

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Available as Masters Projects: Yes

35. Developing computational approaches to analyse development and disease

The use of complex 3D tissues derived from stem cells affords many significant advantages for the study of development and disease. The analysis of the resulting tissue is, however, complex given their size and cellular complexity. Advances in imaging technology, transcriptional profiling resolution and machine learning provide the tools that should allow high throughout characterisation of such complex structures. This project aims to develop novel computational approach to handle high content image datasets for the interrogation of disease mechanism. The applicant should have some basic understanding of computational biology and/or imaging.

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Available as Masters Projects: **Yes**

36. Defining islet composition for furture treatment of type 1 diabetes

Type 1 diabetes is an autoimmune disorder resulting in the destruction of the insulin-secreting beta-cells that reside in islets of the pancreas, resulting in blood glucose dysregulation. Current treatments are limited to exogenous insulin therapies through injection or delivery via an insulin pump, which are both onerous and imprecise; or allogeneic islet transplantation, with islets sourced from deceased donors. Although often efficacious, implementation of allogeneic islet transplantation as a therapy is hampered by both the scarcity of the source (donors) and also by inconsistencies in composition of the-donor derived islet preparations. In order to understand cellular composition of the human pancreas, we have used single cell transcriptional profiling (scRNAseq) of human pancreata to identify a cohort of markers that display expression profiles specific for particular endocrine cell types in the pancreas. We hypothesize that these cell surface markers can be used to quantify the abundance of specific endocrine cell subsets in pre-transplantation material derived from both tissue donors and pluripotent stem cells, enabling the correlation of transplantation outcomes with composition of pre-transplantation materials. This laboratory based project will involve validation of identified cell surface markers using immunofluorescence staining, flow cytometry, and RNAseq on human pancreas samples and/or pluripotent stem cell-derived endocrine cells.

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Available as Masters Projects: **Yes**

Non-Laboratory based research

Infection and Immunity

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

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

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Available as Masters Projects: Yes

38. Auto-titrating positive airway pressure in Paediatric patients for the treatment of obstructive sleep apnoea.

Introduction: Obstructive sleep apnea (OSA) is a sleep breathing disorder associated with multiple neurobehavioral &medical problems in children. The first-line treatment of OSA in children is adenotonsillectomy however many have residual symptoms of OSA postoperatively &require continuous positive airway pressure (CPAP). CPAP therapy involves the provision of pressure via a face mask to treat upper airway obstruction. Currently the gold-standard for determining appropriate treatment pressure is a manual pressure titration by a sleep scientist during attended in-laboratory sleep study. This method of in-laboratory titration is labour intensive, costly &subject to hospital waitlists. Auto-titrating positive airway pressure (APAP) devices provide variable pressure delivery by constantly monitoring the patient's airflow using algorithms developed by each company. APAP for the treatment of OSA has been widely used in adult patients, particularly during the initiation phase of therapy, however there is a paucity of data in children.

Aims: To assess the efficacy of APAP in treating OSA in children.

Methods: All children with OSA requiring an in-laboratory CPAP titration study at the Royal Children's Hospital (RCH), February -July 2021 will undergo an unattended titration study using the ResMed Airsense 10 APAP device with portable sleep monitoring equipment to determine their appropriate treatment pressure. The sleep studies will be set-up &data collated &analysed by the student. The titration study will be analysed by Sleep Scientists to determine efficacy of APAP for treatment of paediatric OSA.

Clinical Implications: CPAP therapy is an effective &safe treatment for OSA in children. In-laboratory titration PSG is standard to determine optimal therapeutic pressure in children with OSA treated with CPAP. The use of APAP devices as an alternative is not well studied in children however has the potential to provide therapeutic pressures in the home without the need for in-hospital titration sleep studies.

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39. Does inflammation contribute to the social gradient of cardiovascular disease?

Non-communicable diseases (NCD) are the leading cause of mortality in Australia and worldwide. The burden of cardiovascular disease (CVD) and other NCD falls disproportionately on those who are socioeconomic disadvantaged. Inflammation may play a role in this 'social gradient' of CVD, through both acute inflammation (e.g. from acute infections) and chronic inflammation over the life course. While elevated inflammation is a known risk factor for CVD and other NCD in adulthood, there is a growing body of evidence that risk of CVD begins to accumulate from early in life. However, the relationship between socioeconomic position, inflammation, and cardiovascular health in childhood is poorly understood. Identifying possible biological mechanisms in childhood contributing to the development of later CVD may open up new opportunities of earlier identification of those most at-risk, and potentially earlier intervention.

We hypothesise that relative socioeconomic disadvantage in childhood is associated with greater inflammation burden, and that inflammation burden in turn is associated with adverse childhood cardiovascular measures. To investigate this, we will explore the relationship between measures of socioeconomic position, blood-based inflammation markers, and non-invasive cardiovascular measures. All these data have already been collected; the project focuses on analyses of the relationships between socioeconomic position, inflammation and cardiovascular risk. We will also consider how heightened inflammation associated with socioeconomic disadvantage might mediate these relationships.

This project is appropriate for students with an interest in biostatistics and epidemiology. It is suitable for an Honours or Master project and potentially may form the basis for a PhD.

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40. Socioeconomic position and metabolomic risk profiles

Cardiovascular disease (CVD) and many other non-communicable diseases disproportionally impact those with greater levels of socioeconomic disadvantage. This 'social gradient' of CVD may begin even prior to conception, and growing evidence supports that accumulation of CVD risk begins from early in life. Socioeconomic position may contribute to this through metabolic differences that promote the accumulation of CVD. In adults, assessment of metabolic profile, using modern techniques such as nuclear magnetic resonance (NMR) 'metabolomic' platforms that measure a large number of metabolites, have revealed metabolic profiles that reflect a higher risk of CVD and metabolic conditions, and similar evidence in older children and young adults have linked metabolic profiles to increased atherosclerosis, a key process in the development of CVD. The relationship of socioeconomic position to metabolomic profiles is poorly characterised, particularly in early life. Identifying possible biological mechanisms in childhood contributing to the development of later CVD may open up new opportunities of earlier identification of those most at-risk, and potentially earlier intervention.

We hypothesise that relative socioeconomic disadvantage is associated with metabolomic differences in infancy and childhood that reflect pro-atherogenic metabolic profiles previously reported in later life. To investigate this, we will explore the relationship between measures of socioeconomic position and plasma NMR metabolomics. We will also consider how anthropometry and health measures associated with socioeconomic disadvantage might influence these relationships.

This project is appropriate for students with an interest in biostatistics and epidemiology. It is suitable for an Honours or Master project and potentially may form the basis for a PhD.

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Available as Masters Projects: Yes

41. Understanding the catch-up vaccination process: a qualitative interview study with migrant parents

This project is an extension to a larger study, the Migrant Immunisation Access (MIA) project, that examines vaccination in migrant children in inner city Melbourne, Victoria. Migrant parents are often unaware of the National Immunisation Program (NIP) requirements in Australia and only learn their children are overdue for vaccinations when enrolling in kindergarten or childcare, as a result of the No Jab No Play policy. The MIA project was undertaken in three phases enabling detailed insight into the impact of catch-up requirements on migrant families. In this extension research piece we plan to explore the experiences and communication needs of migrant parents accessing immunisation services. The student will undertake qualitative interviews with parents (already identified) to understand available resources and their experience of accessing immunisation services. We are seeking to interview 20-25 parents from the City of Melbourne. Qualitative data will be thematically analysed using

NVivo. The student will be supported to undertake qualitative interviews and during the analysis process.

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Available as Masters Projects: No

42. Examining the relationship between SA3 vaccination coverage and the Vaccine Communication Framework

This project will use data collected as part of the Vaccine Barriers Assessment Tool (VBAT) project. The VBAT project is about understanding the reasons why some children are not vaccinated on time. Population based metrics on vaccine coverage are important, but may not reflect true vaccine hesitancy. The Vaccine Communication Framework (VCF) asks parents to respond to a statement on their vaccine beliefs for their child. Similarly, childhood vaccine coverage is determined at the SA3 level and reflects a geographical areas vaccination rates. In this research project we plan to use survey data collected as part of the VBAT project to determine how well SA3 reflects the VCF. The student will be supported to undertake quantitative data analysis.

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Population Health

43. Health Promoting Schools

WHO and UNESCO's Health Promoting Schools (HPS) is a whole-school approach to promoting health and wellbeing that recognises the strong links between health and wellbeing, and education and learning. A health promoting school is one that is 'constantly strengthening its capacity as a setting for living, learning, and working' which includes government investment, school leadership and policies, the school curriculum, school social-emotional and physical environment, local community partnership and school health services. HPS has been shown to be effective at improving several aspects of student health including social and emotional wellbeing, fruit and vegetable intake and physical activity. Our HPS suite of work at the Centre for Adolescent Health, MCRI, led by Professor Susan Sawyer, focusses on research and knowledge translation activities which have influenced global practice and policy. https://www.rch.org.au/cah/research/Health_Promoting_Schools/

The exact scope of this project will be determined on a case-by-case basis and matched to students' skills and interests, and those of our highly interdisciplinary team. For example, projects could include reviewing the effectiveness of HPS for a particular health outcome, mapping policy, or evaluating measurement tools for school health. Projects could be global or national in focus, with the opportunity for translation activities such as developing policy briefs. Projects would be suited to students with an interest in adolescent health and wellbeing, public health, and school systems.

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44. 2000 stories: Victorian Adolescent Health Cohort Study (VAHCS) and Victorian Intergenerational Health Cohort Study (VIHCS)

The 2000 Stories: Victorian Adolescent Health Cohort Study (VAHCS) is a landmark longitudinal study spanning over 29 years. The project began in 1992, when a group of around 2000 Year 9 students across Victoria (14-15 years of age) were selected to participate. Participants completed six interviews at school age (from Years 9 - 12), and five interviews in adulthood (aged around 21, 24, 29, 35 and 42). Many of the original 2000 stories participants have had children of their own, creating a unique opportunity to explore the ways in which the health of one generation may be related to the next. The Victorian Intergenerational Health Cohort Study (VIHCS) was launched in 2006 and aims understand the processes that might influence many aspects of health and wellbeing across generations. 2000 stories based at the Centre for Adolescent Health at MRCI and is led by Professor George Patton and Dr Liz Spry. https://www.mcri.edu.au/2000-stories

The exact scope of this project will be determined on a case-by-case basis and matched to students' skills and interests, and those of our team. For example, projects could include reviewing the evidence

for the role of economic and educational determinants on health or analysing longitudinal data to explore continuities of health outcomes across generations. Projects would be suited to students with an interest in youth and perinatal (mental) health, biostatistics, and epidemiology.

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45. Statewide outcomes for babies in special care nurseries - a pilot study

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

The 'Generation Victoria' cohort is targeting all 160,000 Victorian births over two years commencing Dec- 2020 for Joan Kirner. Within GenV, we are establishing a depth data collection for all newborns admitted to Victoria's 40 SCNs, covering important events during pregnancy and the postnatal admission. These unique whole-state data will complement data already available for the 5 neonatal ICUs and build a statewide evidence base for better physical, mental and developmental outcomes for these vulnerable babies.

Project objective: For the expected 200 babies admitted to Joan Kirner hospital in Dec 2020 to 2021 (pilot study), we aim to determine the population incidence of morbidities (eg respiratory distress, hypoglycaemia, infection, jaundice, and feeding difficulties) in the neonatal period, and the characteristics of the babies who experience them.

Working with the GenV and the SCN study team, the student will learn how registries are set up, assist with data extraction and develop definitions, coding and recording of morbidities and characteristics before proceeding to quantitative analyses to address the study objective.

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

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Available as Masters Projects: Yes

Genetics

46. How do rare neurogenetic disorders impact gait patterns in children?

It has long been assumed that different genetic conditions impact a person's gait in unique and important ways. Sometimes this leads to severe gait difficulties as in the neurogenetic disorder Angelman syndrome, while at other times it leads to more subtle differences in gait, as in neurogenetic disorders linked to autism spectrum disorder, such as Fragile X syndrome. Quantitative gait analysis with wearable sensors offers a potentially useful approach to measure and compare gait patterns across groups.

In this project the student will join the Diagnosis and Development Laboratory at the Murdoch Children's Research Institute. The group comprises a dynamic team of researchers and diagnostic staff that interact to solve problems of both genetic and clinical nature. The project aims to measure and compare gait patterns using wearable motion analysis sensors in children with three rare neurogenetic conditions (Fragile X syndrome, Angelman syndrome and Prader-Willi syndrome).

The student will build upon an existing dataset and will gain expertise in working with children who have neurogenetic disorders. The student will perform intergroup comparisons for specific spatiotemporal parameters (e.g., step time) to make hypotheses about the neurological underpinnings of the gait pattern in each group. The student will also assess how different genetic subtypes within each group interact with the gait pattern (i.e., deletion versus non-deletion in Angelman syndrome and Prader-Willi syndrome; and mosaic versus full mutation in Fragile X syndrome).

This project is cross-disciplinary, spanning fields of gait assessment, digital health, neuroscience, neurogenetic disorders and genetics. Findings will facilitate the development of an innovative approach to deep phenotyping using wearables technology in the rare disorders field.

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Available as Masters Projects: Yes

Clinical Sciences

47. Examination of psychological service need for children with Anorectal Malformations (ARM), Hirschsprung Disease (HD) and Chronic Constipation (CC) and their families

The Colorectal and Pelvic Reconstruction Service (CPRS) was established in 2019. It is a multi-disciplinary service that aims to deliver comprehensive clinical care to children and families with complex colorectal and pelvic conditions such as Anorectal Malformations (ARM), Hirschsprung Disease (HD) and Chronic Constipation (CC).

There are very few research studies that look at what psychological support parents perceive as important for their child with a complex colorectal condition, within a paediatric hospital setting. The research program has 3 core studies. The aim of these studies is to inform psychological clinical care within the CPRS and contribute to the limited available literature in these areas.

1) This project is a quantitative online study that asks parents of children aged 0-18 years to complete a brief survey on psychological service need across the journey of their child's medical care. Survey results available from February 2022 to analyse.

2) This project aims to conduct semi structured interviews with parents of children with ARM, HD and CC to explore the impact of illness, hospitalisation and surgery on the infant and child (aged 0-4 years) and their family.

3) Study examining traumatic stress reactions in parents following the diagnosis of their baby with ARM or HD. Parents will be recruited while inpatients and asked to complete an online survey within 4 weeks of diagnosis/hospitalisation, and then 4, 8, and 18 months later.

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Available as Masters Projects: No

48. Sleep patterns, physical activity and fatigue in children with multiple sclerosis

Introduction Multiple sclerosis (MS) is an immune-mediated disease of the central nervous system that was once considered an adult disease. Paediatric onset MS (POMS) accounts for ~5% of all MS cases with a median age of onset of 11-13 years. Fatigue is a common symptom, reported by up to two-thirds of children with MS and impacts mental health, academic performance, social interaction and development, and quality of life. The Department of Neurology, RCH hosts the statewide paediatric MS clinical service, and the RCH has a tertiary sleep service. We have previously studied the prevalence of fatigue and sleep disturbance in children with MS.

Aims To further investigate sleep and fatigue in children with MS attending RCH, this study aims to:

- evaluate sleep patterns with actigraphy (a movement sensor) and a sleep diary
- evaluate physical activity levels with actigraphy and correlate these findings with physical activity questionnaires
- evaluate sleep habits and sleep hygiene (questionnaire based)
- evaluate the relationship between sleep patterns and physical activity (as measured by actigraphy) with mood, fatigue, family functioning, sleep habits/hygiene, quality of life, and MS disease activity.

Methods All children with POMS attending RCH will be included. Participants and their parents/carers will complete sleep, fatigue, physical activity, mood, quality of life, and family functioning questionnaires. Children will also wear an actigraph for a period of 7 days to evaluate sleep patterns and levels of physical activity when awake. The data collected will be collated and analysed by the student.
Clinical implications Poor sleep quality and fatigue impact quality of life and physical, cognitive and social functioning in children with MS. A better understanding of sleep patterns, factors impacting fatigue and poor sleep quality, and their relationship to physical activity, mood, family functioning, and quality of life will optimise medical management of children with MS.

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Available as Masters Projects: No

49. Improving the care of children with cerebral palsy

Cerebral palsy (CP) is a complex and lifelong condition. Our team is developing a new CP Flagship Program that aims to improve the healthcare of children with CP. This will be achieved by working with families to implement evidence-based care, facilitate care coordination, and to introduce consistent assessments and rigorous data collection, where these processes are not in place. This honours project is a pilot project for the CP Flagship and will be based within the Neurodisability and Rehabilitation Group at MCRI. The project will involve the study of children with CP who attend the Complex Care Hub at the Royal Children's Hospital. The Complex Care Hub delivers a range of services to meet the needs of patients, and partners with families and community providers to deliver the best care closest to home.

The student will study the characteristics of children with CP attending the Complex Care Hub (approximately 70 children) to determine factors including health status, disability (level of functional impairment) and socio-demographic profile (age, geographical background etc) and compare these characteristics with a similar group of children with CP who do not attend the Complex Care Hub. For example, differences in rates of hospital admission and outpatient appointments will be compared for the two groups. Once this baseline information is obtained, the student will interview selected families to determine the benefits of the Complex Care Hub, and areas where the program could be improved. Families will also be invited to share their thoughts about research priorities for the CP Flagship moving forwards.

This project will provide important information to guide the development of the CP Flagship and in turn, enhance care for children with CP and their families.

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Available as Masters Projects: Yes

50. Reducing the burden of radiation exposure to neonates needing intubation

The placement of an endotracheal tube (intubation) to support breathing is often required in critical care medicine. In neonates it is easy for the tube to be placed too far into the lungs, which can be dangerous. Consequently an X-Ray is usually performed after intubation. This project will evaluate whether a new, faster and radiation-free method of lung imaging called EIT can guide correct tube position better than X-Ray. Students will work with Clinicians and Scientists in the MCRI Neonatal Research group to perform an observational study involving newborn babies needing Intensive Care. Students will gain skills in clinical research, lung imaging, data analysis and governance.

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Available as Masters Projects: Yes

51. Trends in haemodynamic support following major non-cardiac surgery in neonates

Following surgery, babies require intensive care support during their recovery. It is essential to provide strong cardiovascular support with IV fluid and medications. In this clinical project, the student will quantify the amount of haemodynamic support required using a validated scoring system, to help us better understand how we support babies in the post-operative period. Students will work with Clinicians and Scientists in the MCRI Neonatal Research group and the RCH Neonatal Intensive Care Unit to gain skills in clinical research, data analysis and governance. This research will pave the way for future interventional studies.

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Available as Masters Projects: No

52. Differences in pre- and post-operative cerebral blood flow markers using ultrasound in neonates undergoing major non-cardiac surgery

Surgery is a high risk time for newborns, because any clinical instability around this time may result in brain injury and poor neurodevelopmental outcomes. This project will record simple ultrasound Doppler studies of arteries in the brain prior to surgery, then at multiple time points after the procedure, to help us understand peri-operative changes in cerebral blood flow and see if there is a correlation with important clinical outcomes. Students will work with Clinicians and Scientists in the MCRI Neonatal Research group to perform an observational study involving newborn babies needing Intensive Care. Students will gain skills in clinical research, ultrasound, data analysis and governance. This study may pave the way for future interventional studies in this area of neonatal intensive care.

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Available as Masters Projects: Yes

53. Can NIRS predict post-op haemodynamic instability in neonates?

Newborn infants needing surgery often experience haemodynamic instability that requires escalating intensive and risks post-operative recovery, as well as risk of longterm organ damage. Near-infrared spectroscopy (NIRS) is a NICU technology that monitors brain and other organ oxygen delivery. This

offers the potential to identify poor oxygenation before problems occur. This observational clinical project will compare NIRS data during the first 48 hours post-operatively with clinical outcomes and pre-operative NIRS in neonates needing surgery at the RCH Neonatal Intensive Care Unit. Students will work with Clinicians and Scientists in the MCRI Neonatal Research group to gain skills in hands-on clinical research, data analysis and governance.

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Available as Masters Projects: Yes

54. Social media and decision-making in the neonatal intensive care unit

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

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Available as Masters Projects: Yes

55. The influence of siblings in end-of-life decision-making

Parents of critically ill babies are sometimes faced with difficult decisions in which they must consider what management plan will best serve the interests of their newborn baby. Sometimes the interests of the patient may be in tension with the interests of the broader family including siblings. This project will seek to understand how siblings influence decision-making from the perspective of parents of critically ill babies admitted to the neonatal intensive care unit through web-based surveys. The student will have the opportunity to learn qualitative analysis and ethical enquiry with exposure to activities of the Children's Bioethics Centre and the neonatal intensive care unit. The student will be supported by a team of neonatal intensivists and clinical ethicists with the opportunity to develop a paper and present at conferences.

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Available as Masters Projects: Yes

56. Are Neonatal Sepsis Calculators useful in a surgical neonatal population?

Neonatal infection is common and impacts short and long-term risk factors and often prolongs NICU admission. But diagnosing infection is difficult. As a consequence, clinicians have to balance risks of infection against potentially unnecessary antibiotic use. Recently validated online calculators to determine the risk of neonatal sepsis have become available for term infants. It is not known whether these calculators are applicable in neonates that need surgery, where alternative sources of inflammation may occur. In this project students will compare the utility and validity of available Neonatal Sepsis Calculators in babies that require surgery at the RCH NICU. Students will work closely with Clinicians and Scientists in the MCRI Neonatal Research group and gain skills in clinical research, data analysis and governance. This research provides the potential to develop tools to reduce the burden of infection in sick neonates.

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Available as Masters Projects: Yes

57. Sleep quality and fatigue in children with Charcot-Marie-Tooth disease

Introduction: Charcot-Marie-Tooth disease (CMT) refers to a group of inherited genetic neuropathies. It is the most common chronic peripheral neuropathy of childhood, affecting 1 in 5000 children. Symptoms often begin in childhood, and include limb weakness, mobility impairment and foot deformity. Fatigue is also common and affects quality of life. An increased prevalence of sleep disorders has been described in adults with CMT. We hypothesise that sleep disturbance is under-recognised, and represents a modifiable contributor to fatigue in children with CMT. Manifestations of sleep disturbance and fatigue are expected to have considerable impact on mental health, academic performance, social interaction and ultimately quality of life in children with CMT. There are no studies evaluating sleep and fatigue in Australian children with CMT and no studies examining the impact of sleep disturbance. The Department of Neurology, RCH hosts a statewide neuromuscular clinical service, and the RCH has a tertiary sleep service.

Aims: In the current population of children with CMT attending the RCH:

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

Methods: All children with CMT attending RCH will be offered participation in this study. Participants and their parents/carer will be asked to complete sleep, fatigue, HRQOL, physical activity and mood questionnaires and referred for overnight sleep study (PSG). The data collected will be collated and analysed by the student. Clinical implications: Sleep disruption may significantly impair health-related quality of life, physical activity, and exacerbate fatigue and mental health problems in children with

CMT. In order to optimise the medical management of children with CMT, it is important to understand the magnitude of sleep disorders and their impact in this population.

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Available as Masters Projects: No

58. What are parent's experiences of the multidisciplinary scoliosis service for children undergoing growth friendly non-fusion spinal scoliosis surgery?

Children with cerebral palsy (CP) have an increased risk of developing scoliosis with an incidence of between 20% and 25%. The definitive treatment for progressive scoliosis in this group is surgical intervention with the aim to halt curve progression. The complication rate of traditional spinal fusion in children with CP has remained relatively high (38%), however despite complications retrospective studies have consistently demonstrated a high satisfaction rate among caregivers. Scoliosis surgery using a new growth friendly non-fusion spinal instrumentation (NFSI) involves a minimally invasive technique and has become the primary surgical technique for children with neuromuscular scoliosis at RCH since June 2017, however there is minimal evidence regarding family satisfaction following this procedure.

The RCH delivers a multidisciplinary scoliosis service for children undergoing scoliosis surgery and to date has performed 145 NFSI surgeries. The aim of this study is

- to evaluate parent/carer satisfaction following bipolar scoliosis surgery and
- to report parent's experience of the multidisciplinary scoliosis service.

Methods: Families participating in the multidisciplinary scoliosis service whose child has undergone NFSI surgery in since June 2017 will be asked to provide data on satisfaction overall, care processes and expected changes in health and function. Content analysis of responses to open-ended questions will be conducted. Significance: Family satisfaction is an important outcome within a patient-centred quality of care framework. We expect our findings will promote strategies to inform the delivery of care in relation to NFSI surgery.

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Available as Masters Projects: No

59. Use of new devices to assess a baby's heart rate immediately after birth

Assessment of the newborn's heart rate immediately after birth is of extreme importance when there are concerns that the baby might be unwell and require resuscitation. An accurate, quick and reliable assessment of the heart rate is important and can be difficult to obtain by auscultation or pulse oximetry. ECG would be beneficial but the application of standard clinical ECG dot electrodes can be difficult in newborns who are moist and covered with vernix. Use of adhesive electrodes can injure the skin of the extremely preterm babies. Several new devices will be tested by the student, initially in the setting of more stable babies in our neonatal intensive and special care nursery and then also in the delivery room context. These devices consist of (1) a system of a modified oximetry probe combined with boot-like ECG electrodes at both feet, (2) an array of three gel covered metal disks in a holder that can be gently held to the baby's chest, and (3) a mat with integrated contact zones to detect the ECG signal.

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Available as Masters Projects: Yes

60. disease control and disordered sleep patterns in children with hepatic glycogen storage disorders (GSDs).

The hepatic glycogen storage disorders (GSD) are a rare group of inherited disorders resulting from deficiency of an enzyme involved in carbohydrate metabolism and the utilisation of glycogen when fasting. Children affected by these disorders are at risk of life threatening hypoglycaemia with minimal fasting. The management of GSDs involves lifelong intensive dietary modifications including either intermittent or continuous overnight feeding to prevent hypoglycaemia. Recent studies in type 1 diabetic populations have explored links between hypoglycaemia and impacts on sleep. One study in a paediatric population indicated the time spent in hypoglycemia to be associated with more nocturnal awakenings and long wake after sleep onset in children with type 1 diabetes. There is currently minimal data available exploring association between disordered sleep and disease control in the GSD population.

The Royal Children's Hospital provides a state-wide service managing all paediatric hepatic GSD patients within Victoria and Tasmania, from birth to 18 years of age. Currently patients are monitored with regular blood glucose finger prick testing and dietary modification based upon these and other biochemical results. Recently continuous glucose monitoring has become available in the diabetic population to assess hypo and hyperglycaemic events. Such monitoring has the potential to better detect unrecognized and asymptomatic periods of hypoglycaemia and hyperglycaemia allowing for improved disease management in GSD patients. This study aims to examine associations and interactions between glycaemic control (both hypo and hyper glycaemia) using continuous glucose monitoring (CGM), dietary management (continuous versus intermittent overnight feeding), quality of

life , and disordered sleep (using sleep questionnaires and actigraphy measurement concurrently with CGM monitoring) in a well defined population of hepatic GSD patients.

This study will define

1. glycaemic control

2. sleep quality and identify disordered sleep patterns in paediatric GSD population

3. quality of life in this population.

Mixed models will then be used to examine associations between these parameters. Ultimately this information will inform decisions around optimizing disease control in this patient population to improve long term outcomes for paeditric patients. This study will be undertaken in the departments of metabolic medicine and respiratory medicine at the RCH and includes supervisors with required expertise from both departments.

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Available as Masters Projects: **Yes**

61. Cardiovascular health literacy promotion for primary school students

The trajectory of a person's lifetime cardiovascular health begins in childhood. For example, there is now good evidence that maintaining a healthy blood pressure from childhood (e.g. through regular physical activity, healthy diet and adequate sleep) is key to long term health and reduces the risk of cardiovascular disease at a relatively young age. However, literacy around childhood blood pressure and cardiovascular health remains poor in our society. This project involves development of an educational program for use in primary schools to raise awareness of the importance of childhood blood pressure. The student will facilitate focus groups with primary school staff and clinicians to design the education package and will undertake pilot testing and evaluation in schools. The student will work closely with a multi-disciplinary team of experts to develop and test this program, and will gain skills in qualitative analysis, health promotion, educational development, and scientific communication. This research also provides the student with the opportunity to prepare a paper for publication and present at conferences.

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Available as Masters Projects: **Yes**

Cell Biology

62. Audit of early death post diagnosis of DMG

Diffuse midline glioma is the deadliest disease of childhood with survival near 0% at 5 years and a median progression free survival of 9 months. Radiation remains the only therapeutic option to extend and maintain quality of life for a period. Early deaths are rare, but have occurred. We intend to look for patterns predicting early death in presentation, imaging and symptoms at diagnosis in our cohort at the RCH and with time, through our collaborators at the DIPG Registry.

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Available as Masters Projects: No

UNIVERSITY OF MELBOURNE HONOURS ENTRY REQUIREMENTS

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

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

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

For further details please visit;

Department of Paediatrics: www.paediatrics.unimelb.edu.au

MCRI: https://www.mcri.edu.au/students/honours-students

MDHS: http://sc.mdhs.unimelb.edu.au/entry-requirements

HOW TO APPLY - MDHS HONOURS

Course Codes:

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

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

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

If you wish to be considered for Honours in 2018, and you would like to undertake your project and coursework with the Murdoch Childrens Research Institute, Royal Children's Hospital, Academic Centre, Faculty of Medicine and Dentistry Sciences with the enrolling unit being Department of Paediatrics, you will need to carry out a FOUR STEP PROCESS.

STEP 1: Look for Projects and Contact Potential Supervisor (Note: 2022 Start Year Intake projects will be available in Sonia by mid-August.) You will need to decide which Supervisor(s) and Project(s) that you wish to apply for. To do this, contact potential supervisors listed in this Handbook, you should speak to them and organise a meeting to discuss the project further. Projects available for 2022 are also listed on the Murdoch Childrens Research Institute and Department of Paediatrics websites.

STEP 2: Submit Online Application: Register for the Honours Application Tracking System (SONIA) before making your application in SONIA. Lodge an online application by Sunday 31 October 2021 (Round 1), and Friday 21 January 2022(Round 2).

http://mdhs-study.unimelb.edu.au/degrees/honours/apply-now#apply-now

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

STEP 4: Respond to Your Offer: Round one offers for entry into 2022 will be issued around mid-December 2021. Students must accept their offer by the Offer Lapse Date notes in their offer letter. Students who meet the minimum entry requirements but are not made a Round 1 offer may be considered for Round 2 under specific circumstances, but that is not guaranteed.

UNIVERSITY OF MELBOURNE MASTER OF BIOMEDICAL SCIENCE

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

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

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

MASTERS RESEARCH PROJECT

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

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

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

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

For commencement in semester one 2022, applications closing dates.
Semester 1 (February) entry - 30 November

Semester 2 (July) entry - 31 May
Semester 1 (February) entry - 15 January
Semester 2 (July) entry - 15 June

*late applications may be accepted based on the availability of places. Only timely applications will be considered for Commonwealth Supported Places (CSP).
http://futurestudents.unimelb.edu.au/admissions/applications/grad-dom