MONASH University

MONASH
CLINICAL AND
MOLECULAR MEDICINE

SF-CaMM Graduate Research Showcase Symposium

9:30 a.m. to 1.00 p.m.

Program

Time	Presenter Name	Title of Presentation	Department / Institute
9:30 am - 9:35 am: Formal opening by Sub Faculty Dean, Prof Eric Morand			
9.30 - 9.45 am	Emily Brennan	Untangling Menstrual Fluid Research	Obstetrics & Gynaecology
9.45 - 10.00 am	Patricia Khoo	Layers of Insight: Sequencing and Spatial Mapping of the Mucosal Microbiome	Paediatrics
10.00 - 10.15 am	Jason Vuong	Extending Acute Stroke Therapies through Innovative Clinical Trials	Medicine
10.15 - 10.30 am	Samara LeGrand	Diet Quality across Shift Schedules in Overweight and Obese Night Shift Workers: A Cross-Sectional Analysis from the SWIFt Study	Nutrition Science and Dietetics
10.30 - 10.45am	Trophy Chen	EValuation Of poLygenic scores and CT imAging In Risk factor modification in patients with diabetes (VOLTAIRE)	Victorian Heart Institute
10.45 - 11.00 am	Bianka Su	Role of CDKs in spermatogonial stem cell function and germline regeneration	Hudson / Department of Molecular and Translational Sciences
11.00 - 11.13 am - 13 min Break with Light Entertainment from SF-CaMM Supervisors			
11.15 - 11.30 am	Cailin Diedericks	Role of the Chest Wall in Newborn Respiratory Function at Birth	Obstetrics & Gynaecology
11.30 - 11.45 am	Grace Huang	Antigen discovery to develop precision immunotherapy for Ewing sarcoma	Medicine
11.45 - 12.00 am	Nur Abdul Jafar	Understanding the Interplay of Sleep and Polycystic ovary syndrome (PCOS)	Monash Centre for Health Research and Implementation (MCHRI)
12.00 - 12.15 am	Sandra Li	Using intra-arterially delivered induced pluripotent cell derived neural stem cells (iPSC-NSC) as therapy for ischemic stroke.	Surgery
12.15 - 12. 30 am	Rui Gao	Short 2'-O-methyl RNA fragments modulate TLR13 sensing.	Hudson / Department of Molecular and Translational Sciences
12.30-12.45 am	Angel Yonehara	Investigating cellular phenotypes of a preclinical model relevant to schizophrenia using single-cell RNA sequencing.	Psychiatry

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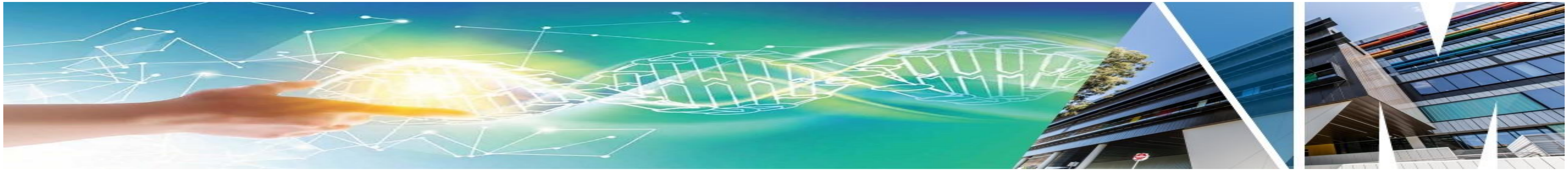
First Place - $500

Second Place - $300

People’s Choice - $100



Emily Brennan, Department of Obstetrics & Gynaecology

Untangling Menstrual Fluid Research

Emily is a second-year PhD student within the Epidemiology and Clinical Trials research group headed by A/Prof Miranda Davies-Tuck. Her project is centred around validating and optimising the use of menstrual fluid as a potential diagnostic for the prevention of adverse pregnancy outcomes. With a background in immunology, Emily's focus is the immune cell fraction of menstrual fluid with a particular interest in the effect of immune challenges on the endometrium and menstruation, and how this may contribute to pregnancy outcomes.

Abstract

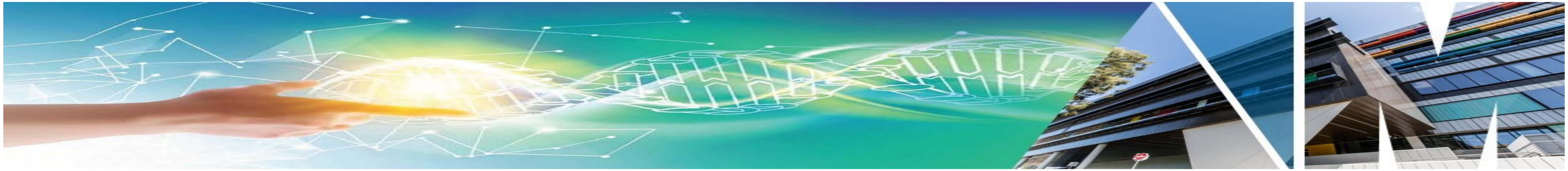
Emily Brennan, Kirstin Tindal, Srikar Vallabhapurapu, Natalie Hollowko, Fiona Cousins, Thomas Tapmeier, Adrienne Gordon, Caroline Gargett, Beverly Vollenhoven, Miranda Davies-Tuck

Menstrual fluid (MF) is a rich source of clinically relevant components including proteins, immune cells and tissue derived from the endometrium and cervix. Though the first recorded MF study was conducted in 1965, MF has gained traction in the last decade as a useful biofluid in diagnosis and management of many obstetric, gynaecological and general health conditions. A critical limitation to the burst in studies in this field is the lack of standardisation in methods for collection, processing and reporting.

Searches were performed in 4 databases using the terms “menstrual fluid”, “collection”, “survey” and “menstruation” to capture the broad range of studies conducted on MF and menstruation. The search results were imported into Covidence for screening and extraction. Forensic studies, reviews and studies that didn’t report collection of menstrual fluid or experiences with menstrual products were excluded. Data from included studies was extracted using a common extraction tool and analysis was performed with R.

118 studies met the inclusion criteria with 102 categorised as quantitative, collecting and analysing menstrual fluid, and 16 categorised as qualitative, reporting on experiences with menstruation or menstrual products. Of quantitative studies, 63.73% didn’t report menstrual cycle length and 41.18% didn’t specify if participants used hormones during the study. 17.65% didn’t report sample collection day and 56.86% collected across multiple days. Only 35.3% of studies used some form of collection media, though each consisted of different combinations of media, buffers, anticoagulants, and antibacterial/fungal agents. 50.1% didn’t use any collection media and 13.73% didn’t specify. Only 26.47% specified the transportation temperature prior to processing or analysis.

These critical discrepancies in the way MF research is conducted and reported introduces confounding variability between studies and impedes meaningful comparison. Standardising the collection, processing and reporting of MF research is critically important in furthering this growing field.



Dr Patricia Khoo, Department of Paediatrics

Layers of Insight: Sequencing and Spatial Mapping of the Mucosal Microbiome

Patricia Koo is a paediatric gastroenterologist at Monash Health. After graduating from Monash University in 2014, she undertook her training at the Monash Children's Hospital and Royal Children's Hospital, receiving her fellowship to the RACP in 2022. Dr Khoo is passionate about improving care for young people living with gastrointestinal conditions through clinical practice and research.

For her PhD, she is investigating the potential roles of the mucosa-associated microbiome in inflammatory bowel disease through sequencing and spatial imaging. Dr Khoo is supported by the National Health and Medical Research Council (NHMRC) postgraduate scholarship and the Academic Enhancement PhD scholarship from Monash Children's Hospital and Monash University.

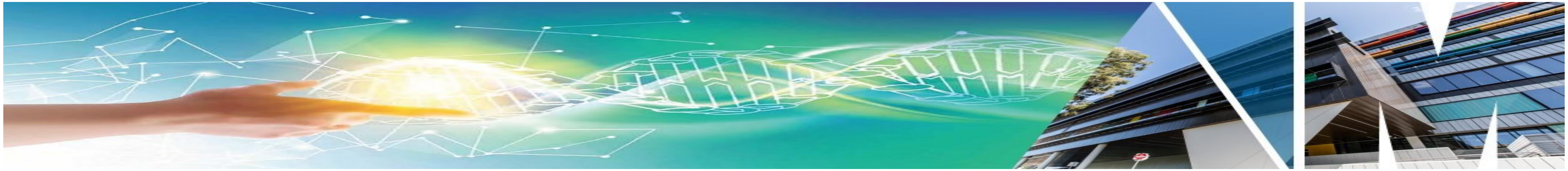
Abstract

The gut microbiome plays a fundamental role in maintaining human health, with disruptions to its composition implicated in a range of conditions, including inflammatory bowel disease. While much progress has been made in cataloguing microbial diversity, less is known about how these microbes are organised within the gut and how they interact in situ. In particular, the spatial distribution and co-occurrence patterns of gut microbes in both health and disease remain poorly understood, largely due to the inherent challenges of directly accessing and studying the human gut.

Spatial organisation of the microbiome can be broadly considered in two dimensions: longitudinally along the gastrointestinal tract, and cross-sectionally across the layers from lumen to mucosa. Longitudinal studies have demonstrated compositional and functional variation of mucosa-associated microbiota across different gut segments. In contrast, cross-sectional examination of microbiota, particularly at the mucosa where host–microbe interactions are most intimate, remains more difficult but is highly relevant to disease processes such as ulcerative colitis (UC).

We are developing an integrative approach to investigate the spatial organisation of bacteria within the mucosa of patients with UC. Using metagenomic sequencing data from UC patients and matched controls, network analyses were performed to identify potential candidate bacterial pairs and co-occurrence networks. These putative interactions are then validated experimentally: specific bacteria are labelled with existing or newly designed fluorescent probes and visualised using high-resolution confocal microscopy.

This combined genomic and imaging strategy allows us to directly map microbial communities in their anatomical context. By characterising multispecies consortia within the inflamed mucosa, we aim to identify potential microbial communities that contribute to disease activity. Ultimately, this work may highlight new therapeutic opportunities, including targeted disruption of pathogenic microbial networks through mechanical, chemical, or microbiome-directed interventions.



Dr Jason Vuong, Department of Medicine

Extending Acute Stroke Therapies through Innovative Clinical Trials

Dr Jason Vuong is an academic neurologist and PhD candidate in the Department of Medicine at the School of Clinical Sciences, Monash Health. He graduated from The University of Melbourne in 2015 and obtained his Fellowship of the Royal Australasian College of Physicians (FRACP) in Neurology in 2022. Clinically, he holds a fractional appointment within the stroke service at Monash Health. His PhD research focuses on the application of advanced neuroimaging techniques in stroke clinical trials.

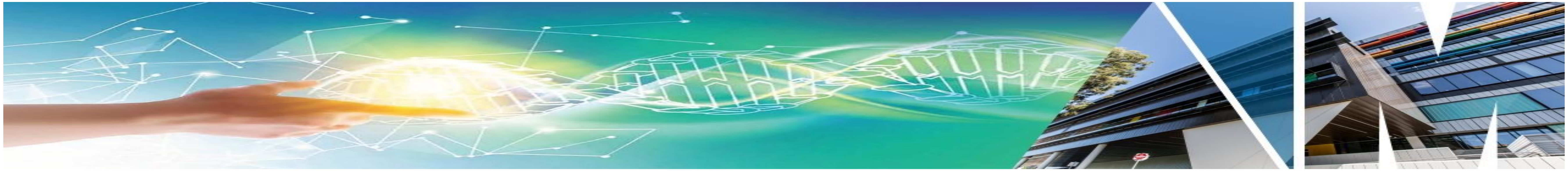
Dr Vuong is a recipient of a National Health and Medical Research Council (NHMRC) scholarship and has received additional support through a grant from Brain Australia.

Abstract

Reperfusion therapies for acute ischaemic stroke (AIS) have undergone a major transformation over recent decades, driven by positive outcomes from thrombolysis and thrombectomy randomised clinical trials. These foundational studies primarily used the modified Rankin Scale (mRS), a global measure of post-stroke disability, as their outcome metric. The mRS is scored from 0 – 6; 0 indicates no disability, 5 indicates severe disability (bedridden), and 6 denotes death. However, the mRS heavily emphasises motor function and is less reliable in patients with comorbidities, lower socioeconomic status, or non-motor manifestations of AIS. As clinical trials increasingly focus on smaller strokes and non-motor presentations, there is a growing need to develop new primary outcome measures for future stroke RCTs.

This PhD addresses this gap in stroke research. First, a systematic review was conducted on thrombectomy outcomes in elderly patients and those with comorbidities. We propose incorporating patient-reported outcomes as primary endpoints, rather than relying solely on the mRS, which may be ill-suited for this population. Second, a review of visual loss secondary to occipital infarcts was undertaken to highlight the impact of vision on quality of life. We analysed the neuroanatomical basis of visual field deficits in the occipital lobe to inform the design of future trials aimed at preserving visual function, thereby reducing morbidity and maintaining the ability to drive. Finally, this PhD will investigate the incidence of post-stroke cognitive impairment (PSCI), with the goal of developing a predictive model for PSCI at the onset of AIS.

Correlation of non-motor patient outcomes to the patient’s neuroimaging requires the development of new tools. Thus, this PhD has also focused on developing a parcellated whole brain template. ASPECTS is a well known and validated scoring system designed to predict clinical outcomes in patients with an AIS in the middle cerebral artery receiving thrombolysis. The ASPECTS-AAL is an expansion of the original ASPECTS, by partnering with the parcelled automated anatomical atlas (AAL) to create a whole brain template. It aims to correlate clinical outcomes with regions of brain involvement, with a view to better correlate an ischaemic stroke location with its’ clinical manifestation.



Samara Legrand, Department of Nutrition Science and Dietetics

Diet Quality across Shift Schedules in Overweight and Obese Night Shift Workers: A Cross-Sectional Analysis from the SWIFt Study

Samara is a PhD candidate in the Department of Nutrition, Dietetics and Food, where her research explores the intersection of technology and nutrition. Her thesis, titled "The Role of Digital Technologies in Personalised Dietary Feedback: A Focus on Diet Quality Scores for Shift Workers", reflects both her academic interest and lived experience as a former shift worker.

With a Bachelor of Nutrition and Dietetics and a Master of Public Health, Samara has a passion for innovative, data-driven approaches to preventative health. By utilising digital tools with personalised dietary strategies, she aims to provide individuals with meaningful, real-time insights to improve diet quality and support long-term wellbeing.

Abstract

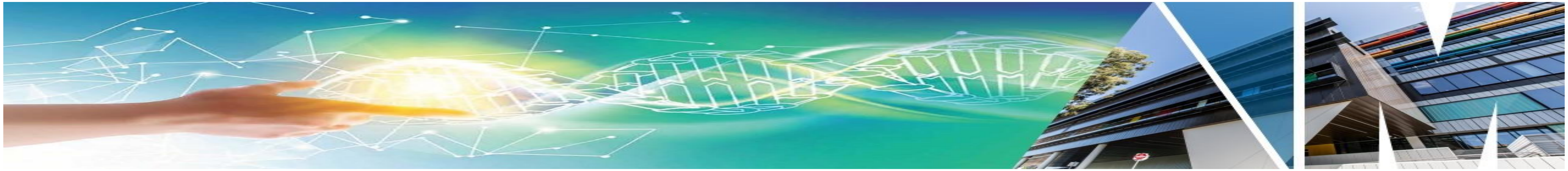
Background: Shift work is essential to maintaining access to critical services and meeting the demands of a 24-hour economy. In 2012, approximately 16% of the Australian workforce were shift workers, with 7% working predominantly at night. Despite its importance, night shift work is associated with an increased risk of chronic disease driven by circadian disruption and irregular eating patterns. The circadian rhythm, which regulates biological and behavioural processes over a 24-hour cycle, becomes desynchronised during night work, impairing glucose and lipid metabolism. This misalignment is compounded by altered eating behaviours, including increased energy intake during biologically inappropriate times and reduced overnight fasting.

Aim: This study aims to assess the diet quality of overweight and obese night shift workers and examine differences across shift types (day shift, night shift and days off).

Methods: This cross-sectional analysis uses baseline data from the SWIFt study, a three-arm, randomised controlled trial. Participants aged 25-65 years completed food and work diaries, capturing dietary intake across various shift types. Diet quality was assessed using an adapted Healthy Eating Index for Australian Adults, allowing comparisons against the Australian Dietary Guidelines.

Results: Following randomisation and matching of food and work diaries, 218 participants and 1150 days of data were included in the analysis. The median age was 48 years (±9.8), and 54% were female. The average HEIFA-2013 score was 48.4 (±10.9) out of a possible 100, indicating suboptimal diet quality across the cohort. After adjusting for gender and age, diet quality was highest on a day shift and lowest when transitioning from a night shift to a day off (p = 006).

Conclusion: This is the first study to assess diet quality across the working schedule in overweight and obese night shift workers. These insights can inform the development of feasible interventions for night shift workers to improve their diet quality and reduce the risk of disease



Trophy Chen, Victorian Heart Institute

EValuation Of poLygenic scores and CT imAging In Risk factor modification in patients with diabetes (VOLTAIRE)

Trophy (Ruofei) Chen is a third-year PhD candidate at the Monash Victorian Heart Institute, with over a decade of clinical experience as a critical care nurse in intensive care. Her research focuses on transforming cardiovascular prevention through the integration of advanced imaging, genetic risk information, and behavioural interventions. She leads the VOLTAIRE study, a randomised controlled trial that combines coronary CT angiography, polygenic risk scores, and health coaching to deliver proactive, patient-centred care for people with type 2 diabetes. With more than five years of experience in clinical trials, Trophy is passionate about translational research that bridges precision medicine and sustainable models of care.

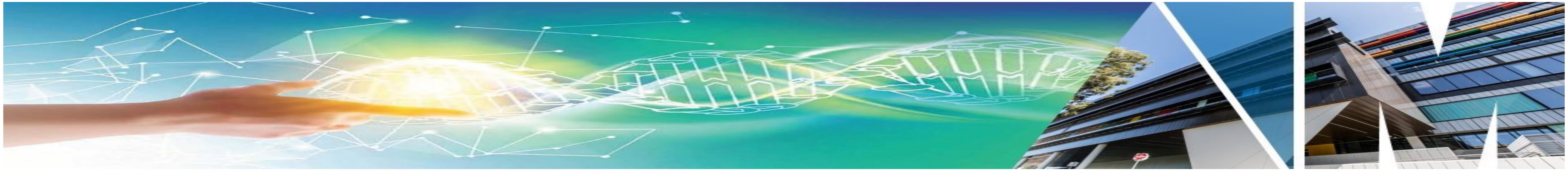
Abstract

Cardiovascular disease (CVD) remains the leading cause of death worldwide, and people with type 2 diabetes are among the most vulnerable. Despite advances in treatment, many patients experience delayed detection and suboptimal adherence to prevention strategies, leaving them at high risk of serious outcomes. This PhD project seeks to transform prevention by combining innovative diagnostics with personalised behavioural support in a nurse-led model of care.

The centrepiece of the work is the VOLTAIRE study, a randomised controlled trial recruiting up to 150 participants with type 2 diabetes at the Victorian Heart Hospital. The trial evaluates whether advanced imaging and genetic risk information can improve cardiovascular risk factor management compared with standard care. Participants undergo computed tomography coronary angiography (CTCA) to detect early, otherwise hidden atherosclerosis, and receive polygenic risk scores to quantify inherited susceptibility to heart disease. These personalised risk profiles are then coupled with health coaching, delivered using motivational interviewing techniques, to support sustained lifestyle changes and improve adherence to medications.

Importantly, VOLTAIRE extends beyond clinical outcomes by also investigating behavioural and psychological responses to genetic and imaging information. The primary outcome is change in non-calcified plaque volume assessed by CTCA. Secondary outcomes include the proportion of participants achieving risk factor control, adherence to medications, levels of patient engagement, and psychological health scores. This comprehensive framework provides insights into both the biological and behavioural impact of personalised prevention.

By integrating technology, precision medicine, and nursing expertise, this project represents a shift from reactive treatment to proactive prevention. Ultimately, VOLTAIRE aims to provide evidence for scalable models of care that can reduce cardiovascular risk, strengthen patient engagement, and ease the growing global burden of CVD.



Bianka Su, Department of Molecular and Translational Sciences

Role of CDKs in spermatogonial stem cell function and germline regeneration

Bianka is a third-year PhD candidate in the Germline Stem Cell Laboratory, led by Associate Professor Robin Hobbs,at the Hudson Institute of Medical Research and the University of Adelaide. She holds a Bachelor of Science from Monash University, along with a Graduate Diploma in Reproductive Sciences and a Master of Clinical Embryology. Her research centres on male fertility and the germline, with a focus on how cell cycle regulators influence the function and fate of spermatogonial stem cells.

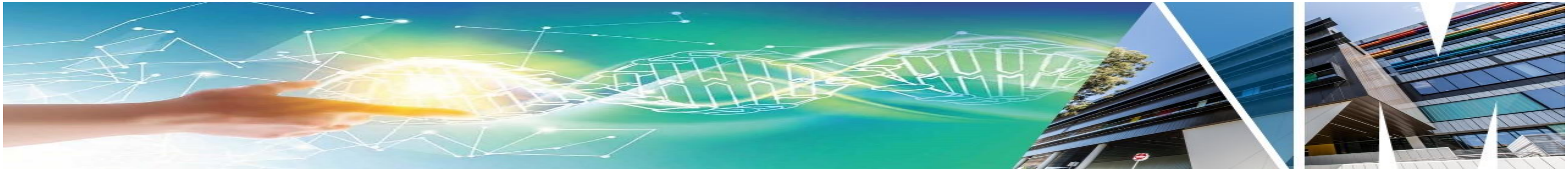
Abstract

Infertility is surprisingly common, affecting 10–15% of couples globally, with male factors contributing to about half of these cases. In men, fertility relies on a population of spermatogonial stem cells (SSCs) located in the testes, which continuously produce sperm through spermatogenesis. Proper regulation of SSC self-renewal and differentiation into sperm is crucial for maintaining germline stability and overall fertility. Despite their importance, the molecular mechanisms that control SSC function remain poorly understood.

Cell division is a vital biological process that occurs in a series of distinct phases and is typically dysregulated in cancer. The progression through these phases is controlled by cyclin-dependent kinases (CDKs), which also play roles during various stages of spermatogenesis. Beyond their role in cell cycle control, a distinct family of CDKs regulates gene activity, transcription and cell function through regulating RNA polymerase. Notably, research indicates that disruptions in germline cell cycle regulation can significantly impact fertility.

My PhD research investigates the role of cell cycle and transcriptional CDKs in regulating SSCs and maintaining the male germline, using both pharmacological and genetic approaches. We employ mouse models along with highly selective CDK inhibitors originally developed for cancer therapy. Through a combination of in vivo and in vitro studies, we show that broad-range CDK inhibition disrupts spermatogenesis and induces defects across multiple germ cell types, ultimately impairing sperm production in adult testes. Further, we have uncovered specific roles of both cell cycle and transcriptional CDKs in control of SSC identity and fate.

This research defines the roles played by CDK family members in function and gene expression of SSCs and other germ cells. Besides providing insight into the molecular mechanisms underpinning SSC control, my study is important in understanding how CDK- targeting drugs used in chemotherapy may have harmful and persistent side-effects on cancer patient fertility.



Morning Tea Break

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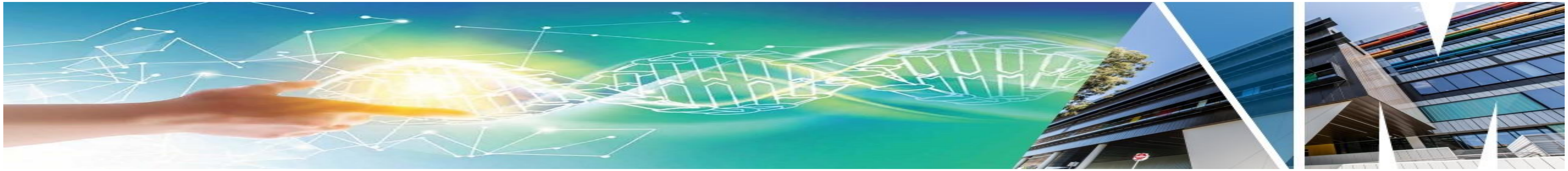


Cailin Diedericks, Department of Obstetrics & Gynaecology

Role of the Chest Wall in Newborn Respiratory Function at Birth

Cailin is a third-year PhD candidate working under the supervision of Dr Kelly Crossley and Prof Stuart Hooper. My research focuses on the role of the chest wall in neonatal respiratory function, which, until now, has been ignored. I have used phase contrast X-ray imaging in near-term rabbit kittens to visualise how changes in chest wall mechanics influence respiratory function, haemodynamics and the cardiorespiratory transition at birth. Through this work, I have discovered that the chest wall plays a critical role in the successful adaptation of the respiratory system at birth, and has major implications for understanding the adverse effects of pulmonary oedema on respiratory function in adults.

Abstract

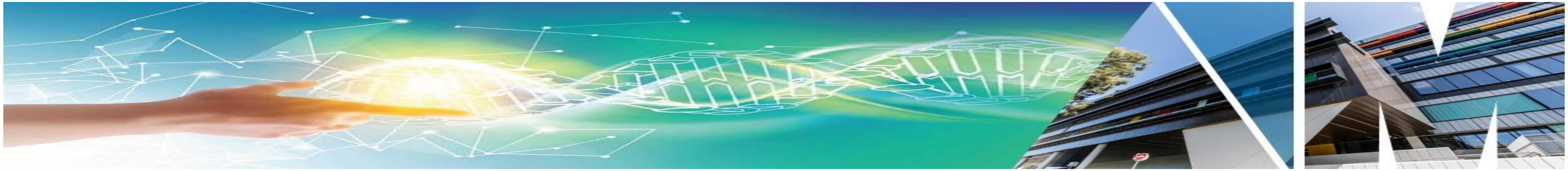
Background: The chest wall significantly impacts respiratory function after birth, but its role in the newborn remains poorly understood as it is structurally and functionally different to adults. In neonates, the chest wall is highly compliant, enabling it to expand and accommodate both the incoming air and liquid cleared from the airways (into the lung tissue) during lung aeration. While the chest wall plays a crucial role in the respiratory transition and breathing immediately after birth, its role has been ignored, leading to clinical practices that may impact chest wall mechanics. This includes external positive pressures (i.e. swaddling), which limit thoracic expansion, and external negative pressures (i.e. negative pressure ventilation), which expand the chest.

Aim: To summarise the role of chest wall function in fetuses and neonates, with particular focus on lung liquid clearance, lung aeration, and breathing after birth.

Methods: Chest wall mechanics were altered by applying external atmospheric (0 $\mathrm{cmH_2O}$), positive (+6 $\mathrm{cmH_2O}$), and negative pressures (-6 $\mathrm{cmH_2O}$) to the thorax of lambs (near-term, 137/147; preterm, 127/147 days gestation age; GA) and rabbit kittens (30/31 days GA). Physiological recordings and respiratory function were investigated using lambs, and phase-contrast X-ray imaging in rabbit kittens was used to assess chest wall expansion and lung aeration.

Results: Positive extra-thoracic pressures limited chest wall expansion and reduced lung compliance, air volumes and pulmonary oxygen exchange capacity in near-term and preterm newborns ($P<0.05$). In contrast, external negative pressures increased thoracic expansion, lung compliance, lung air volumes and pulmonary oxygen exchange compared to external atmospheric pressures ($P<0.05$).

Conclusion: External positive pressures compress the chest wall, reduce lung air volumes and impair respiratory function, whereas external negative pressures expand the chest, increase lung air volumes and improve respiratory function after birth.



Grace Huang, Department of Medicine

Antigen discovery to develop precision immunotherapy for Ewing sarcoma

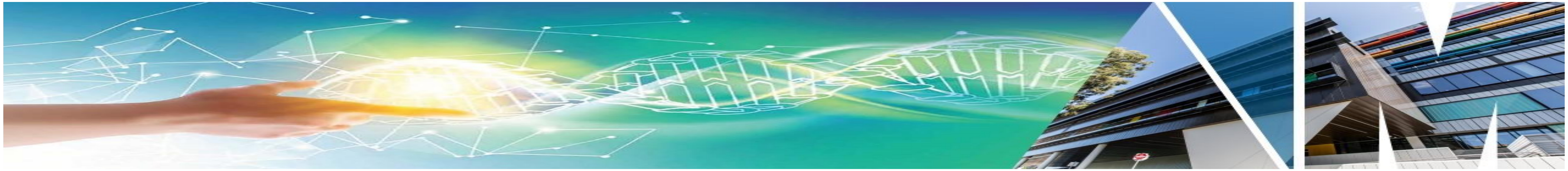
Grace is a third-year PhD student at the Hudson Institute of Medical Research, Centre for Cancer Research. She began her research journey in 2022 as an Honours student in the Translational Antigen Discovery Lab, led by Associate Professor Pouya Faridi. Co-supervised by Associate Professor Jason Cain, Grace is investigating the immunopeptidome of Ewing sarcoma to identify therapeutic targets for HLA-dependent treatments, including cancer vaccines and T-cell therapies. Her research integrates multi-omics approaches—specifically immunopeptidomics and transcriptomics—with translational oncology, aiming to advance precision immunotherapy for paediatric Ewing sarcoma.

Abstract

Ewing Sarcoma (ES) is the second most common primary bone cancer in children, adolescents, and young adults. Its aggressive nature and poor prognosis—especially in recurrent or metastatic cases, with a five-year survival rate below 30%—urges the need for novel therapies. Precision immunotherapies, such as cancer vaccines and T-cell therapies, offer a promising strategy by training the immune system to target tumour-specific peptide antigens presented on human leukocyte antigens (HLAs). This study presents a comprehensive immunopeptidomics analysis of ES cell lines to identify targets for immunotherapy.

Eight ES cell lines were cultured with or without 100 IU/mL IFNγ for 72 hours. Post-treatment, 100 million cells per condition were harvested, lysed using a mild buffer to preserve HLA-peptide complexes, and isolated using magnetic beads bound to pan-HLA class I antibody. Peptides were eluted and analysed by LC-MS/MS (Orbitrap Exploris 480). Data were searched against the human proteome using PEAKS 12.5, and potential targets were filtered using various databases such as TANTIGEN and other published databases.

Our cohort of Ewing Sarcoma (ES) cell lines collectively expresses 24 distinct HLA alleles, covering over 96% of the global population. Across all samples, we identified 59,129 peptides (8–12 amino acids in length), which mapped to 10,250 unique source proteins. Each cell line presented 100-350 tumour-associated antigens, including LOXHD1, LIPI, and IGF2BP1—proteins known to be implicated in ES and with potential immunotherapeutic relevance. We also detected a peptide derived from the EWSR1-FLI1 fusion breakpoint, offering a highly specific and potential target for precision immunotherapy in Ewing Sarcoma. This study presents the most comprehensive immunopeptidomic analysis of Ewing Sarcoma to date, with a look into tumour-associated antigens and tumour-specific antigens. These findings provide a rich foundation for developing peptide-based vaccines and T-cell therapies, advancing precision immunotherapy for Ewing Sarcoma.



Nur Abdul Jafar, Monash Centre for Health Research and Implementation (MCHRI)

Understanding the Interplay Between Sleep and Polycystic ovary syndrome (PCOS)

Nur Abdul Jafar is a PhD candidate with a Bachelor of Science (Honours) and a Master of Science in Public Health, with an academic background in sleep epidemiology. Her research focuses on sleep health across the lifespan, from early childhood to maternal populations, examining chronotype, sleep health measures, and their links to metabolic and emotional well-being. She has contributed to journals such as *Sleep Medicine* and *The American Journal of Clinical Nutrition*, advancing understanding of sleep's impact on health. Currently, her PhD project investigates the interplay between sleep and polycystic ovary syndrome (PCOS), aiming to better understand and develop strategies to improve sleep in this population.

Abstract

Polycystic ovary syndrome (PCOS) is a common endocrine disorder affecting up to 18% of reproductive-aged women worldwide, characterized by reproductive, metabolic, and psychological complications. Key features of PCOS include hyperandrogenism, insulin resistance, central adiposity, and obesity, all of which contribute to a higher prevalence of sleep problems, including poor sleep quality, restless sleep, and obstructive sleep apnea (OSA). Sleep problems exacerbates insulin resistance and metabolic dysfunction, further worsening PCOS symptoms and negatively impacting quality of life. Although the relationship between sleep and PCOS is recognized, the underlying pathophysiological mechanisms, particularly the role of sex hormones, and the extent of sleep problems in adolescent populations remain poorly understood.

This PhD research seeks to advance understanding of sleep health across the lifespan in women with PCOS and to explore potential strategies to improve sleep quality in this population. A narrative review synthesizes existing literature on sleep disturbances in PCOS beyond OSA, highlighting gaps and treatment approaches. A systematic review and meta-analysis examine the prevalence and severity of OSA in women with PCOS compared to controls, adjusting for key confounders such as BMI, age, and ethnicity, contributing to the 2023 International PCOS Guideline recommendations. An additional meta-analysis explores the associations between sex hormones, sex hormone-binding globulin, and sleep problems, providing insights into potential pathophysiological links.

Longitudinal data from the Raine Study cohort is also analysed to examine associations between sleep behaviours and body mass index (BMI) from childhood through early adolescence in girls with and without PCOS. This analysis explores specific sleep behaviours linked to adolescent PCOS risk and investigates bidirectional relationships between sleep and BMI over time, with consideration of PCOS as a potential modifying factor.

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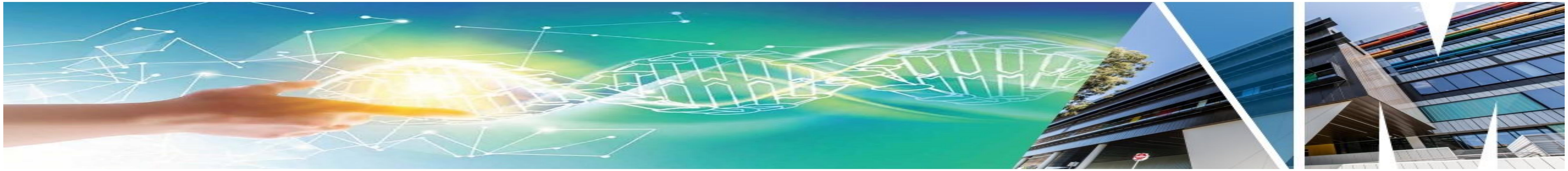
Together, these comprehensive studies aim to elucidate the complex interactions between sleep, hormonal factors, and metabolic health across critical developmental stages, ultimately guiding lifestyle interventions to improve health outcomes for women with PCOS.



Sandra Li, Department of Surgery.

Using intra-arterially delivered induced pluripotent cell derived neural stem cells (iPSC-NSC) as therapy for ischemic stroke.

Sandra is a current MD-PhD candidate based at The Ritchie Centre and Department of Surgery. With an interest in neurosurgery, her project investigates the therapeutic potential of genetically modified neural stem cells as an adjunct treatment for ischaemic stroke. Her project combines regenerative neuroscience, genetic engineering and translational therapeutics to address the unmet need for neuroprotective and neuro-regenerative therapies post-stroke. Sandra previously completed her BMedSc(Hons) at School of Clinical Sciences in 2023 with the Department of Neurosurgery. After thoroughly enjoying her year, she chose to continue with a PhD to further develop her research skills and clinical insight. Sandra is passionate about bridging bench-to-bedside gaps, improving patient outcomes and aspires to become a future clinician-scientist.

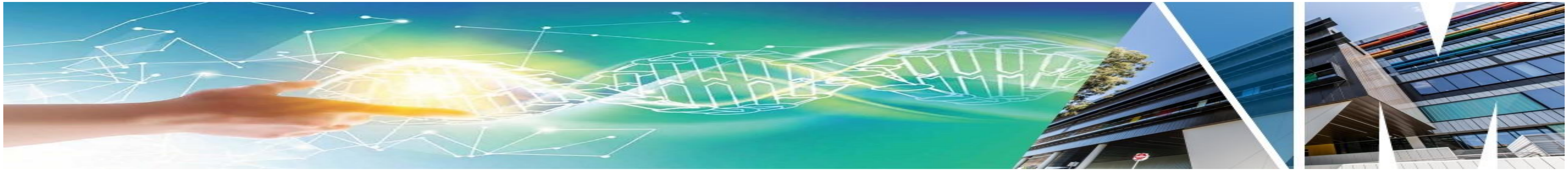
Abstract

Background: Stroke is a leading cause of death and permanent neurological disabilities. Existing treatment only restores perfusion without addressing post-stroke brain damage. Clinical trials using neural stem cell (NSC) therapy have shown promise, yet poor cell survival and migration remain key limitations. Preclinical studies suggest genetic engineering may enhance the therapeutic efficacy of NSCs. My PhD investigates whether genetically modified induced pluripotent derived-neural stem cells (iPSC-NSCs) delivered intra-arterially could serve as an effective regenerative therapy for neonatal and adult ischaemic stroke.

Method: NSCs are differentiated from human iPSCs using a commercial neural induction kit. iPSC-NSCs are validated across passages through conducting immunocytochemistry, comparative quantitative PCR (qPCR), testing cell proliferation and downstream cell type differentiation potential. Lentivirus transduction is used to overexpress C-C chemokine receptor 5 (CCR5) and basic fibroblast growth factor (bFGF) to enhance migratory and survival capacities of the iPSC-NSCs. Functional validation of these modifications is conducted *in vitro* using Boyden chamber assays and oxygen-glucose deprivation models. *In vivo* testing is conducted using a neonatal rat photothrombotic stroke model. Cells are administered at 24-hours post-stroke via the carotid arteries. Short term animals are sacrificed at 3 days post therapy with brains harvested for histology staining and molecular studies.

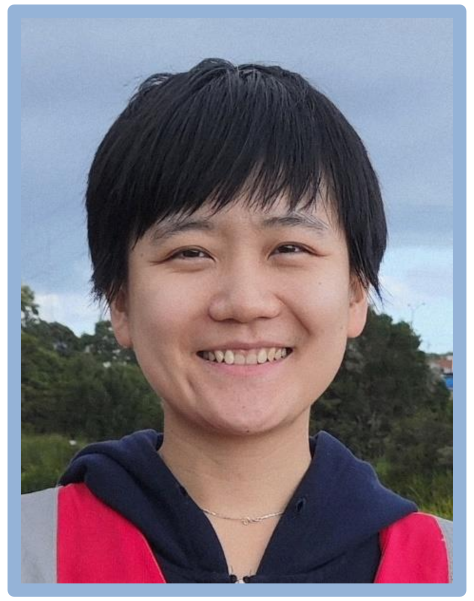
Result: iPSC-NSCs have been successfully generated and validated. Immunocytochemistry and qPCR confirmed expression of NSC specific markers (PAX6, Nestin, SOX1) and loss of pluripotency markers (OCT4, Nanog). Differentiation into neurons and astrocytes was confirmed. Lentiviral transduction was optimised at a multiplicity of infection (MOI) of 5, without polybrene and 24-hour exposure time. The intra-arterial cell delivery protocol is currently being refined, with preliminary *in vivo* data collected.

Conclusion: Currently, regenerative and neuroprotective therapies for stroke is non-existent. This study aims to address this gap by developing a clinically translatable NSC-based intervention. By genetically enhancing iPSC-derived NSCs and delivering them intra-arterially, we aim to improve cell survival and migration, ultimately offering a promising new treatment for stroke recovery.



Rui Gao, Dept of Molecular and Translational Sciences

Short 2'-O-methyl RNA fragments modulate TLR13 sensing.



Rui Gao completed her bachelor’s degrees at Michigan State University in 2016. She began her career as a chemist at Neogen Corporation in the US before pursuing a Master’s degree at Monash University in 2019. Following this, she worked as a PK/PD scientist and project manager at Henlius Biologics in Shanghai. In 2023, she commenced her PhD at the Hudson Institute in Associate Professor Michael Gantier's lab, where she is investigating the regulation of toll-like receptors.

Abstract

Toll-like receptors (TLRs) are a family of innate immune sensors that recognise pathogenic molecules to initiate immune responses and protect the host. Among them, nucleic acid sensing TLRs also have the capacity to be aberrantly engaged by host RNA/DNA and lead to autoimmunity. Our laboratory has recently discovered that TLR7 and 8 are normally kept in check against host RNA detection by the activity of antagonistic RNA fragments released from ribosomal RNA recycling1. TLR13 is a key bacterial RNA sensor in rodents. Recently, *in vivo* depletion of RNase T2 was linked to spontaneous neuro- and splenic inflammation due to aberrant TLR13 activation (1, 2). Here, we investigated whether this aberrant TLR13 signalling could be related to a lack of natural TLR13 antagonism, mediated by RNase T2 fragmentation of 2’-O-methyl (2’-OMe)-modified ribosomal RNA (rRNA). We confirmed that rRNA antagonises TLR13 sensing of its canonical agonist Sa19. We also found that short 2’-OMe Guanosine oligonucleotides can antagonise TLR13, similar to our findings for TLR7 and TLR8. Systematic analyses of short oligos with different base modifications showed that, unlike TLR7/8 antagonism, which is driven by 5’-end 2’-OMe-Guanosine RNA fragments, TLR13 antagonism depends on a 3’-end penultimate 2’-OMe-Guanosine residue. We propose that such 3’-end penultimate 2’-OMe-Guanosine RNA fragments are uniquely generated by RNase T2, to prevent endosomal TLR13 from erroneous activation. Critically, this work confirms that the natural antagonism of endosomal TLRs, mediated by short 2′-OMe-Guanosine RNA fragments, extends beyond TLR7 and TLR8 and is pivotal in mitigating autoinflammation driven by these receptors.

1. Alharbi, A.S. *et al.* 2’-O-Methyl-guanosine 3-base RNA fragments mediate essential natural TLR7/8 antagonism. *bioRxiv*, 2024.2007.2025.605091 (2024).
2. Sato, R. *et al.* RNase T2 deficiency promotes TLR13-dependent replenishment of tissue-protective Kupffer cells. *J Exp Med* 222 (2025).
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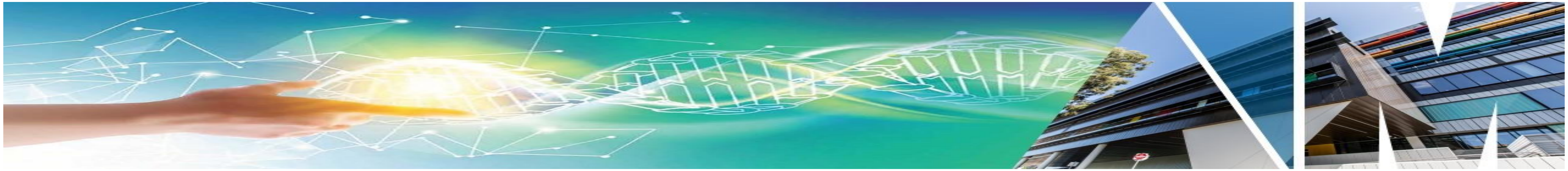

Angel Yonehara, Department of Psychiatry, Monash University

Investigating cellular phenotypes of a preclinical model relevant to schizophrenia using single-cell RNA sequencing.

Angel Aki Yonehara is a PhD candidate in Psychiatry at Monash University, studying the molecular mechanism of schizophrenia. Her research focuses on the role of mutation ArxR264Q in GABAergic interneuron migration and development and single-cell RNA sequencing of mice brains. Her future directions include developing an induced pluripotent stem cell (iPSC) model of the ARXR264Q mutation to study human-specific impacts GABAergic differentiation and migration. Angel's work combines developmental neurobiology, high-throughput transcriptomics and bioinformatics to uncover gene networks underlying inhibitory neuron dysfunction, with the aim of advancing understanding of schizophrenia development and identify therapeutic targets for this disorder.

Abstract

Background:
The homeobox gene Arx, located on the X chromosome, encodes a transcription factor critical for embryonic brain development, where it regulates cell fate specification and neuronal positioning. Mutations in this gene have been linked to several neurodevelopmental disorders including intellectually disability, epilepsy, autism spectrum disorder, and schizophrenia. Our lab identified a missense mutation (ArxR264Q) where glutamine replaces a proline residue. The proband presented with schizophrenia and a family history of mental illness. To study this mutation, we next generated an ArxR264Q mutant mouse. Adult ArxR264Q mice showed reduced GABAergic cell density and behavioural phenotypes relevant to schizophrenia.

Aims and Methods:
This study investigated how the ArxR264Q mutation alters gene expression within specific cell populations using single-cell RNA sequencing (scRNA-seq) of postnatal day 3-4 mouse brains. We hypothesised that the mutation would result in cell-type-specific transcriptional changes, particularly for GABAergic interneuron subtypes parvalbumin and somatostatin. Fresh mouse brains (~4,500 cells per sample) were processed using 10x Chromium Next GEM Single Cell 3' reagent kits.

Results:
scRNA-seq identified 16 distinct cell types, including GABAergic populations. Sub-clustering of GABAergic cells revealed medial and caudal ganglionic eminence-derived subtypes (MGE and CGE), including both mature and immature cells. Immature MGE cells, exhibited differential expression of *C1qa*, *C1qb*, and *C1qc*, core components of the complement pathway, and *Apoe*, *Tyrobp*, and *Fcer1g*, known to modulate complement activity and immune-related processes.

Discussion:
The *Arx*R264Q mice show altered expression of complement-related genes in immature MGE-derived GABAergic neurons. These transcriptional changes may underlie the GABAergic cell density reductions and behavioural phenotypes observed in adulthood, supporting a link between early complement pathway dysregulation and neurodevelopmental *outcomes in this model.*