ASMR
AUSTRALIAN SOCIETY FOR MEDICAL RESEARCH

Victorian Annual Scientific Meeting

Thursday, 31 July 2025
Deakin Downtown, Melbourne

Get in touch
+61 (02) 9230 0333 vic@asmr.org.au www.asmr.org.au/vic/

ACKNOWLEDGEMENT OF COUNTRY

We acknowledge the traditional owners of the land that we meet on today and pay our respects to the people of the Kulin Nation. We also acknowledge that our research institutes are located on the lands of many Traditional Custodians in Victoria and around Australia. We recognise their ongoing connection to the land and contributions to research, university and wide Australian society. We pay our respects to Indigenous Elders, past, present and emerging and will continue to acknowledge their living culture and their continuing roles in the life of this region.

The ASMR's vision is for a healthy and equitable Australia. There is no doubt that a significant gap remains between the health outcomes of First Nations people and other Australians, and the ASMR will continue to work towards closing this gap.

The ASMR believes that our diversity is our strength: health and medical research belongs to everyone, and everyone belongs in health and medical research.

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ABOUT THE AUSTRALIAN SOCIETY FOR MEDICAL RESEARCH

The Australian Society for Medical Research (ASMR) is a non-politically aligned, non-profit organisation established in 1961. ASMR is the peak organisation representing health and medical researchers in Australia through public, political, and scientific advocacy. ASMR's members include individuals from diverse career stages and research areas, as well as affiliate and associate members drawn from specialist medical societies, medical colleges and institutes, and consumer groups.

The ASMR is dedicated to achieving a secure and sustainable health and medical research workforce to facilitate increased productivity in Australian health and medical research.

ASMR's activities focus on:

- fostering excellence in health and medical research
- expanding the interface between basic science and clinical research
- promoting community understanding and support
- holding annual scientific meetings, including our National Scientific Conference and state Scientific Meetings
- creating opportunities for Australian health and medical researchers through the ASMR Research Awards and student travel grants
- keeping members up to date about medical research activites around Australia through our eBulletin
- offering Professional and Career Development Programs
- helping to foster new relation between current members

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OUTLINES OF ASMR VICTORIAN ANNUAL SCIENTIFIC MEETING PROGRAM

8:00 - 8:30 am	REGISTRATION			
8:30 - 8:35 am	Acknowledgement of Country Conference overview			
8:35 - 10:30 am	Keynote Presenter: Dr. Shane Huntington (CEO, ASMR) *Communication and Grant Writing Workshop*			
10:30 - 10:40 am	Sponsor talks: Beckman Coulter Life Sciences, GenScript Biotech, and Stago			
10:40 - 11:00 am	Morning tea			
11:00 - 11:30 am	Keynote Presenter: Dr. Gunveen Kaur (Institute for Physical Activity and Nutrition, Deakin University) *Developing a career of excellence between research and teaching*			
11:30 - 11:40 am	Sponsor talks: Qiagen, Abacus dx, John Morris Group, and MP Biomedicals			
11:40 - 11:50 am	Break			
11:50 - 12:50 pm	Session 1A: Oral Presentations Sponsor: CSL Pages 25-30	1. Mr Chen Wang 2. Ms Grace Osmond 3. Ms Natalie Tsiang 4. Ms Hannah Phillips 5. Ms Marina Yakou 6. Ms Pranita Shrestha	Session 1B: Oral Presentations Sponsor: CSL Pages 31-36	1. Ms Dima Abdu 2. Mr Sachintha Wijegunasekara 3. Ms Caitlin Vella 4. Ms Qing Lin 5. Mr Innocent Okpako 6. Ms Sandra Li
12:50 – 1:40 pm	Lunch / Poster Presentations			
1:40 - 2:40 pm	Session 2A: Oral Presentations Sponsor: Murdoch Children's Research Institute Pages 42-47	1. Mr Yan Kuan Chen 2. Mr Seyheeran Naidu 3. Ms Christina Ni 4. Ms Nanditha Hareesh 5. Ms Lily Anthony 6. Ms Maya Robertson	Session 2B: Oral Presentations Sponsor: Murdoch Children's Research Institute Pages 48-52	1. Ms Emily Whalen 2. Ms Kaitlin Clarke 3. Mr Amal Jayawardena 4. Mrs Dian Hasanah 5. Ms Jooa Kwon
2:40 – 2:50 pm	Break			
2:50 - 3:50 pm	Session 3A: Oral Presentations Sponsor: University of Melbourne Pages 53-58	1. Dr Katherine Colman 2. Mr Patrick Bajan 3. Dr Bernadette Jones-Freeman 4. Dr Pavitha Parathan 5. Dr Jennifer Devlin 6. Dr Saeedeh Darzi	Session 3B: Oral Presentations Sponsor: University of Melbourne Pages 59-64	1. Mrs Farzaneh Bazregari 2. Ms Cailin Diedericks 3. Ms Jaidah Fergus-Mackie 4. Ms Fahmida Islam 5. Ms Paula Volchek 6. Mr Tan Nguyen
3:50 - 4:20 pm	Afternoon Tea			
4:20 - 5:20 pm	Session 4A: Oral Presentations Sponsor: Burnet Institute Pages 65-69	1. Dr Ishmael Inocencio 2. Dr Nadia Mazarakis 3. Mrs Rachel Higgins 4. Dr Sohinee Sarkar 5. Dr Winnie Tan	Session 4B: Oral Presentations Sponsor: Burnet Institute Pages 70-75	1. Ms Erin Crellin 2. Ms Rachel Xu 3. Ms Anusuiya Bora 4. Ms Fenella McAndrew 5. Ms Brianna Kline
5:20 - 5:30 pm	Break			
5:30 - 6:00 pm	Awards announcement & Close			
6:00 – 7:00 pm	Social drinks and networking at the Hightail Bar			

A MESSAGE FROM THE ORGANISING COMMITTEE

Dear Delegates,

On behalf of the ASMR Victorian Committee, we look forward to welcoming you to the 2025 Annual ASMR Victorian Scientific Meeting.

Researchers from across Melbourne have submitted their abstracts, and we are pleased to provide a platform where Victoria's researchers can share their work and engage in meaningful discussions with their peers. Presentations from a breadth of disciplines will be showcased, and researchers at all stages of their career will be able to engage in interdisciplinary networking and relationship-building opportunities.

This symposium would not have been possible without the hard work and support from various people. We would like to extend our gratitude to the ASMR Victorian committee members who have dedicated much of their time in organising this symposium.

We would also like to thank the various sponsors and supporters of this year's ASMR Medical Research Week®. We encourage you to interact with generous sponsors and supporters who may be present on the day.

We wish all delegates an enjoyable and rewarding conference.

Organising Committee,
ASMR Victorian Scientific Meeting

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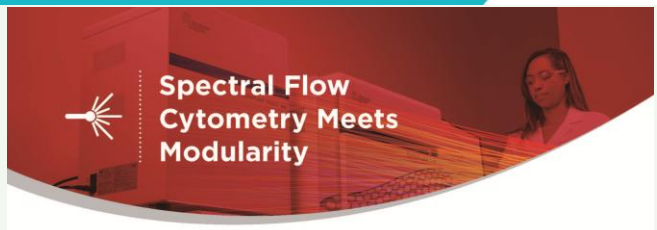

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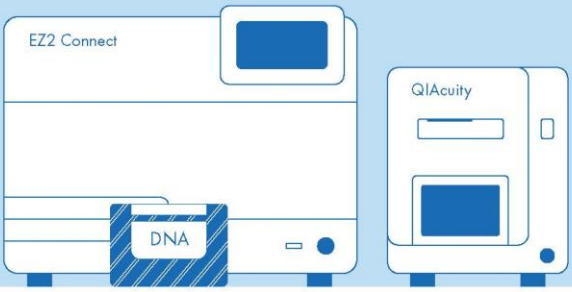

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DR SHANE HUNTINGTON OAM

ASMR, Chief Executive Officer
Science Communications Expert
Presenter at Einstein A Go-Go, RRR

Dr Shane Huntington is the inaugural Chief Executive Officer of the Australian Society for Medical Research. Until March 2025, he was the Chief Executive Officer of Little Big Steps; a charity helping kids with cancer. In this role he has acquired more than $3.5million to support kids with cancer in just 3 years.

Shane is also a speaker, trainer, and facilitator. He has been providing consulting services in communication and strategy for over 25 years. He is the host and producer of 3RRR's science radio program Einstein A Go Go. Over the last 31 years, he has interviewed thousands of scientists and explained hundreds of scientific concepts to the public. In 2020 he was awarded an Order of Australia in recognition of his science communication work. Shane is a prolific writer with articles on Medium.com read more than 100,000 times. He is the Founder and Director of the Innovation Group Pty Ltd, a scientific equipment supplier in Australia and New Zealand since 1999 and is a Senior Associate with consulting firm Outside Opinion.

Until January 2019 he was Deputy Director of the Melbourne Academic Centre for Health (MACH) which he established in 2011. Prior to his work in the Faculty of Medicine, he was Principal Strategy Adviser to the Vice-Chancellor of The University of Melbourne, Prof. Glyn Davis. From 2005 to 2008 he was the CEO and Founder of Quantum Communications Victoria within the School of Physics at the University of Melbourne. Quantum Communications Victoria was a $9.3Million Government funded centre which developed telecommunications security based on Quantum Physics and exported Australia's first quantum product. Shane's specialty was in Photonics and Imaging, and he has published more than 75 refereed journal papers during his 10 years in research. Shane was the Founder of the Telescopes in Schools Program, a Victorian based initiative designed to bring the wonders of Astronomy and education to low SES schools in Melbourne's Northern and Western suburbs and rural districts through the prevision of research-grade telescopes and support.

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DR GUNVEEN KAUR

SENIOR LECTURER, NUTRITIONAL SCIENCES
SCHOOL OF EXERCISE AND NUTRITION SCIENCES, INSTITUTE FOR PHYSICAL ACTIVITY AND NUTRITION (IPAN), DEAKIN UNIVERSITY

Dr Gunveen Kaur is a Senior Lecturer in Nutritional Sciences at Deakin University. Her teaching interests include physiology, nutrition and chronic diseases. Dr Kaur is also a member of Deakin's Institute for Physical Activity and Nutrition (IPAN) and is the Domain Co-ordinator of Biology of Health and Disease domain within IPAN. Her work focuses on the role of dietary fats—especially omega-3 fatty acids—in preventing chronic diseases like type 2 diabetes and cardiovascular conditions. Alongside a strong publication record, she is deeply committed to teaching and mentoring the next generation of nutrition scientists, blending cutting-edge research with a passion for student development.

CSL ORAL PRESENTATION SESSION A
(SESSION IA)

Session Chair: Ms Natasha Letunica

Time	Speaker	Presentation Title	Affiliation
11:50 – 12:00	Mr Chen Wang	Assessing Reliability and Optical Fogging Effects in a Web-Based Contrast Sensitivity Test: A Pilot Study	Monash University
12:00 – 12:10	Ms Grace Osmond	Developing a beta-synuclein specific regulatory T cell therapy for multiple sclerosis	Monash University
12:10 – 12:20	Ms Natalie Tsiang	Characterising The Role of Interferon Epsilon On T-regulatory Cell Function in Endometriosis Lesion Development	Hudson Institute of Medical Research
12:20 – 12:30	Ms Hannah Phillips	Assessing the Need for Post-operative ICU in Children with Complex Neuromuscular and Syndromic Scoliosis	The University of Melbourne
12:30 – 12:40	Dr Marina Yakou	Investigating Sex-Specific Microbial Networks to Boost Colorectal Cancer Immunity	Doherty Institute for Infection and Immunity
12:40 – 12:50	Ms Pranita Shrestha	Building Consensus on Artificial Intelligence (AI) Rules for Detecting Harmful Body Image and Eating Disorder Content: A Delphi Study	Monash University

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CSL ORAL PRESENTATION SESSION B
(SESSION IB)

Session Chair: Ms Ankita George

Time	Speaker	Presentation Title	Affiliation
11:50 – 12:00	Ms Dima Abdu	Determining the efficacy of delayed interleukin-1 receptor antagonist on diffuse white matter injury in preterm fetal sheep	Monash University/ Ritchie Centre
12:00 – 12:10	Mr Sachintha Wijegunasekara	The microbiome and genomic epidemiology of Buruli ulcers in Southeastern Australia	Deakin University
12:10 – 12:20	Ms Caitlin Vella	Inflammatory Endothelial Cell-derived Apoptotic Bodies Modulate Innate and Adaptive Immune Processes	La Trobe Institute for Molecular Science
12:20 – 12:30	Ms Qing Lin	Exploring targeted therapies for KIF1A-Associated Neurological Disorder	Murdoch Children's Research Institute
12:30 – 12:40	Mr Innocent Okpako	Engineering EphB1-CAR T cell Immunotherapy for Paediatric High-Grade Gliomas	Walter and Eliza Hall Institute
12:40 – 12:50	Ms Sandra Li	Using intra-arterially delivered genetically modified induced pluripotent stem cell-derived neural stem cells (iPSC-NSC) as therapy for ischemic stroke.	Monash University

POSTER SESSION
12:50 – 13:40

Speaker	Presentation Title	Affiliation
Ms Kathleen Whipp	Sleep Quality and Fatigue in Children with Charcot-Marie Tooth Disease (CMT)	Murdoch Children's Research Institute
Ms Naomi Drego	Development of Novel Agonists for the Gut Microbial Short-chain Fatty Acid Receptor FFAR2/GPR43	Monash University
Mr Ali Mulayim	Therapeutic potential of novel tumour target ROR1 in the treatment of advanced prostate cancer	The Peter MacCallum Cancer Centre
Ms Jessica Canning	Investigating germinal centre B cells following infection and vaccination in malaria	Burnet Institute
Mrs Deborah Hilton	A statistical tribute to the late Australian Professors and Doctors namely Hopper, Del Mar, Silagy, Speare, Krum and Gabel.	Deborah Hilton Statistics

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MURDOCH CHILDREN'S RESEARCH INSTITUTE ORAL PRESENTATION SESSION A
(SESSION 2A)

Session Chair: Ms Natasha Letunica

Time	Speaker	Presentation Title	Affiliation
13:40 – 13:50	Mr Yan Kuan Chen	Impact of Preoperative Anaemia on Transfusion and Outcomes in Paediatric Cardiac Surgery: A Retrospective Analysis at The Royal Children's Hospital	University of Melbourne
13:50 – 14:00	Mr Seyheeran Naidu	Two stage procedures for primary surgical management of cervical cancer: A harm minimisation approach	Monash University
14:00 – 14:10	Ms Christina Ni	The Benefits of Neonatal Resuscitation Video Review 1:1 Coaching, a Qualitative Analysis	Monash University
14:10 – 14:20	Ms Nanditha Hareesh	Triple Elimination of Mother-to-child Transmission of HIV, Hepatitis B and Syphilis in Asia-Pacific: A Systematic Review	Monash University
14:20 – 14:30	Ms Lily Anthony	Uncovering the immunobiology and biomechanics of Human Fascia Lata as an autologous graft for Pelvic Organ Prolapse treatment.	Hudson Institute of Medical Research
14:30 – 14:40	Ms Maya Robertson	Targeted lipid nanoparticle delivery of short interfering RNA to treat preeclampsia	University of Melbourne

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MURDOCH CHILDREN'S RESEARCH INSTITUTE ORAL PRESENTATION SESSION B
(SESSION 2B)

Session Chair: Dr Jonas Benjamim

Time	Speaker	Presentation Title	Affiliation
13:40 – 13:50	Ms Emily Whalen	Sulforaphane as a Future Therapeutic for Preeclampsia: The Next Steps in Clinical Translation	Monash University
13:50 – 14:00	Ms Kaitlin Clarke	Uncovering the Potential of Bacterial Autotransporters: A Journey from Pathogenesis to Therapeutic Applications	La Trobe University
14:00 – 14:10	Mr Amal Jayawardena	Decoding SNAPPs: Molecular Insights into Next-Generation Antibacterial Polymers	University of Melbourne
14:10 – 14:20	Mrs Dian Hasanah	All-trans Retinoic Acid in Lipid Nanoparticles (ATRA-LNP) as an Immunomodulator to Treat Glomerulonephritis	Monash University
14:20 – 14:30	Ms Jooa Kwon	Multi-omics Data Analytics Identifies Subtype-Specific Plasma Signatures in Juvenile Idiopathic Arthritis	Murdoch Children's Research Institute

UNIVERSITY OF MELBOURNE
ORAL PRESENTATION SESSION A
(SESSION 3A)

Session Chair: Dr Lewan Parker

Time	Speaker	Presentation Title	Affiliation
14:50 – 15:00	Dr Katherine Colman	Venetoclax-based therapy as a bridge to haematopoietic stem cell transplantation in relapsed or refractory paediatric acute leukaemia	Walter and Eliza Hall Institute
15:00 – 15:10	Mr Patrick Bajan	Development of novel lateral flow assays (LFA) for active syphilis and liver health screening	Burnet Institute
15:10 – 15:20	Dr Bernadette Jones-Freeman	The Impact of Gender-Affirming Hormone Therapy on Skeletal Muscle Physiology and Molecular Profiles	Monash University
15:20 – 15:30	Dr Pavitha Parathan	CGRP and RAMP1 promotes tumorigenesis in the human gastrointestinal tract	Olivia Newton-John Cancer Research Institute
15:30 – 15:40	Dr Jennifer Devlin	A CDK11-CDK9 regulatory axis controls the RNA polymerase II pausing-to-elongation transition	Peter MacCallum Cancer Centre
15:40 – 15:50	Dr Saeedeh Darzi	Foreign Body Response to Implanted Human Fascial Lata in a Mouse Model: Implications for Enhancing Pelvic Reconstructive Surgery	Hudson Institute of Medical Research

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UNIVERSITY OF MELBOURNE
ORAL PRESENTATION SESSION B
(SESSION 3B)

Session Chair: Ms Suelyn Van Den Helm

Time	Speaker	Presentation Title	Affiliation
14:50 – 15:00	Mrs Farzaneh Bazregari	Therapeutic targeting of MLKL with nanobodies to inhibit necroptosis	Walter and Eliza Hall Institute
15:00 – 15:10	Ms Cailin Diedericks	Optimising Lung Aeration using External Negative Pressures in Near-Term Rabbit Kittens.	Hudson Institute of Medical Research
15:10 – 15:20	Ms Jaidah Fergus-Mackie	Questioning the Causative Role of FANCA Variants in Premature Ovarian Insufficiency: A Multiomic Investigation	Murdoch Children's Research Institute
15:20 – 15:30	Ms Fahmida Islam	Can dual specific CAR NK cells enhance solid tumor targeting?	Monash University
15:30 – 15:40	Ms Paula Volchek	Investigating the Therapeutic Potential of Extracellular Vesicles for Fetal Brain Injury	Hudson institute of Medical Research
15:40 – 15:50	Mr Tan Nguyen	Economic evaluation of smoking cessation interventions to prevent periodontitis compared to standard care in Australia	Monash University

BURNET INSTITUTE
ORAL PRESENTATION SESSION A
(SESSION 4A)

Session Chair: Mr Patrick Banjan

Time	Speaker	Presentation Title	Affiliation
16:20 – 16:30	Dr Ishmael Inocencio	The Therapeutic Potential of Extracellular Vesicles: Unlocking the Next Frontier of Regenerative Medicine.	The Ritchie Centre/Hudson Institute of Medical Research
16:30 – 16:40	Dr Nadia Mazarakis	The persistence of immunogenicity and efficacy following a fourth dose of a bivalent mRNA or protein-based COVID-19 vaccine	Murdoch Children's Research Institute
16:40 – 16:50	Mrs Rachel Higgins	Effect of time-of-day vaccination on the antibody response to mRNA and protein COVID-19 vaccine in adults	Murdoch Children's Research Institute
16:50 – 17:00	Dr Sohinee Sarkar	A stem-cell based drug discovery pipeline for nontuberculous mycobacteria	Murdoch Children's Research Institute
17:00 – 17:10	Dr Winnie Tan	MORC2 is a phosphorylation-dependent DNA compaction machine	The Walter and Eliza Hall Institute of Medical Research

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BURNET INSTITUTE
ORAL PRESENTATION SESSION B
(SESSION 4B)

Session Chair: Dr Jonas Benjamim

Time	Speaker	Presentation Title	Affiliation
16:20 – 16:30	Ms Erin Crellin	Enhancing parents' experiences of paediatric genomic testing in usual outpatient care: insights from a multi-perspective qualitative study	University of Melbourne
16:30 – 16:40	Ms Rachel Xu	Harnessing CD19 CAR T Cell Therapy for Solid Tumour Treatment via a Novel Adaptor Approach	Peter MacCallum Cancer Centre
16:40 – 16:50	Ms Anusuiya Bora	On The Reproducibility and Reliability of Enrichment Analysis	Burnet Institute
16:50 – 17:00	Ms Fenella McAndrew	Evaluating the impact of COVID-19 vaccination strategies on infections and hospitalisations in Victoria in the context of non-seasonal epidemic waves	Burnet Institute
17:00 – 17:10	Ms Brianna Kline	The powerhouse of fertility: a novel mitochondrial cause identified in two unrelated patients diagnosed with premature ovarian insufficiency	Murdoch Children's Research Institute

Assessing Reliability and Optical Fogging Effects in a Web-Based Contrast Sensitivity Test: A Pilot Study

Chen Wang[1,2], Marc Sarossy[1,2]

1. Monash University, Faculty of Medicine, Nursing and Health Sciences, Clayton, Melbourne, Victoria, Australia
2. Centre for Eye Research Australia, University of Melbourne, Melbourne, Victoria, Australia

Introduction: Contrast sensitivity (CS) is an important visual function often omitted from routine assessments due to the need for costly and specialised equipment. CS evaluates the ability to detect objects across a range of contrast levels and spatial frequencies, making it particularly valuable in identifying functional vision impairments for populations with early-stage ocular disease, neurological conditions or age-related vision decline. Despite its clinical importance, CS testing remains underutilised in ophthalmology services in Australia.

Objective: This pilot study evaluates the test-retest reliability and optical fogging effects of a free, open-source web-based CS test developed using R Shiny.

Methods and Results: Participants (n = 40 eyes) completed a CS function test across four conditions: Baseline, Retest (15 minutes post-baseline), Optical Fogging (+3.00D reading glasses to simulate blur), and Retest. CS was assessed across a range of optotype sizes (6/6 to 6/60) and contrast levels at a 3.1 m distance from the laptop screen. Test-retest reliability was high, with ICCs of 0.974 (95% CI: 0.941 - 0.988) for normal vision and 0.963 (95% CI: 0.916 - 0.983) for fogging. Optical fogging disproportionately reduced sensitivity for smaller optotypes (e.g 6/6), consistent with existing literature showing greater blur effects at higher spatial frequencies. The high 6/6 threshold may suggest display-related limitations. Mean testing time was 9.2 $\pm$ 1.5 minutes across conditions. Participants rated the ease of use of the web-based CS test with a median score of 5 (IQR: 4 - 5) on a 5-point Likert scale (1 = Very difficult, 5 = Very easy).

Conclusions: The open-source test is validated with high test-retest reliability and shows plausible results, showing promise to be an accessible alternative to traditional contrast sensitivity testing. The next steps include validation against commercially available CS function tests and enrolment of clinical cohorts.

Developing a beta-synuclein specific regulatory T cell therapy for multiple sclerosis

Grace Osmond[1], Joshua Ooi[1], Yi Tian Ting[1], Nevin John[1,2]

1. Department of Medicine, School of Clinical Sciences, Monash University, Melbourne, Victoria, Australia
2. Department of Neurology, Monash Health Clayton, Melbourne, Victoria, Australia

Introduction: Grey matter damage and progression independent of relapse activity are now known to affect many MS patients - even those not diagnosed with progressive subtypes - but are poorly treated by available therapies. Engineered T cell receptor-regulatory T cell (TCR-Treg) therapies are a cutting-edge strategy to ameliorate autoimmune diseases, using an antigen-specific TCR to localise the anti-inflammatory, pro-neural healing effects of Tregs. One such disease-relevant antigen is beta-synuclein, a grey matter protein that is released from neurons and provokes an immune response in some progressive MS patients.

Objective: This project aims to select immunogenic beta-synuclein peptides to begin development of a TCR-Treg therapy targeting beta-synuclein, and to investigate the molecular basis of beta-synuclein antigen presentation on HLA DRB1*15:01 (DR15).

Methods and Results: In silico methods were used to identify peptides that may be presented on HLA DR15 and to begin investigating the structural basis of this presentation. HLA DR15 was produced in mammalian cells and successfully peptide exchanged to present two beta-synuclein peptides. Coculture of dendritic cells and T cells from a healthy DR15+ donor with flow cytometry cell lineage tracing tested the immunogenicity of selected beta-synuclein peptides, which identified several immunogenic peptides. Colocalisation of stained HLA-peptide with activated T cells confirmed antigen specific T cell presence. Future experiments will include single-cell RNA sequencing to find the TCRs used by antigen-specific T cells, and X-ray crystallography to solve the structure of HLA-DR15 presenting beta-synuclein peptides.

Conclusions: Immunogenic antigens within beta-synuclein have been identified and antigen specific T cell presence confirmed within healthy DR15+ donors. Protein studies also indicated that HLA-DR15 can present several beta-synuclein peptides. This research ultimately aims to contribute to explaining HLA-DR15's link to autoimmune susceptibility and develop a TCR-Treg therapy that could improve quality and length of life for MS patients.

Characterising The Role of Interferon Epsilon On T-regulatory Cell Function In Endometriosis Lesion Development

Natalie Tsiang[1,2], Claire Davison[1,2], Thomas Tapmeier[1,2,3], Fiona Cousins[1,2]

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Introduction: Endometriosis affects approximately 1 in 7 reproductive aged women and is a major cause of chronic pelvic pain and infertility. Whilst the pathogenesis of endometriosis is poorly understood, it is hypothesised that a dysregulated immune response contributes to lesion formation and progression. Interferon epsilon (IFNε), a type I interferon, is an immunomodulatory and anti-viral cytokine that is constitutively expressed by epithelial cells and immune cells in the female reproductive tract. IFNε has known protective functions against bacterial and viral infections, as well as cancers. Given its immunomodulatory properties, we have investigated a role for IFNε in regulating T cell function in endometriosis pathogenesis.

Objective: An endometriosis murine model was used to investigate T-regulatory cell function between wild-type, *Ifnε*$^{-/-}$, and *Ifnar1*$^{-/-}$ mice. Donor mice were ovariectomised and received hormone treatment to mimic human-like menstruation. Menstrual fragments were collected, minced and intraperitoneally inserted into recipient mice to induce artificial endometriosis. Endometriotic lesions were allowed to develop for 3 weeks.

Methods and Results: Endometriotic lesions harvested from recipient mice were analysed by immunofluorescence and quantified using HALO AI. A Kruskal-Wallis and Dunn's multiple comparisons test was performed. Co-localised (Foxp3+CD4+) cells showed increasing trends in *Ifnε*$^{-/-}$ mice compared to controls, although not statistically significant ($p>0.05$).

Conclusions: Endogenous IFNε may play a protective role by limiting T-regulatory cell infiltration, which could otherwise enhance inflammation. Although not statistically significant, lesion morphology and location may influence their development, offering qualitative insights into their appearance despite the absence of clear quantitative trends or differences. Future research may explore additional leukocyte markers in both lesions and peritoneal fluid involved in endometriosis-related inflammation.

Assessing the Need for Post-operative ICU in Children with Complex Neuromuscular and Syndromic Scoliosis

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Introduction: Neuromuscular scoliosis refers to spinal deformity in patients with an underlying neurological diagnosis or syndrome. These children are often medically complex, associated with higher perioperative risks. A multidisciplinary team (MDT) meeting was established to assess these patients before scoliosis surgery, with a key goal of determining the need for postoperative intensive care unit (ICU) admission.

Objective: The study aims to (1) determine the proportion of patients reviewed by the MDT meeting who proceed to surgery, and (2) evaluate compliance with MDT meeting recommendations.

Methods and Results: A retrospective review was conducted on all patients who underwent an MDT meeting at a single paediatric institution between 2019-2024. Preoperative, operative, postoperative, and complications data were collected and summarised descriptively. A total of 173 patients (53% female) were reviewed. Diagnoses include Cerebral palsy (63%), other (34%, e.g. Marfan's and Prader-Willi). Rett syndrome (4%) and Muscular dystrophy (1%); 73% were non-ambulant. In total, 142 (82%) were deemed suitable for surgery, 31 did not proceed (3 deaths, 9 patient/parent declined,19 deemed unfit by MDT meeting). Post-operatively, 9% (16/173) had an unplanned ICU admission. The MDT recommended ICU care for 51 patients post-surgery; three were decided not to need ICU after a pre-operative anaesthetics review (PARC). Nine patients initially not recommended for ICU by the MDT were sent to ICU based on PARC. Among 79 patients where both meetings agreed ICU wasn't needed, 13 (16%) had unplanned ICU admissions. Of 39 patients with unclear MDT recommendations, 3 (8%) required unplanned ICU admissions.

Conclusions: The MDT meeting helps determine post-operative ICU needs. This project lays the groundwork for a scoring tool to guide ICU decisions in high-risk patients.

Investigating Sex-Specific Microbial Networks to Boost Colorectal Cancer Immunity

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Introduction: Colorectal cancer (CRC) is a global health burden, responsible for over 500,000 deaths annually. Despite the promise of immunotherapy in many malignancies, clinical efficacy in CRC remains modest, largely due to gaps in our understanding of how anti-tumour immunity is regulated within the colonic environment. Tissue-resident memory T (T_{RM}) cells are critical for local tumour surveillance, yet the signals that shape their function in the colon, particularly the interaction between sex hormones and the gut microbiota, are poorly defined. Compounding this issue, standard preclinical models rely on specific-pathogen-free (SPF) mice with low microbial diversity, limiting translational relevance.

Objective: We aimed to define how microbial diversity and sex-specific factors regulate colonic T_{RM} cell populations, to better understand how host physiology influences anti-tumour immunity in CRC.

Methods and Results: We generated microbially diverse mice via faecal microbiota transfer from wild mice into genetically identical hosts. Using this human-relevant system, we observed striking sex-specific disparities in colonic T_{RM} cells whereby males showed a significant increase in colonic T_{RM} abundance compared to females. These differences were absent in SPF mice, indicating that microbial diversity is required for sex-biased immune regulation in the colon. These findings suggest that the microbiota modulates T_{RM} cell development in a sex-dependent manner, with implications for tumour immunity and therapeutic response.

Conclusions: This study identifies a novel interaction between the microbiota and host sex in shaping tissue-resident immunity within the colon. By uncovering the sex-specific, microbiome-driven regulation of T_{RM} cells, our work lays the foundation for personalized immunotherapeutic strategies in CRC that account for host-intrinsic factors such as sex and microbial composition.

Building Consensus on Artificial Intelligence (AI) Rules for Detecting Harmful Body Image and Eating Disorder Content: A Delphi Study

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Introduction: Artificial Intelligence (AI) tools are increasingly used to moderate harmful content on social media, but they often misclassify nuanced posts related to body image and eating disorders (ED). Harmful content may be overlooked, while recovery-oriented posts are wrongly flagged. There is an urgent need to establish context-aware, ethically grounded AI moderation rules informed by domain-specific expertise, particularly for individuals at-risk or experiencing ED.

Objective: This study aimed to develop consensus-based rules to guide the design of AI systems for detecting harmful social media content related to body image and ED, by incorporating the perspectives of clinical experts, researchers, and individuals with lived experience of ED.

Methods and Results: A two-round Delphi study was conducted with experts by profession (clinicians, researchers) and experts by lived experience (individuals with past ED history). Prior to Delphi rounds, a six-member steering committee, representing clinical, research, and lived experience perspectives, guided the refinement of AI harm detection rules. These rules were initially developed through interviews with n=12 experts by profession and focus groups with n=18 experts by lived experience. In Round 1, participants rated each rules using a 5-point Likert scale. Rules with <80% agreement or substantive feedback were revised and re-evaluated in Round 2 after participants reviewed the group responses. The final result includes expert-informed rules across eight categories: General content, Drugs, supplements and surgeries, Beauty products, Filters and edited images, Food and nutrition, Exercise, Body measurement and comparisons, and ED recovery. Participants highlighted the importance of distinguishing harmful content from recovery narratives, considering intent and context and balancing freedom of expression with user protection.

Conclusions: This study offers a foundational set of consensus-based rules for context-aware moderation of body image and ED-related content using AI. These rules will inform the development of nuanced moderation tools powered by LLM in our future research.

Determining the efficacy of delayed interleukin-1 receptor antagonist on diffuse white matter injury in preterm fetal sheep

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Introduction: During perinatal infection/inflammation, induction of the pro-inflammatory effector cytokine IL-1β is associated with white matter injury and poor neurodevelopmental outcomes. Preclinical studies show that systemic administration of interleukin-1 receptor antagonist (IL-1Ra) before or immediately after inflammation-induced brain injury is neuroprotective; however, our understanding of the therapeutic window of IL-1Ra is limited.

Objective: In this study, we investigated whether delayed administration of IL-1Ra, 24 hours after induction of LPS-induced inflammation, would reduce markers of white matter injury in preterm fetal sheep.

Methods and Results: Chronically instrumented preterm fetal sheep (102 days gestational age) were randomly assigned to received saline infusions (control, n=9), repeated LPS infusions (0 h = 100 ng, 24 h = 200 ng, 48 h = 400 ng, n=8) or repeated LPS + IL-1Ra infusions (10 mg/kg infused over 2 minutes) starting 24 h after each LPS infusion (n= 8). Sheep were killed 12 days later for assessment of CSF inflammation and brain pathology. LPS-exposure increased CSF cytokines (IL-1β and IL-6; $P<0.05$, LPS + vehicle vs. control). LPS-exposure reduced numbers of total oligodendrocytes (Olig-2+cells) and increased numbers of microglia (Iba-1+ cells) and A1 (reactive) astrocytes (STAT3+/GFAP+ cells) within the intragyral and periventricular white matter tracts ($P<0.05$, LPS+vehicle vs. control). Delayed IL-1Ra infusions reduced CSF IL-1β and IL-6 concentrations, improved oligodendrocyte survival and reduced gliosis in the periventricular and intragyral white matter tracts ($P<0.05$, LPS+IL-1Ra vs. LPS+vehicle).

Conclusion: Delayed administration of IL-1Ra, 24 h after LPS-induced inflammation, reduces markers of white matter inflammation and injury in preterm fetal sheep.

The microbiome and genomic epidemiology of Buruli ulcers in Southeastern Australia

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Introduction: Buruli ulcer (BU), caused by *Mycobacterium ulcerans* (MU), is a neglected tropical disease that leads to severe skin infections, which can result in disability or amputation if left untreated. Despite Australia's temperate climate, BU incidence is increasing in the southeastern region.

Objective: This study investigated the microbiome and genomic epidemiology of BU in collaboration with the University Hospital Geelong.

Methods and Results: Metagenomic analysis of 30 samples identified 70 species, notably *Cutibacterium*, *Corynebacterium*, and *Staphylococcus* in pre-treatment samples in addition to MU, and *Malassezia restricta* during treatment. Post-treatment microbiomes were dominated by skin commensals, including *Cutibacterium modestum* and *Staphylococcus epidermidis*. Severe ulcers in pre-treatment samples exhibited higher alpha diversity, whereas beta diversity analyses clearly distinguished between the pre-treatment and treatment phases. Drug resistance profiling revealed resistance to multiple antibiotics but not to those currently recommended for BU treatment. Genomic epidemiology analysis, conducted through the direct sequencing of MU from 108 clinical swabs across the Mornington Peninsula, Bellarine Peninsula, and Geelong, demonstrated that the isolates aligned with the established MU population structure in southeastern Australia. Isolates from Geelong closely matched those from the Bellarine Peninsula, indicating significant genomic similarity.

Conclusions: This research highlights the polymicrobial complexity of BU, confirms the genomic structure of MU in southeastern Australia and demonstrates that direct sequencing is a faster alternative to traditional culture-based MU analysis.

Inflammatory Endothelial Cell-derived Apoptotic Bodies Modulate Innate and Adaptive Immune Processes

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Introduction: The death of endothelial cells (EC) within a highly inflammatory environment is a hallmark of chronic inflammatory vascular conditions, including atherosclerosis. During disease pathogenesis, extensive EC death triggers plaque growth and increases the risk of thrombosis. Apoptotic bodies (ApoBDs) are small (~1-5mm) membrane bound extra-cellular vesicles generated exclusively through the apoptotic cell disassembly pathway that are widely regarded as mediators of intercellular communication. However, the role of EC-derived ApoBDs in intercellular communication within an inflammatory environment, is poorly characterized.

Objective: To characterise the functional properties of EC-derived ApoBDs, identifying their capacity for intercellular communication and modulating immune processes.

Methods and Results: Through an *in vitro* model of vascular inflammation, Human Umbilical Vein ECs (HUVECs) were pre-treated +/- TNF-a for 24h followed by induction of apoptosis with a BH3-mimetic cocktail and ApoBDs were isolated via differential centrifugation. Our proteomics analysis of ApoBDs generated with TNF-a treatment (iApoBDs) identified enrichment of inflammatory cytokines/chemokines, adhesion molecules and antigen presentation machinery. The upregulation of key immunomodulatory proteins in iApoBDs were validated using cytometric bead arrays, chemotaxis and engulfment assays. iApoBDs were further shown to have functional impacts: releasing cytokines over time, correlating with membrane lysis and promoting monocyte chemotaxis; increasing efferocytosis by macrophages in an ICAM-1 dependent manner; and eliciting a greater IFN-g response from human patient T cells co-cultured with iApoBD from antigen pulsed ECs. This altered phenotype translated *in vivo* where there was increased engulfment of iApoBDs by resident macrophages when administered intraperitoneally.

Conclusions: These findings demonstrate a novel mode of intercellular communication by apoptotic ECs during inflammation. The ability of EC-derived ApoBDs to propagate inflammatory signalling may serve as a therapeutic target in the development of treatments for vascular inflammatory diseases.

Exploring targeted therapies for *KIF1A*-Associated Neurological Disorder

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Introduction: Kinesin-3 Family Member 1A (KIF1A) is a motor protein specifically expressed in the neurons, responsible for transporting synaptic vesicles, dense core vesicles and lysosomes carrying important cargo proteins for healthy synaptic function. Genetic variants in the *KIF1A* gene cause rare, severe, progressive neurodegenerative conditions, collectively known as the KIF1A-associated neurological disorder (KAND). More than 550 people have been genetically diagnosed with KAND, but no cure exists.

Objective: In this project, we aim to explore the potential of small molecule drug screening and/or gene replacement therapy as therapeutic opportunities for KAND and test drug candidates on cortical neurons differentiated from patient-derived induced pluripotent stem cells (iPSCs).

Methods and Results: KAND individual iPSCs along with their isogenic control lines will be differentiated into the cortical neurons. Cellular and molecular phenotypes of the differentiated neurons will be evaluated through determining the effect of KIF1A deficits on i) neuron development and survival, ii) development of healthy, long, branched axons, and ii) endogenous KIF1A protein level and function in neuronal environments. The effect of small molecule candidates and gene replacement therapy will be determined by evaluating for i) correction of any cellular phenotypes identified and ii) improved KIF1A trafficking using fluorescently labelled KIF1A cargo live-cell confocal imaging. Our anticipated outcomes involve successful full or partial restore of cellular and molecular phenotypes.

Conclusions: By testing the efficacy of small molecules and gene replacement therapy on physically relevant patient-derived model system, our work lays the foundation for the future *in vivo* validation and clinical trials, thereby advancing the development of potential therapeutics for KAND.

Engineering EphB1-CAR T cell Immunotherapy for Paediatric High-Grade Gliomas

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Introduction: Paediatric high-grade gliomas (pHGGs) are a group of aggressive brain tumours with a median survival of only 11–18 months. Chimeric antigen receptor (CAR) T cell therapy has shown early potential in targeting these tumours; however, its effectiveness is limited by antigen heterogeneity, highlighting the need for novel therapeutic targets. EphB1 was identified as a promising candidate due to its high expression in fresh primary pHGG samples and cell lines following cell surface proteomic analysis.

Objective: To develop novel EphB1-targeting CAR T cells as a potential immunotherapy for pHGGs.

Methods and Results: Twelve antibody clones reactive to recombinant EphB1 were generated using a human phage display screen, and ten were successfully converted into single-chain variable fragments (scFvs) with an 8-fold range in binding affinity. These scFvs were assembled into 432 second-generation CAR constructs in different orientations and combined with various spacer lengths, transmembrane domains (TMDs), and signalling tail variants. The constructs were lentivirally transduced into primary human T cells and to identify the construct with the best functional phenotypes, the T cells (carrying the library), pooled CAR T cells, were co-cultured with EphB1-expressing paediatric high-grade glioma (pHGG) cells. CAR T cell activation was assessed by CD137 expression using flow cytometry. The genomic DNA of activated and non-activated T cells populations was extracted, and Oxford Nanopore sequencing was used to profile activated CAR constructs, revealing that activation was mainly influenced by the binding affinity of the scFv clone and the nature of signalling tail variants, while spacers, TMDs, and scFv orientation exerted less influence.

Conclusions: These findings demonstrate the feasibility of engineering EphB1-targeting CAR T cells through high throughput library screening. Ongoing work aims to further characterise and validate lead CAR constructs as potential candidates for clinical translation in pHGGs immunotherapy.

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

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Introduction: Stroke is a leading cause of death and permanent neurological disabilities worldwide. Existing gold standard therapies are unable to achieve neuroregeneration and do not have neuroprotective properties. Stem cell therapy, especially neural stem cells (NSCs) are promising as they can target underlying pathophysiology and facilitate neuroregeneration. Preclinical studies with promising results have mostly utilised intracerebral transplantation to overcome NSC's limited homing abilities. However, such invasive transplantation methods complicate clinical translation. Therefore, intra-arterial delivery poses as a promising minimally invasive route which can integrate well with existing clinical workflow. Moreover, key NSC limitations can be overcome through genetic engineering.

Objective: To investigate whether intra-arterially delivered genetically modified NSCs could be effective and result in better treatment outcomes for ischaemic stroke.

Methods and Results: We have successfully generated induced pluripotent stem cell-derived NSCs expressing appropriate NSC specific markers; Nestin, PAX6 and SOX1, and have lost the pluripotency marker OCT-4. Our NSCs will be genetically modified via lentivirus transduction to overexpress factors improving their homing (CCR5) and survival abilities (bFGF). A neonatal photothrombotic stroke rat model will be used to test our modified NSCs against naïve NSCs and a vehicle control group. Cells will be administered intra-arterially at 4-hours post-stroke. Efficacy will be assessed through histological and molecular studies of the brain and behavioural tests of the animals.

Conclusions: Currently, regenerative and neuroprotective therapies for stroke do not exist. We hope our results will show that intra-arterial delivery of genetically modified NSCs has promising potential in becoming adjunct therapy for ischaemic stroke.

POSTER SESSION

Sleep Quality and Fatigue in Children with Charcot-Marie Tooth Disease (CMT)

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Introduction: Charcot-Marie Tooth disease (CMT) describes a group of heterogeneous inherited peripheral neuropathies, affecting approximately 1 in 2,500 children. While its primary motor and sensory symptoms are well understood, secondary symptoms including fatigue and sleep disorders are only beginning to emerge as significant comorbidities in the adult literature and remain under-investigated in children. This study aims to bridge that gap by investigating sleep quality and fatigue in Australian children with CMT.

Methods: We aim to recruit 20 children (=<18 years) with CMT attending the neuromuscular clinic at the Royal Children's Hospital, Melbourne. Depending on age, participants and their parent/guardian will complete up to 8 validated questionnaires assessing sleep, fatigue, physical activity, pain, mood and quality of life. Each child will also undergo an at-home overnight polysomnography (PSG) to assess for sleep disorders.

Results: Recruitment commenced in May 2025 and is ongoing (currently n=7; mean age 15.7 years). Early findings indicate that all participants report elevated fatigue levels, with a mean PedsQL-MFS score of 43.2/100. Sleep disturbance is also prevalent, with a mean SDSC score of 55 (scores >39 are consistent with sleep disturbance). Five PSGs have been completed to date.

Conclusion: Although recruitment is ongoing, we anticipate that fatigue and sleep disorders will be prevalent and multifactorial, as seen in adult cohorts. In the absence of curative treatments for CMT, early identification and management of modifiable factors such as sleep may offer an opportunity to improve quality of life in affected children.

Development of Novel Agonists for the Gut Microbial Short-chain Fatty Acid Receptor FFAR2/GPR43

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Introduction: Free fatty acid receptor 2 (FFAR2, formerly GPR43) is a G protein-coupled receptor (GPCR) which is activated by short-chain fatty acids (SCFAs), generated via the gut microbial fermentation of dietary fibre. Research has implicated FFAR2 as an important modulator of cardiovascular health, with its absence increasing the risk of high blood pressure in experimental models and humans. The paucity of high-potency ligands has limited the therapeutic targeting of FFAR2 but may provide a novel avenue to treat cardiovascular and inflammatory diseases.

Objective: To identify novel, selective small-molecule agonists for FFAR2 using a semi-high-throughput screening approach.

Methods and Results: An in-silico screen was conducted using our in-house library of small molecule compounds to identify those with a high potential to bind to FFAR2. A targeted library of the top 113 compounds was ordered and screened *in vitro* to identify potential FFAR2 ligands. These compounds were tested at a single point concentration of 50 µM in CHO cells overexpressing FFAR2. Those significantly inhibiting cAMP accumulation, an indicator of FFAR2 activation, were considered preliminary hits. Those preliminary hits are being further investigated and validated through dose-response assays to determine potency (EC_{50} values).

Conclusions: This study has developed a robust experimental pipeline for identifying FFAR2 agonists. The potential identification of novel ligands contributes to our understanding of FFAR2 pharmacology and supports the early-stage development of therapeutic strategies for cardiovascular and inflammatory diseases.

Therapeutic potential of novel tumour target ROR1 in the treatment of advanced prostate cancer

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Introduction: Receptor tyrosine kinase-like orphan receptor 1 (ROR1) has emerged as a promising therapeutic target in various cancers, including advanced prostate cancer (PCa), due to its tumour-restricted expression and role in oncogenic signalling. Yet, no effective ROR1-targeted therapies have been established, and the precise role of ROR1 in cancer emergence and progression remains poorly understood. One key unknown is how the relationship between ROR1 and sister protein, ROR2—typically absent in PCa and a proposed tumour-suppressor—-influences PCa progression, and whether this relationship can be exploited for therapeutic purposes.

Objective: To investigate the role of ROR1 in the regulation of ROR2 expression and identify a candidate mechanism through which to develop ROR1-targeted treatment strategies for PCa treatment.

Methods and Results: Human PCa cell, PC3, was treated with type I interferon (IFN-b), a proposed regulator of ROR1 expression, to assess (i) alterations in ROR1 and ROR2 protein expression by flow cytometry and (ii) corresponding transcriptional changes by real-time (RT)-qPCR. Concurrently, C4-2 cells were engineered to overexpress ROR1 with matching ROR1-negative controls. Modified C4-2 cells were treated with enzalutamide, a non-steroidal anti-androgen proposed to induce ROR2, to test if constitutive ROR1 expression prevents ROR2 upregulation at the protein and transcriptional level using flow cytometry and RT-qPCR. PC3 cells treated with IFN-b for 5 days exhibited a time-dependent decrease in ROR1 protein and mRNA expression, accompanied by a significant increase in ROR2. Conversely, the upregulation of ROR1 was sufficient to block treatment-induced ROR2 expression at 10 days post-enzalutamide treatment.

Conclusions: These novel results reveal an inverse relationship between ROR1 and ROR2 in PCa, suggesting high ROR1 may suppress ROR2 expression. This knowledge may be exploited therapeutically, whereby blocking ROR1 expression with a drug, may limit its tumourigenic signalling, while promoting ROR2 expression along with its tumour-suppressive effects.

Investigating germinal centre B cells following infection and vaccination.

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Introduction: Malaria remains a global health priority and in 2023, the WHO reported nearly 600,000 deaths, the majority of which were children under the age of five. Protection from malaria is mediated by antibodies that can be induced by infection or vaccination. Infection-induced antibodies are slow to develop in previously exposed individuals, and responses to vaccination are less robust, with booster doses failing to provide adequate protection.

Protective antibodies are dependent on the activation of B cells within germinal centres (GCs). To date, no studies have characterised malaria specific B cells within GCs nor following vaccination in children.

Objective: Here we used tonsil cells from Ugandan children with prior malaria exposure or asymptomatic infection to investigate the phenotype of malaria-specific B cells within the GCs.

Methods and Results: Samples comprise of tonsils and matched PBMCs from Ugandan children aged 2-11 (n=103, 33% infected at collection). The control malaria-naïve cohort comprise of tonsils from age matched Australian children.

Expression of malaria antigens CSP, MSP1, AMA1, MSP2 was conducted in Expi293F mammalian cells with BirA enzyme. *In vivo* biotinylation allowed for site-specific tagging with fluorescent streptavidins to form tetramers. Tetramers bind to antigen specific B cells with high affinity and identified using high-dimensional spectral flow cytometry.

Conclusions: We have successfully optimised a 29-marker spectral flow cytometry panel including five unique malaria tetramer markers in both PBMCs and complex human tonsil tissue. Preliminary results indicate that asymptomatic malaria infection may disrupt B cell responses to unrelated pathogens such as SARS-CoV-2. That is, individuals with asymptomatic malaria infection at the time of tonsillectomy have reduced SARS-CoV-2-specific B cells compared to both uninfected individuals and naïve individuals. This knowledge may inform the impact of prior infections on vaccination responses and provide insights into antigen inclusion in future malaria vaccines.

A statistical tribute to the late Australian Professors and Doctors namely Hopper, Del Mar, Silagy, Speare, Krum and Gabel.

Deborah Hilton[1,2,3].

1. Deborah Hilton Statistics Online https://sites.google.com/site/deborahhilton/, Melbourne, Vic, Australia.
2. ResearchGate https://www.researchgate.net/profile/Deborah-Hilton. Melbourne, Vic, Australia.
3. Roy Morgan Research https://www.roymorgan.com/ Melbourne, Vic, Australia.

Introduction: Six late Australian male statistical research leaders who have strived to comprehend, decipher, analyse and report on important, relevant and significant research findings are worthy of this tribute.

Objective: Statisticians, researchers and health professionals are not immune to disease, illness, accidents and/or misfortune. This tribute collates statistics and presents their research work highlights.

Methods and Results: ResearchGate and worksites located the author's manuscripts, book chapters and citations generating statistical summaries. A Medline publication search of scientists' life expectancy ["Life Expectancy"[Mesh] AND researchers] enabled a life course comparison. Six researchers had approximately 2795 articles [sourced from ResearchGate [RG] profiles or RG name identification even though no direct profile, hence as affiliated with Melbourne, South Australia or Monash University websites. Uncertainty over research work type [unspecified retrieval; 889 Henry Krum]. Three researchers [CDM, HK, JH] wrote 10 books and 71 book chapters. Six researchers had 186,618 citations [minimum 149; maximum 56,015]. The mean age of death (MAD) and longevity for 54,256 men professionally involved in research work: assigned to; physics, chemistry, medicine and biology, mathematics, economics, and humanities was published [Russian/USSR scientist's data;1724-2013]. The minimum MAD for mathematicians;72.1y, maximum MAD for economic scientists was 74.6y. MAD was 3.5y higher for scientists involved in university teaching. Increases in life expectancy and longevity were evident in males involved in intense scientific work. I worked on projects with four researchers in the tribute [employed, invited guest monthly speaker, contract work] or attended a workshop or I utilised their research on general practice literature searching, twin registry, coenzyme Q10, slacklining and head lice. The average age of passing of these research leaders was 62 yrs [min 41; max 74].

Conclusions: These six late Australian statistical research leaders will have long continued Australian and overseas science and research impact as a result of incredible publication records.

MURDOCH CHILDREN'S RESEARCH INSTITUTE

ORAL PRESENTATION SESSION A

Impact of Preoperative Anaemia on Transfusion and Outcomes in Paediatric Cardiac Surgery: A Retrospective Analysis at The Royal Children's Hospital

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Introduction: Haemoglobin is critical for oxygen transport, and adequate levels are essential to meet metabolic demand. Anaemia, defined by low haemoglobin relative to age-specific thresholds, is common in children and may influence outcomes in cardiac surgery. In paediatric patients undergoing cardiac surgery with cardiopulmonary bypass (CPB), haemodilution and intraoperative blood loss are managed with packed red blood cell transfusions. While transfusions can be lifesaving, they also carry risks including infection, immune reactions, and other complications. Children with congenital heart disease may have a higher prevalence of anaemia due to feeding difficulties, renal and heart failure. Accurate assessment of anaemia in this population is further complicated by a lack of standard definitions in cyanotic patients and age-related haemoglobin changes in infancy. In adults and paediatric non-cardiac surgical cohorts, preoperative anaemia has been linked to higher transfusion rates and poorer outcomes, but these relationships are less well defined in the paediatric cardiac population, marking a growing need to understand the implications of anaemia in this setting.

Objective: To investigate the prevalence of preoperative anaemia and its association with transfusions and postoperative outcomes in paediatric patients undergoing cardiac surgery with CPB at The Royal Children's Hospital, Melbourne.

Methods and Results: We retrospectively analysed 3,198 patients <18 years who underwent cardiac surgery with CPB (2016–2025). Anaemia was defined using age-specific institutional thresholds. Anaemia was present in 23% of patients. In neonates and infants, anaemia did not increase transfusion incidence but was associated with greater volumes and donor exposures. In older children and adolescents, anaemia was linked to increased transfusions, longer hospital stays, ventilation duration, and higher mortality.

Conclusions: Preoperative anaemia is prevalent and associated with increased transfusions and poorer outcomes in paediatric cardiac surgery, highlighting the potential value of targeted preoperative optimisation in this population and warrant further investigation in larger, multicentre cohorts.

Two stage procedures for primary surgical management of cervical cancer: A harm minimisation approach

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Introduction: Morbidity amongst cervical cancer patients remains high, largely due to complications associated with their treatment.

Objective: (1) To evaluate the clinical and oncological outcomes of single stage versus two stage surgical approaches in the management of early-stage cervical cancer; (2) To determine the false-negative rate and negative predictive value (NPV) of positron emission tomography (PET) and magnetic resonance imaging (MRI) in preoperative nodal staging.

Methods and Results: This was a retrospective cohort study of patients undergoing surgical management for early-stage cervical cancer (FIGO stage IA1–IIB) at Monash Health over a 9-year period (2016–2024). Comparative analyses were conducted on diagnostic imaging performance (PET/MRI), treatment pathways, and oncological outcomes between single stage and two stage surgical cohorts. PET and MRI were performed in 113 and 97 patients respectively, with 96 undergoing both. PET demonstrated limited discriminatory value, with no significant difference in uptake patterns between node-negative and node-positive patients (p=0.34) and an NPV of 83.7%. MRI showed modestly improved performance, with significantly fewer node-positive patients exhibiting negative MRI findings (65.0% vs 82.7%, p=0.04) and an NPV of 86.2%. Patients undergoing a single stage procedure were significantly more likely to require adjuvant radiotherapy (30.8% vs 15.1%, p=0.046) and demonstrated a trend towards worse overall outcomes including higher rates of composite adverse events (61.5% vs 45.3%, p=0.078) and late complications (p=0.03).

Conclusions: These findings highlight the limited accuracy of PET and MRI in preoperative nodal assessment for early-stage cervical cancer, underscoring the risk of false-negative imaging and its implications for treatment planning. The observed trends suggest a potential oncological benefit to a two-stage surgical approach, particularly in reducing adjuvant treatment rates and late morbidity. Larger, prospective studies are needed to validate these findings and evaluate the cost-effectiveness and broader clinical impact of staged surgical strategies in cervical cancer care.

The Benefits of Neonatal Resuscitation Video Review 1:1 Coaching, a Qualitative Analysis

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Introduction: Neonatal resuscitation is a common emergency required to support an infant's physiological adaptation to extrauterine life. This is a high stress environment involving high risk patients, as such, errors such as communication breakdowns and resuscitation algorithm deviations commonly occur. Neonatal resuscitation video review (NRVR) is a novel resuscitation teaching tool involving recording neonatal resuscitations and reviewing the video for education and quality improvement.

Objective: We hypothesise that 1:1 NRVR sessions between a neonatal fellow or nurse (learner) and a neonatal consultant or nurse educator (coach) improves communication and situational awareness during neonatal resuscitation.

Methods and Results: With prospective consent, learners at Monash Medical Centre video recorded neonatal resuscitations in which they provided patient care. Candidate videos were processed with multiple synchronised views of the neonate and available physiological data. Learners reviewed their own video with a coach using a 'pause and reflect' approach. Learners attended semi-structured interviews to investigate the impact of coaching on their learning. A thematic analysis of participant responses was conducted using a social constructivist viewpoint. Nine learners (7 fellows and 2 nurses) had 14 NRVR 1:1 coaching sessions with 7 coaches. Three key themes were identified 1) Debrief accuracy: better recall of events and improved situational awareness. 2) Individual coaching: learner-centred feedback, exploring their own learning trajectories in a meaningful way. Specific areas for improvement are identified for clinical upskilling. 3) Psychological safety: learners experienced differing levels of comfort reviewing themselves, but all learners reported that the education benefits superseded these anxieties.

Conclusions: Learners reported NRVR 1:1 coaching to be a safe and effective method for reviewing and improving their clinical management during neonatal resuscitations. This study supports NRVR coaching should be available for neonatal clinicians. Further studies exploring repeated NRVR 1:1 coaching sessions over time and the coaches' perspective is needed.

Triple Elimination of Mother-to-child Transmission of HIV, Hepatitis B and Syphilis in Asia-Pacific: A Systematic Review

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Introduction: Human Immunodeficiency Virus, Hepatitis B, and Syphilis are sexually transmitted infections (STIs) that can be transmitted from mother to child in the perinatal period. World Health Organisation (WHO) introduced the concept of triple elimination to address all three conditions in an integrated manner and set targets for a range of outcomes to be achieved by 2030. WHO Regions of Southeast Asia and Western Pacific have committed to meeting these, with three countries already validated. However, progress in the remaining countries remains unclear with several targets having no up to date data.

Objective: To evaluate the progress made in Fiji, Papua New Guinea, Solomon Islands, Mongolia, Indonesia, Nepal, Bangladesh, and Timor-Leste towards achieving the triple elimination targets set in the WHO *Regional Framework for the Triple Elimination of Mother-to-Child Transmission*.

Methods: A review protocol was developed as per the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline. It included peer-reviewed studies from the selected countries post 2010, reporting on pregnant women and/or children, as well as grey literature and database values. Studies were screened and extracted on Covidence and analysed through descriptive analysis and narrative synthesis.

Results: The review screened 4421 studies and extracted 37 of them, in addition to five non-study sources. 182 data points were available across the ten outcomes which showed that no country is on track to achieve the targets. Data availability was uneven across outcomes and countries. Studies also varied in sample size (25 to 109,262) and were primarily single centre studies with a cross-sectional design.

Conclusions: This review highlights that data availability for triple elimination is inconsistent and that countries are not on course to achieve the 2030 targets. Upstream challenges such as lack of resources and barriers in accessing care affect service coverage and data collection, subsequently hindering progress. This review joins only one other in evaluating triple elimination, emphasising the need for accelerated action and further research.

Uncovering the immunobiology and biomechanics of Human Fascia Lata as an autologous graft for Pelvic Organ Prolapse treatment.

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Introduction: Pelvic Organ Prolapse (POP) is a condition where the female pelvic organs descend outside the pelvic cavity, with a 50% prevalence in women, often occurring in post-menopausal women. POP was previously treated with polypropylene mesh; however, it was banned due to adverse complications. Urogynaecologists currently utilise alternative treatments, such as autologous fascia lata (FL) grafts, a multilayered, dense fibrous connective tissue sheath that envelops the thigh musculature, enhancing biomechanical efficiency through tension regulation, venous return facilitation, and joint stabilisation. Clinicians are concerned that important questions remain regarding the impact of patient characteristics, such as age, on patient outcomes.

Objective: We aimed to characterise the immunobiological and biomechanical properties of the Human Fascia Lata to establish evidence-based guidelines for confident clinical applications of autologous FL grafts for POP treatment.

Methods and Results: Human fascia lata (FL) was harvested using a lateral thigh incision with a 3cm transverse cut, mobilising and dissecting tissue during sacrocolpopexy, with a tiny sample retained post-ethical approval. Rupture testing was completed with the CellScale UniVert Tensiometer. Ultimate tensile strength (MPa) and strain at max force (mm/mm) showed an increase with age. Further, FL immunofluorescence of fibrillar collagens and decorin revealed a localisation of collagen V towards the basement membrane, and decorin was localised within the collagen matrix. Moreover, Collagen I and III stains were expressed extensively across FL samples.

Conclusions: The detection of collagen V and decorin within the FL allowed us to assess if this is impacted by age. Additionally, the increase in Ultimate Tensile Strength and strain at max force demonstrated that autologous FL grafts may be effective across all ages. This research could help improve the understanding of autologous grafts and optimise their real-world applications.

Targeted lipid nanoparticle delivery of short interfering RNA to treat preeclampsia

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Introduction: Preeclampsia is a severe pregnancy complication resulting in the deaths of >76,000 mothers and >500,000 neonates annually. Central to its pathogenesis is placental dysfunction, and excess circulating maternal antiangiogenics. The only cure is very of the placenta, which can have profound consequences in cases of early-onset preeclampsia. Lipid nanoparticles (LNPs) offer a promising option to deliver gene-silencing nucleic acid therapies to the placenta, halting pathogenesis, due to their biocompatibility and reduced off-target effects, reducing risk.

Objective: We aim to target LNPs to the placenta, delivering short interfering RNA (siRNA) to silence pathogenic drivers of preeclampsia.

Methods and Results: Cyanine 5-labeled non-functional siRNA (siRNA-Cy5) encapsulated within LNPs was conjugated with a placental-specific target moiety via thiol-maleimide chemistry. CytoFLEX Nano Flow Cytometry was used to validate moiety-LNP conjugation, revealing highly efficient moiety conjugation, >97% moiety attachment, with no detectable signal in controls. Targeting efficiency was assessed by incubating targeted and untargeted LNPs (500ng siRNA/well) with human placental cytotrophoblast cells for 1 hour. Flow cytometry identified significantly higher fluorescence in cytotrophoblasts treated with targeted LNPs compared to untargeted and control groups ($p<0.0001$), confirmed by confocal microscopy. I*n vivo;* pregnant mice (D14.5) were injected with PBS (control), untargeted, or targeted LNPs (0.3mg/kg) via tail vein. After 24 hours (D15.5), maternal organs, fetuses and placentas were imaged using In Vivo Imaging System (IVIS) to detect siRNA-Cy5 uptake. Preliminary findings demonstrated significantly higher Cy5 radiant efficiency in mouse placenta treated with targeted LNP compared to untargeted ($P=0.0008$).

Conclusions: These findings establish the feasibility of targeted siRNA delivery to the placenta, paving the way for therapeutic application of LNPs in pregnancy. This demonstrates strong potential to revolutionise placental drug delivery, representing a significant advancement for maternal-fetal medicine.

MURDOCH CHILDREN'S RESEARCH INSTITUTE

ORAL PRESENTATION SESSION B

Sulforaphane as a Future Therapeutic for Preeclampsia: The Next Steps in Clinical Translation

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Introduction: Preeclampsia is characterised by hypertension with maternal end-organ dysfunction and/or fetal growth restriction. In recent years, in vitro studies have demonstrated sulforaphane, a naturally occurring antioxidant in broccoli sprouts, can mitigate oxidative stress and inflammation in placental tissue, and protect against endothelial dysfunction in human blood vessels. These findings suggest that sulforaphane, via a broccoli sprout extract, may offer protective effects in preeclampsia.

Objective: This study aimed to compare circulating sulforaphane concentrations from three extracts in pregnant women and determine whether sulforaphane crosses the placenta to the fetus.

Methods and Results: Healthy non-pregnant (n=18) and uncomplicated pregnant women (n=18, gestation between 28-36 weeks) were assigned to one of three broccoli sprout extracts (EnduraCell, AVMACOL®, or BROQ™; ~21mg sulforaphane). Blood was collected over 8 hours and sulforaphane levels were measured using liquid chromatography-mass spectrometry (LCMS). Additionally, uncomplicated pregnant patients (n=8) scheduled for elective caesarean sections received a single dose of EnduraCell pre-operation, with maternal blood, urine, umbilical cord blood, and placenta collected at birth. A second dose was administered postnatally, followed by maternal blood and breast milk collection two hours later. The area under the curve of sulforaphane was analysed and compared across three extracts in the non-pregnant group (EnduraCell: 343.1 ± 90.13, AVMACOL®: 90.97 ± 30.78, BROQ™: 245.3 ± 17.67) and pregnant participants (EnduraCell: 179.2 ± 22.63, AVMACOL®: 42.05 ± 15.67, BROQ™: 105.0 ± 10.66). Sulforaphane was detected in maternal (70.10ng/ml ± 11.90) and umbilical cord blood (vein: 23.91ng/mL ± 3.11, artery: 18.81ng/mL ± 2.36), placental tissue (10.99ng/mg ± 2.11) and breast milk (1.33ng/mL ± 2.29).

Conclusions: Different extracts demonstrated distinct circulating sulforaphane profiles in pregnant and non-pregnant women. Further, sulforaphane is present in umbilical cord and breast milk, providing the world's first evidence of sulforaphane maternal-fetal transfer and opening avenues for future research into fetal implications.

Uncovering the Potential of Bacterial Autotransporters: A Journey from Pathogenesis to Therapeutic Applications

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Introduction: Autotransporters (ATs) are bacterial nanomachines that drive virulence through diverse mechanisms including immune evasion, adhesion, and biofilm formation. Evolving alongside us for millennia, ATs represent a versatile molecular toolkit that bacteria use to manipulate human biology. Although widespread across many pathogens, functional studies have largely focused on *Escherichia coli*, leaving many ATs from clinically relevant species unexplored.

Objective: This project both exploits the wealth of accumulated knowledge for well-characterised ATs and uncovers new mechanisms for poorly characterised ATs.

Methods and Results: Our multidisciplinary approach spans structural biology, biophysics, cell biology, and microbiology to both understand and exploit the molecular mechanisms by which ATs contribute to pathogenesis. First, we exploit the extensive knowledge of *E. coli* ATs to engineer the protein Pet for intracellular drug delivery. Second, we investigate under-characterised ATs from *Bordetella pertussis*, the causative agent of whooping cough.

Conclusions: We have reprogrammed Pet to deliver therapeutic peptides into epithelial cells, triggering targeted, cargo-dependent cell death. This proof of principle will lead the way into using this platform to deliver other peptide drugs, increasing their efficacy by delivering them directly into the cytoplasm. Meanwhile, our phylogenetic classification revealed that Vag8 and TcfA, two adhesins from *B. pertussis*, likely employ distinct mechanisms. Vag8 combines local host adhesion with remote immune suppression via complement inhibition, facilitated by its presence in outer membrane vesicles. In contrast, TcfA is ungrouped, highly specific to *B. pertussis*, and lacks homologs. Our studies have found that TcfA is functionally competent, promoting host cell adhesion, yet exhibits no distinct structural features (via multiple methods of structural determination), pushing us to rethink rigid structure-function paradigms.

Decoding SNAPPs: Molecular Insights into Next-Generation Antibacterial Polymers

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Introduction: Multi-drug resistant (MDR) bacteria pose a significant threat to global health and the economy. Structurally Nanoengineered Antimicrobial Peptide Polymers (SNAPPs), composed of multiple arms of amino acid residues, have demonstrated superior antibacterial performance against Gram-negative and Gram-positive bacteria compared to traditional antibiotics. Although experiments confirm their effectiveness, the molecular mechanisms underlying their action and corresponding design parameters remain incompletely understood.

Objective: This study aims to elucidate the antibacterial mechanism of SNAPPs and examine how lipidation influences their structural stability, membrane interactions, and bactericidal efficacy, ultimately supporting rational design of optimized SNAPPs.

Methods and Results: Molecular dynamics (MD) simulations were employed to investigate interactions between SNAPPs and bacterial model membranes. Simulations of SNAPPs composed of valine and lysine residues revealed a stepwise pore formation process potentially responsible for bacterial cell death. Further, lipidated SNAPP variants with hexanoic acid (C6), lauric acid (C12), and stearic acid (C18) tails were modelled. Lipidation enhanced the α-helical stability of SNAPP arms, promoting deeper insertion into the bilayer. Among the variants, C12-SNAPP induced the greatest membrane disruption, while C18-SNAPP's excessive hydrophobicity caused back-folding and reduced efficacy. Potential of mean force calculations showed lipidation lowered the energy barrier for membrane translocation.

Conclusions: This study provides detailed molecular insights into how SNAPPs disrupt bacterial membranes. Atomistic simulations showed that hydrophilic and hydrophobic amino acid arrangements determine membrane binding, secondary structure, and pore formation. Lipidation enhanced α-helical stability and reduced energy barriers for bilayer penetration, especially in C6- and C12-SNAPPs, promoting deeper insertion and greater disruption. In contrast, C18-SNAPP's excessive hydrophobicity induced arm back-folding, limiting efficacy. These findings underscore the importance of tuning lipid chain length and sequence composition to balance membrane interactions and avoid structural collapse. This work offers a framework for designing advanced SNAPPs to combat multidrug-resistant bacterial infections effectively.

All-trans Retinoic Acid in Lipid Nanoparticles (ATRA-LNP) as an Immunomodulator to Treat Glomerulonephritis

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Introduction: Autoimmune diseases can induce glomerulonephritis. While standard treatments have improved patient outcomes, they also present challenges, including general immune suppression and the development of drug resistance. Immunomodulatory and tissue-repairing properties of ATRA-LNP present a promising therapeutic approach.

Objective: To investigate ATRA-LNP therapeutic capacity in glomerulonephritis.

Methods and Results: Studies were conducted using NTN and anti-MPO AAV C57BL/6 mice, human T cells, and podocyte cell lines. *Ex vivo* imaging revealed that DiR-tagged ATRA-LNP were detected at higher intensity within and remained elevated in NTN mice kidneys ($7.81 \times 10^{\wedge 8}$ at 24 hours and $8.56 \times 10^{\wedge 8}$ at 72 hours), in contrast to the kidneys of healthy mice ($2.19 \times 10^{\wedge 8}$ at 24 hours and $1.45 \times 10^{\wedge 8}$ at 72 hours). In extended NTN mice, the survival rate in ATRA-LNP group was higher than in empty LNP group (83.3% vs 33.3%). ATRA-LNP reduced glomerular sclerosis by 23% in anti-MPO AAV mice. Flow cytometric analysis revealed that in anti-MPO AAV mice, ATRA-LNP reduced TNF-α expression in kidney T cells (MFI 8.202 ± 524.1 vs 7.596 ± 262.0) and increased TGF-β expression in kidney Treg cells (MFI 14.606 ± 886.7 vs 15.508 ± 155) compared to non-treated mice. Doses up to 10 times higher than the therapeutic dose had no significant toxic effects on the kidneys and liver. ATRA-LNP induced podocyte maturation, as shown by reduced VIM mRNA (log2RQ -0.9 ± 0.6) and S1A100 mRNA (log2RQ -2.4 ± 0.5). IL-6 level in the DMSO-induced podocyte culture medium of ATRA-LNP group was lower than in non-treated group (OD 0.51 ± 0.14 vs 0.80 ± 0.14). ATRA-LNP also increased Treg percentage in human T cell culture by fourfold.

Conclusions: ATRA-LNP is a potential disease-targeted therapy for glomerulonephritis that ameliorates kidney injury, modulates cytokine levels, induces podocyte maturation, and increases Treg number while exhibiting minimal cytotoxicity.

Multi-omics Data Analysis Identifies Subtype-Specific Plasma Signatures in Juvenile Idiopathic Arthritis

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Introduction: Juvenile idiopathic arthritis (JIA) is an umbrella term for a heterogeneous group of chronic rheumatic diseases characterised by persistent joint inflammation lasting at least six weeks with onset before age 16 affecting 1 to 4 per 1000 Australian children. JIA is classified into several subtypes based on clinical presentations including systemic (sJIA), oligoarticular (oJIA), polyarticular rheumatoid factor positive and negative (pJIA RF+/-). However, the current clinical features-based JIA classification presents significant limitations as clinical symptoms overlap substantially between subtypes and with other inflammatory conditions, leading to diagnostic misclassification and delays in immunologically aligned treatment. The absence of molecular and cellular biomarkers that distinguish JIA subtypes and track disease activity represents a critical barrier to improving diagnostic and prognostic of JIA.

Objective: To identify molecular and cellular clinical biomarkers of JIA.

Methods and Results: This includes high-dimensional data analytics across three complementary molecular and cellular profiling techniques: Nuclear magnetic resonance (NMR) metabolomics, Multiplex cytokine analysis and flow cytometry. Multi-step data preprocessing including data normalisation, quality control and filtering biological outliers was performed prior to statistical analysis. To discover JIA-associated patterns across molecular and cellular layers, non-parametric comparisons, multivariable linear regression models adjusting covariates with multiple testing correction, correlation analysis and network analysis. The findings were visualised into diverse formats of graphs including volcano plots, forest plots, heatmaps, network diagrams, box plots, scatter plots. The study demonstrates the molecular and cellular heterogeneity across JIA subtypes. The plasma of sJIA emerges as molecularly distinct, with 24 metabolites significantly altered including elevated GlycA while there were no changes in other subtypes. Cytokine profiling identifies sJIA-specific elevation of IL-18, M-CSF and LIF, with the most distinct correlation networks, while oJIA shows a decreased inflammatory profile in plasma. Flow cytometry further supports systemic cellular heterogeneity across JIA subtypes, showing differential monocyte subset distributions between active and inactive sJIA. GlycA outperforms hsCRP in distinguishing disease activity and better integrating with inflammatory networks in JIA subtypes, suggesting superior utility for disease monitoring in systemic inflammation within JIA.

Conclusions: These findings provide the foundation for future diagnosis and prognosis research to apply immunologically aligned treatment strategies in JIA subtypes.

UNIVERSITY OF MELBOURNE

ORAL PRESENTATION SESSION A

Venetoclax-based therapy as a bridge to haematopoietic stem cell transplantation in relapsed or refractory paediatric acute leukaemia

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Introduction: Relapsed and/or refractory (R/R) acute paediatric leukaemia, associated with chemotherapy resistance, portends dismal outcomes, particularly in patients unable to achieve sufficient remission to proceed to haematopoietic stem cell transplantation (HSCT). BCL-2 inhibitor venetoclax targets aberrant cell survival pathways, with promising pre-clinical and phase I studies, however minimal literature describes its real-world use.

Objective: To understand the real-world experience of venetoclax-based therapy, both with curative intent bridging to HSCT and with palliative intent.

Methods and Results: We reviewed patients <18 years treated with venetoclax-based therapy at our site for R/R acute leukaemia. The primary outcome was best ORR and secondary outcomes included number receiving HSCT, overall survival (OS), event free survival (EFS), and toxicities. 20 children (ten female, ten male) received 22 episodes of venetoclax-based therapy: 19 with curative intent and three with palliative intent. Patients were median 4.9 years (range 0.8-17.4) and received mean 2.3 (range 1-5) prior lines of therapy. 50% had morphological disease and 50% detectable measurable residual disease (MRD). When given with curative intent, ORR post venetoclax-based therapy was 78% (14/18) of evaluable patient-episodes, with 89% (16/18) resulting in complete morphological remission: ten MRD-negative (56%) and six MRD-positive (33%). It facilitated immediate progression to HSCT in 79% (15/19) of patients, with another two (11%) requiring further bridging therapy prior to HSCT. The median time from first venetoclax dose to HSCT was 2.5 months (range 0.9-6.0). 76% (13/19) are alive at a median follow-up of 20.6 months (range 1.2-63.2), with two-year OS 78.1% and EFS 40.7%. Therapy was very well tolerated, with median Lansky (<10yo) or Karnovsky (≥10yo) score of 80/100 (range 50-90/100).

Conclusions: This is Australia's largest paediatric single-centre experience of venetoclax-based therapy in acute leukaemia, demonstrating venetoclax-based therapy should be considered as an effective salvage therapy, bridge to HSCT, or even a valid palliative option.

Development of novel lateral flow assays (LFA) for active syphilis and liver health screening

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Introduction: Access to affordable and reliable diagnostic testing is a persistent barrier to health equity that often undermines efforts to improve health outcomes for those in under-resourced communities. Lateral flow assays (LFAs) provide an easy to use, low-cost solution that is scalable for use in decentralised settings and can be used to detect both infectious and chronic disease.

Objective: The Burnet Diagnostics Initiative (BDI) are committed to closing the gap in health equity through developing innovative lateral flow technology that can be used globally and in low-resource settings. Through this initiative, they have achieved early success in the development of two distinct prototypes that take a novel approach to identifying both infectious and chronic disease.

Methods and Results: We have developed and optimised two lateral flow systems which represent a unique approach to identifying and monitoring both infectious and non-communicable disease for acute and chronic conditions. To overcome a major limitation in current diagnostic testing for syphilis, we have engineered a rapid treponemal antibody test that can distinguish active syphilis from that of past-treated infections. From 10 µL of blood, this test can provide results within 15 minutes with an overall sensitivity of 98%. This could greatly improve confidence in decentralised testing and reduce the unnecessary use of antibiotics. In addition, we have also developed a liver health screening tool that can be used to assess liver damage in both acute and chronic conditions. This test utilises the well-categorised liver biomarker, *alanine transaminase* (ALT, *isotype* ALT1), and provides a quantitative result that can be accessed by health practitioners to provide insight as to patient liver-health status.

Conclusions: Our work in diagnostic assay development demonstrates the pivotal role that lateral flow can play in strengthening health equity both globally and in low-resource settings through innovation and scalable, accessible testing solutions.

The Impact of Gender-Affirming Hormone Therapy on Skeletal Muscle Physiology and Molecular Profiles

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Introduction: Gender-affirming hormone therapy (GAHT) is a critical intervention for transgender individuals to align physical traits with gender identity, usually involving testosterone for transgender men (TM) and estrogen for transgender women (TF). While GAHT's effects on secondary sex characteristics are well established, its impact on skeletal muscle, a highly hormone-sensitive tissue crucial for metabolic and physical health, remains underexplored.

Objective: This study aimed to characterise changes in skeletal muscle physiology and underlying molecular profiles in transgender adults undergoing GAHT longitudinally over 12 months.

Methods and Results: A longitudinal, multimodal study was conducted on transgender adults initiating GAHT. Measures included circulating sex hormone levels, body composition assessed via dual-energy X-ray absorptiometry (DXA), muscle fibre type distribution, aerobic capacity testing, and muscle strength using the isometric mid-thigh pull test. A baseline skeletal muscle transcriptomic reference for cisgender men and women was generated from publicly available data. In TM participants, testosterone increased from ~3 to 21 nmol/L, accompanied by a ~4% decrease in fat mass, ~3% increase in lean mass, and improved muscle strength. In TF participants, testosterone declined from ~16 to 0.4 nmol/L and estrogen rose from ~64 to 223 pmol/L, corresponding with a ~4% increase in fat mass, ~4% reduction in lean mass, and reductions in aerobic capacity and strength. A trend toward a higher proportion of type I (slow-twitch) fibres was observed in TF muscle. While not all changes reached statistical significance within 12 months, consistent patterns indicate progressive musculoskeletal adaptation. RNA sequencing and proteomics from the same cohort are underway.

Conclusions: This study offers early evidence of how GAHT influences skeletal muscle health. The trends suggest continued changes beyond 12 months, highlighting the need for longer-term studies. Integrating molecular data will deepen our understanding of hormone-driven muscle adaptation and help inform better, evidence-based care for transgender people.

CGRP and RAMP1 promotes tumorigenesis in the human gastrointestinal tract

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Introduction: The gastrointestinal (GI) tract is richly supplied with nerve fibres, forming a critical network for gut function. Tumour cells are highly adaptive and exploit their environment, including nerves to support and accelerate tumour growth. However, the molecular mechanism mediating nerve cell function during GI tumorigenesis remains unknown.

Objective: Investigate the expression and function of sensory neuropeptide calcitonin gene-related peptide (CGRP) and its receptor component, receptor activity-modifying protein 1 (RAMP1), to elucidate novel mechanisms by which cancer cells exploit neuropeptides.

Methods and Results: We analysed 126 patient samples using multiplex-immunohistochemistry to assess the expression of RAMP1 in primary human colorectal cancers (CRC), CRC liver metastasis (mCRC) and gastric cancer (GC). We assessed RAMP1 tumour expression in correlation with patient gender, age and tumour characteristics including pathological features, molecular subtype and genomic subtypes. Associations with patient survival were elucidated using data from The Cancer Genome Atlas Program (TCGA). Finally, we confirmed the function of CGRP on human tumour cell growth using *in vitro* stimulation assays and RNA-sequencing. *RAMP1* expression was significantly associated with decreased patient survival in both CRC and GC. We found that RAMP1 was highly expressed by over 60% of human CRC and GC cells. In addition, RAMP1 expression was more significantly expressed in CRCs with microsatellite instability and younger GC patients. Finally, CGRP stimulation of RAMP1-expressing CRC and GC cell lines enhanced tumour growth alongside increased expression of genes linked to proliferation, metabolism and migration.

Conclusions: Together, this work highlights new mechanism by which nerves and neuropeptides promote tumour growth in the GI tract. Our data highlight the potential for existing CGRP antagonists to be further investigated as treatments in both CRC and GC, leading to a reduction of tumour cell growth and improving patient survival.

A CDK11-CDK9 regulatory axis controls the RNA polymerase II pausing-to-elongation transition

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Introduction: Transcriptional cyclin-dependent-kinases (tCDKs) modulate RNA polymerase II (Pol II) progression through distinct phases of 'transcription cycles' including recruitment, initiation, pausing/release, elongation, and termination. Tight regulation of Pol II transcription ensures controlled gene expression and dysregulation of this process underpins all disease including cancer. tCDK inhibitors have emerged as a potential therapeutic approach that can selectively exploit cancer cell dependencies on abnormal gene expression. Haematological malignancies with over-expression of MYC or translocations involving the histone methyltransferase MLL and super-elongation-complex (SEC) subunits are particularly vulnerable to inhibition of CDK9, which releases Pol II from promoter-proximal pausing. New findings suggest that CDK11, a tCDK that regulates pre-mRNA splicing, has an important role for the control of Pol II pause-release checkpoint and for sustaining oncogenic gene expression.

Methods: Complementary pharmacological and chemical-genetic approaches (auxin-induced protein degradation, analog-sensitive kinase mutants) and global transcriptomic, genomic, and proteomic approaches technologies have been used to assess the impact of acute CDK11 blockade. Human cell line and syngeneic models of aggressive blood cancer have been used to dissect the biological/therapeutic impact of CDK11 inhibition.

Results: Acute CDK11 inhibition/degradation induces global Pol II pausing at promoter-proximal regions accompanied by rapid ablation of nascent RNA synthesis near the beginning of transcriptional units. CDK11 activity is dispensable for Pol II recruitment to genes in response to external stimuli, but necessary for transition from pausing to active elongation. *In vitro* recombinant kinase assays demonstrate that CDK11 is capable of phosphorylating the Pol II C-terminal-domain, with global decreases in phosphorylated Pol II observed in cells following CDK11i. High resolution ChIP-nexus indicate that CDK11i Pol II pausing peaks are distinct from pausing peaks induced by CDK9 inhibition (CDK9i), and precision nuclear-run-on (PRO-seq) assays indicate that CDK11 regulates Pol II upstream of the CDK9-dependent checkpoint. Importantly, CDK11 inhibition (CDK11i) exhibits potent therapeutic efficacy in pre-clinical mouse models of MLL-rearranged acute-myeloid-leukaemia (AML) and MYC-driven B-lymphoma.

Conclusion: These data identify and dissect a CDK11-CDK9 regulatory axis that modulates Pol II-dependent transcription and is a therapeutic vulnerability that can be targeted in aggressive blood cancer cells.

Foreign Body Response to Implanted Human Fascial Lata in a Mouse Model: Implications for Enhancing Pelvic Reconstructive Surgery

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Introduction: Pelvic Organ Prolapse (POP) is an increasingly common condition, yet options for surgical grafts remain limited, especially following the withdrawal of all transvaginal and sacrocolpopexy meshes. Human Fascia Lata (HFL) grafts have long been used in incontinence procedures and are now being explored as alternatives for prolapse repair. However, limited data exist on the Foreign Body Response (FBR) to HFL, particularly in comparison to synthetic mesh.

Objective: This study aimed to compare the FBR to HFL and synthetic mesh to understand immune responses and integration mechanisms essential for clinical adoption.

Methods and Results: HFL samples were collected from 26 women undergoing prolapse surgery. C57BL6 mice (n=8/group/timepoint) received abdominal implants of HFL or synthetic mesh, with analysis at 7- and 90-days post-implantation. Gene expression and spatial proteomics were used to assess immune responses. At day 7, spatial imaging and gene analysis showed fewer neutrophils and lower E-selectin expression around HFL, indicating reduced acute inflammation. By day 90, HFL showed increased expression of myeloid (e.g., *Mrc1*, *Nos2*), leukocyte trafficking (*Ccr1*, *Cxcr3*), T cell (*Cd3*, *Cd4*), and regulatory markers (*Foxp3*, *Cd274*) compared to mesh. Spatial imaging confirmed higher presence of dendritic cells, helper T cells, and regulatory double-negative T cells in the HFL group. Angiogenic and ECM-related genes were also upregulated, alongside a higher number of CD31+ cells, suggesting improved vascularization and matrix deposition.

Conclusions: HFL demonstrates superior performance over polypropylene mesh in terms of tissue integration and durability, making it an appealing choice for surgical grafts in pelvic reconstruction. Employing advanced techniques including Spatial Tissue Imaging and Fluidigm® 96.96 Real-Time PCR, this study revealed a significant contrast in the activation of immune cells in response to HFL compared to synthetic mesh. We observed an intricate interplay between the innate and adaptive immune systems following HFL implantation, leading to heightened angiogenesis and deposition of extracellular matrix ninety days post-implantation, thereby facilitating the seamless integration of HFL into the host tissue.

UNIVERSITY OF MELBOURNE

ORAL PRESENTATION SESSION B

Therapeutic targeting of MLKL with nanobodies to inhibit necroptosis

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Introduction: Necroptosis is a form of inflammatory cell death implicated in infections, cancer, and sterile autoinflammation. This pathway is initiated by the engagement of death receptor and Toll-like receptor signalling, culminating in activation of the pseudokinase MLKL. Active MLKL oligomerizes and translocates to the plasma membrane, where it disrupts the lipid bilayer, causing cellular rupture and release of immunogenic molecules.

Objective: In this study, I hypothesized that necroptotic cell death could be blocked via intracellular expression of MLKL-targeting nanobodies, which represent the smallest antigen-binding fragments of camelid antibodies. To test this hypothesis, I aimed to generate mouse MLKL-targeting nanobodies, then characterize the function and structure of these nanobodies. To test the therapeutic potential of MLKL targeting nanobodies, I plan to use an in vivo MLKL-driven disease model and deliver MLKL nanobody mRNA via lipid nanoparticles (LNPs) to diseased tissue.

Methods and Results: Alpacas were immunized with recombinant N-terminal MLKL, and phage display panning identified 14 nanobodies with distinct CDR3 regions. FLAG tagged nanobodies were expressed in mammalian cells and their expression levels examined by immunoblotting, and their ability to bind intracellular endogenous MLKL shown via immunoprecipitation. Functional screening for their ability to block necroptosis identified six nanobodies that provided complete protection against necroptotic cell death. Surface plasmon resonance (SPR) analysis demonstrated that MLKL targeting nanobodies bound MLKL in the low nanomolar and subnanomolar range, while crosslinking mass spectrometry indicated that MLKL nanobodies interacted with the MLKL N-terminal 3α helix, which is required for MLKL membrane binding and necroptosis execution. Mechanistically, I showed that intracellular expression of MLKL targeting nanobodies inhibited MLKL translocation to the membrane and, unexpectedly, promoted MLKL degradation. Future studies will investigate the mechanism of nanobody-driven MLKL degradation and will focus of generating MLKL nanobody mRNA for therapeutic LNP delivery.

Optimising Lung Aeration using External Negative Pressures in Near-Term Rabbit Kittens.

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Introduction: Respiratory distress in term infants (TRD) is primarily caused by elevated airway liquid at birth. As liquid is cleared from the airways into lung tissue at birth, the lungs become oedematous. However, elevated liquid increases the degree of oedema, impairing respiratory function. Previous research demonstrated that external negative pressures (-6 cmH_2O) improve lung aeration, and we hypothesise that the optimal level of external negative pressure will vary depending on the volume of airway liquid.

Objective: Determine the external negative pressure level that optimises lung aeration in near-term rabbit kittens with and without elevated airway liquid.

Methods and Results: Rabbit kittens (30/32d) were randomised to Control or Elevated Liquid (EL) groups. Control kittens had lung liquid drained, simulating expected volumes after vaginal delivery. EL kittens had lung liquid drained and 30 mL/kg liquid returned, simulating expected volumes after caesarean section. Kittens were delivered into a water-filled plethysmograph and external pressures adjusted to 0 cmH_2O (Control n=7; EL n=6), -3 cmH_2O (Control n=7; EL n=8), -6 cmH_2O (Control n=6; EL n=7), or -9 cmH_2O (Control n=6; EL n=7). Kittens were ventilated with a tidal volume of 8 mL/kg and PEEP of 0 cmH_2O. Phase contrast X-ray imaging measured lung aeration (functional residual capacity; FRC). In Control kittens, FRC levels increased with the external negative pressure level, but were similar in kittens exposed to -6 and -9 cmH_2O (31.6 ± 0.9 vs 39.0 ± 1.3 mL/kg). In EL kittens, FRC increased with the levels of external negative pressure (0 cmH_2O, 7.6 ± 2.0; -3 cmH_2O, 15.1 ± 1.3; -6 cmH_2O, 22.1 ± 1.6; -9 cmH_2O, 28.3 ± 3.1 mL/kg; $P \leq 0.05$).

Conclusions: Optimal lung inflation (FRC≈30 mL/kg) was achieved with an external -6 cmH_2O in *Control* kittens, whereas external -9 cmH_2O caused over-inflation (FRC≈40 mL/kg). In *EL* kittens, optimal lung aeration was achieved with external 9 cmH_2O. External negative pressures enhance lung aeration after birth.

Questioning the Causative Role of *FANCA* Variants in Premature Ovarian Insufficiency: A Multiomic Investigation

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Introduction: Premature ovarian insufficiency (POI) affects up to 4% of women under 40, with 15-31% having positive family history suggesting genetic aetiology. DNA damage repair gene variants, particularly in the Fanconi anaemia (FA) pathway, are emerging as prominent aetiologies. While biallelic loss-of-function *FANCA* variants cause FA, the role of heterozygous *FANCA* variants in isolated POI remains controversial.

Objective: To evaluate the causative role of *FANCA* variants in POI.

Methods and Results: WES analysis revealed five POI patients with *FANCA* variants. We conducted proteomics, RNAseq analysis, and functional assays including DNA damage hypersensitivity testing, protein expression analysis, and FA pathway assessment. Whole genome sequencing and comprehensive DNA damage repair assays are being performed to identify potential missed variants and assess subclinical pathway defects. Analysis of five POI patients with *FANCA* variants revealed diverse genetic patterns. WES identified compound heterozygous *FANCA* variants in two sisters with isolated POI, yet functional studies showed no DNA damage hypersensitivity. Two unrelated patients shared the same monoallelic pathogenic *FANCA* deletion (c.2602-9_2602-8del), and another patient carried maternally inherited FANCA variants. Proteomic analysis of the patient with maternal *FANCA* variants (missense and splice region) revealed depleted FANCA and FANCG protein levels, suggesting FA core complex disruption. Gene ontology analysis showed overrepresentation of cell cycle and mitosis pathways. Subsequent analysis identified a heterozygous nonsense *MCPH1* variant, with RNAseq confirming nonsense-mediated decay of variant transcripts. Western blot analysis showed normal FANCA protein expression despite the patient's phenotype. FANCD2 ubiquitination assays are ongoing to assess FA pathway functionality.

Conclusions: The pathogenic role of heterozygous *FANCA* variants in POI remains uncertain. Despite proteomic evidence of FA core complex disruption, normal protein expression and absence of detectable DNA damage hypersensitivity raise questions about *FANCA*'s causative role. The identification of an additional variant in *MCPH1* suggests potential oligogenic inheritance or alternative pathogenic mechanisms.

Can dual specific CAR NK cells enhance solid tumor targeting?

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Introduction: Antigen heterogeneity in solid tumors is a primary driver of immune evasion, including from common mono-specific chimeric antigen receptor (CAR) T cell therapy. To overcome this mode of tumor escape, we developed dual CAR natural killer (NK) cells targeting TAG-72, a pan-adenocarcinoma antigen, and CD47, broadly upregulated in cancers, complementing the array of endogenous NK killer receptors. Since CD47 is expressed on healthy cells, a truncated, non-signalling CD47 CAR variant was included to enhance target binding avidity while minimizing off-target toxicity.

Objective: To evaluate whether dual CAR NK cells offer functional advantages over single-target CARs in solid tumor models.

Methods and Results: Using CRISPR-Cas9, CAR constructs were integrated into induced pluripotent stem cells (iPSCs), then differentiated into NK cells via a 24-day embryoid body-based protocol. Flow cytometry confirmed successful CAR expression and NK phenotype. Anti-tumor efficacy was assessed against ovarian cancer cells with differential TAG-72 expression using real-time cytotoxicity (xCELLigence), 3D spheroid killing, CD107a degranulation, and IFN-γ assays. All constructs successfully differentiated into $CD45^{+}CD56^{+}$ iNK. Dual CAR demonstrated superior cytotoxicity, particularly against TAG-72^{high} OV-90 cells, achieving 60-70% elimination by 90hours, and enhanced CD107a degranulation across all cell lines compared to single CAR ($p<0.001$), suggesting improved synapse formation and multi-antigen engagement. However, while enhancing cytotoxic potential, dual CAR constructs exhibited significantly reduced IFNγ production (<400pg/ml) compared to single CAR (>800pg/ml) following soluble antigen stimulation, suggesting receptor competition and signal dilution. Using 3D spheroid targets, dual CAR showed a trend to increasing killing at 1:1 E:T ratio but not at lower ratios. TAG-72^{low} MESOV cells remained resistant to all constructs (20-50% cytotoxicity), demonstrating limitations in targeting antigen-poor environments despite dual recognition strategy.

Conclusions: While dual CAR NK cells offered improved tumor recognition and killing, their functional tuning—particularly cytokine output and impact on effector cells, if targeting CD47, require further optimization for clinical translation.

Investigating the Therapeutic Potential of Extracellular Vesicles for Fetal Brain Injury

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Introduction: Chorioamnionitis (bacterial infection of the fetal membranes) results in a fetal proinflammatory response, subsequent brain injury. This increases the risk of long-term neurodevelopmental disorders such as cerebral palsy. Human amnion epithelial cell derived extracellular vesicles (hAEC-EVs) demonstrate anti-inflammatory, angiogenic, and regenerative properties, making them an attractive therapy for antenatal brain injury. However, the assessment of acute toxicity, indicated by immediate physiological response, has not been investigated. Additionally, non-specific uptake of EVs by organs such as the liver and lungs, necessitate higher dosing to achieve neuroprotective effects. Given the complexities and costs associated with EV production, improving brain specific delivery is critical for advancing it clinical translation.

Objective: Using a large animal model of fetal brain injury, we aim to evaluate acute physiological responses to hAEC-EV therapy and enhance efficacy through the development of brain targeted EVs.

Methods and Results: hAECs were cultured in chemically defined media. EVs were isolated from conditioned media using tangential flow filtration and size exclusion chromatography. EVs were also modified to enhance their targeting to the brain. Fetal sheep were randomly assigned to one of four groups: (1) Saline control, (2) Injury via intravenous LPS exposure, (3) treatment with hAEC-EVs or (4) treatment with brain targeting EVs. Physiological signals (blood pressure, heart rate, oxygen saturation) were collected from 95-105 (dGA). Fetuses were then euthanised and brains collected for histological analysis. LPS exposure resulted bradycardia and hypoxia. In contrast physiological signals remained stable following hAEC-EVs exposure.

Conclusions: Our current results show LPS exposure induces physiological signs of fetal distress, consistent with systemic inflammatory response. This is not seen following EV exposure, suggesting fetal safety. To enhance the neuroprotective efficacy, future work within this project will involve the use of EVs engineered to deliver therapeutic effects directly to the fetal brain.

Economic evaluation of smoking cessation interventions to prevent periodontitis compared to standard care in Australia

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Introduction: Periodontitis is one of the most prevalent oral diseases globally. There is limited health economic evidence to inform reimbursement policy decision to support smoking cessation interventions provided by dental practitioners in Australia.

Objective: This study aims to economically evaluate three smoking cessation interventions provided by dental practitioners to prevent periodontitis in Australia compared to standard care: 1) one session of behavioural support, 2) two sessions of behavioural support, and 3) one session of behavioural support and nicotine replacement therapy.

Methods and Results: The healthcare perspective was taken. The base-case scenario included the intervention and healthcare costs with one-year time horizon. Sensitivity analysis included other healthcare costs (e.g. periodontic services, extractions, etc.). Extrapolation modelling extended the model to a three-year time horizon. The reference year is 2020 with 3% discount rate. The willingness-to-pay threshold chosen was AUD$50,000 per disability-adjusted life year (DALY) averted, and AUD$28,033 per quality-adjusted life year (QALY). There was 0% probability for cost-effectiveness for all three interventions under the base-case analysis. Cost-effectiveness results did not change with sensitivity analysis or extrapolation modelling. The incremental cost-effectiveness ratio, in order of the most favourable intervention were AUD$216,279/DALY averted and AUD$65,889/QALY gained, AUD$311,484/DALY averted and AUD$$94,893/QALY gained, $470,459/DALY averted and AUD$143,325/ QALY gained for one session of behavioural support, one session of behavioural support and nicotine replacement therapy, and two sessions of behavioural support, respectively.

Conclusions: Modelled smoking cessation interventions provided by dental practitioners for the Australian context were not cost-effective to improve health outcomes by preventing periodontitis (≤3 years). Incorporating co-benefits for smoking cessation interventions provided by dental practitioners, and longer time horizon has potential merit for reimbursement policy implementation.

BURNET INSTITUTE

ORAL PRESENTATION SESSION A

The Therapeutic Potential of Extracellular Vesicles: Unlocking the Next Frontier of Regenerative Medicine

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Introduction: Mesenchymal stromal cells (MSCs) and amnion epithelial cells (AECs) demonstrate potent anti-inflammatory and regenerative effects for several inflammatory diseases. However, clinical translation has been hindered following concerns regarding immunogenicity, tumorigenicity, and complexities with scalability and storage. Extracellular vesicles (EVs), paracrine mediators released by all cells, possess therapeutic bioactivity comparable to their parent cells. Furthermore, EVs are non-immunogenic and non-tumorigenic, and, compared to whole cells, they are cheaper and easier to manufacture and store. EVs circumnavigate the limitations associated with whole-cell therapy, making them an attractive novel agent for regenerative medicine. However, current therapeutic evidence is limited to in-vitro and small animal studies. Therefore, their therapeutic potential in different inflammatory diseases and more clinically relevant large-animal models remains unknown.

Objective: To determine if MSC- and AEC-derived EVs can (1) mitigate or reverse injury in multiple preclinical models of inflammatory injury, and (2) be scaled for clinical production while retaining therapeutic efficacy.

Methods and Results: EVs were isolated using tangential flow filtration and size exclusion chromatography. Production was successfully scaled for use in small animal models (µg) to clinically relevant large animal doses (mg). Inflammatory organ injury was induced in mice as follows: antenatal brain and lung injury by lipopolysaccharide (LPS) and hyperoxia; adult liver injury by a high-fat diet and carbon tetrachloride; and adult kidney injury by myeloperoxidase sensitisation. In sheep, antenatal brain injury was induced via intravenous LPS. EVs were administered after injury onset as rescue therapy. Inflammatory injury (immune cell infiltration, fibrosis, and proinflammatory cytokine release) was evident in the brain, lung, liver, and kidney across all models. Both MSC- and AEC-derived EV treatments mitigated these indices.

Conclusion: EV treatment improved organ injury in multiple models of inflammatory disease, demonstrating broad therapeutic potential. Further, EV production scaled for clinically relevant doses retained therapeutic potency.

The persistence of immunogenicity and efficacy following a fourth dose of a bivalent mRNA or protein-based COVID-19 vaccine

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Introduction: Regular COVID-19 booster vaccinations are recommended to improve protection against COVID-19 by broadening immunity to emerging SARS-CoV-2 variants. Yet the duration and breadth of protection against SARS-CoV-2 following multiple booster vaccination, particularly against emerging variants, remains unclear.

Objective: We conducted a randomised controlled trial (RCT) to compare the immunogenicity, reactogenicity and safety of a fourth dose bivalent mRNA (mRNA-1273.214/mRNA-1273.222) or protein-based (NVX-CoV-2373) COVID-19 vaccine in Melbourne, Australia. This paper presents longitudinal 12-month follow-up data on immunogenicity and a detailed analysis of breakthrough infections.

Methods and Results: Participants were randomised into either the bivalent mRNA (n=177) or protein (n=176) vaccine groups. A non-randomised control group was also recruited (n=143). Participants were followed up at 6- and 12-months post-vaccination. The geometric mean ratio of anti-Spike binding IgG antibody levels against Ancestral strain and Omicron BA.1, BA.4/5 and JN.1 variants, remained ~1.5-fold and 1.2-fold higher in the mRNA group than in the protein group at 6 months and 12 months post-vaccination, respectively. However, no differences in cellular immunity, as measured by IFNγ release, were observed between mRNA and protein at each timepoint. Vaccine efficacy against SARS-CoV-2 breakthrough infection across the 12-month follow up were similar between mRNA (46%, 95% CI: 41%-50%) and protein group (40%, 96 % CI: 35%-44%) (p=0.39). Eighteen adverse events were reported over the 12-month follow up period, with 7 seven mild cases considered possibly related to vaccination (n=5 mRNA, and n=2 protein).

Conclusions: Overall, this study found that both bivalent mRNA vaccine and protein ancestral strain-based vaccine, were highly immunogenic and provided additional protection against SARS-CoV-2 Omicron variants (JN.1) compared to no vaccination over a 12-month period. These results will have important implications for COVID-19 booster vaccination recommendations, particularly in settings where updated COVID-19 vaccines are not available.

Effect of time-of-day vaccination on the antibody response to mRNA and protein COVID-19 vaccine in adults

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Introduction: Time-of-day vaccination has been suggested as a feasible method to boost COVID-19 vaccine immunogenicity. However, several studies report inconsistent findings.

Objective: We explored if time-of-day vaccination influences antibody responses to a fourth dose of mRNA (Moderna bivalent vaccine; mRNA-1273.214/mRNA-1273.222) or protein (Novavax; NVX-CoV-2373) COVID-19 vaccine as part of a randomised controlled trial (RCT) in Melbourne, Australia. Furthermore, we assessed if time-of-day vaccination effects differed by vaccine type or sex.

Methods and Results: Participants were healthy adults (≥18 years) who have previously received their third dose of COVID-19 vaccine for at least six months and had no self-reported SARS-CoV-2 infection confirmed by PCR or RAT within the last three months. Participants were randomized 1:1, stratified by age (<50 and ≥50 years), to receive either a fourth dose of Moderna or Novavax COVID-19 vaccine. In the Moderna group, 87 participants were vaccinated in the morning (<12:00) and 89 participants in the afternoon (≥12:00). In the Novavax group, 92 participants received their vaccination in the morning and 84 in the afternoon. Blood samples were collected at day 0 and day 28 post-vaccination. Spike IgG and neutralising antibodies to SARS-CoV-2 variants (Wuhan, Omicron BA.1 and BA.4/5) were measured. At day 28 post-vaccination, antibody responses to all variants were higher for morning compared to afternoon vaccination in the Moderna group. For Novavax, Spike IgG and neutralising antibodies were similar for morning and afternoon vaccination. We also found that male participants in the Moderna group responded with higher antibodies to all variants tested when vaccinated in the morning compared to the afternoon, while female antibody responses were not influenced by the time-of-day vaccination. There was no interaction between sex and time-of-day vaccination in the Novavax group.

Conclusions: Overall, our study found that time-of-day vaccination had more effect in the Moderna group and for males only.

A stem-cell based drug discovery pipeline for nontuberculous mycobacteria

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Introduction: Nontuberculous mycobacteria (NTM) are emerging opportunistic pathogens causing a wide spectrum of diseases in individuals with structural lung defects (bronchiectasis, cystic fibrosis) or with compromised immune systems. Infections can range from tuberculosis-like lung disease to localised and systemic infections. Treatment of NTM infections is complex, prolonged and associated with high failure rates due to its innate resistance to several classes of commonly used antimicrobials.

Objective: To develop a drug screening pipeline for antibiotic resistant NTM with physiologically relevant, human stem cell derived infection models.

Methods and Results: NTM are mostly intracellular pathogens, primarily targeting macrophages. Our team has developed an innovative drug screening model for the most resistant NTM species (*Mycobacterium abscessus*), located within human stem cell derived macrophages. This infection model was successfully scaled up for automated, high-throughput screening of >4000 FDA-approved, off-patent compounds in a drug repurposing approach. We have identified ~150 drugs from an array of diverse compound classes. These compounds either have direct anti-mycobacterial activity or target the host macrophage to potentiate its ability for bacterial clearance, without causing any host cell cytotoxicity. Our drug screening pipeline further incorporates stem cell derived mini-lung models of donor-matched airway and alveolar epithelial cells. We have also optimised a TNF-alpha deficient mouse model to mimic a natural route of infection for efficacy testing of different drugs via intranasal or systemic deliveries. Ongoing studies are investigating in-depth dose response profiles of shortlisted drug candidates, which will then be validated in these preclinical infection models.

Conclusions: We have undertaken a drug repurposing approach to meet the immediate and unmet need for better and safer NTM treatment options. Our unique screening/validation pipeline with a broad-spectrum drug library has identified anti-mycobacterial compounds that will undergo further testing with existing standards of care to identify 'best-performing' drugs/combinations against treatment-refractory NTM lung disease.

MORC2 is a phosphorylation-dependent DNA compaction machine

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Introduction: MORC2, an oncoprotein possessing a GHKL-type ATPase domain, is associated with H3K9me3-mediated epigenetic silencing and DNA damage response, implicated in various cancers and neurological disorders, including autosomal dominant early-onset Charcot-Marie-Tooth disease. Its complex biological functions require phosphorylation by the P21-activated kinase 1 (PAK1) pathway. Despite being phosphorylated and linked to gastric cancer progression, the precise mechanism underlying MORC2's phosphorylation-dependent chromatin remodeling activity remains poorly understood.

Objective: We hypothesise that structural investigation of MORC2 and imaging MORC2 dynamics in live cells will generate mechanistic insights into its role in chromatin remodelling. This project aims to investigate the DNA binding mechanism of human MORC2 using integrative structural biology, proteomics, genomics and single molecule imaging techniques.

Methods and Results: Here, we purified full-length MORC2 and investigated its phosphorylation activity with various DNA substrates. Cryo-electron microscopy and quantitative crosslinking mass spectrometry reveals symmetric dimer formation upon phosphorylation and large rearrangements through the protein C-terminal domain. Hydrogen-deuterium mass spectrometry, surface plasmon resonance and DNA binding assays showed MORC2 possess multiple DNA biding sites with different binding affinities. Fluctuation Fluorescence Spectroscopy confirms MORC2 homodimerization in live cells. Chromatin immunoprecipitation coupled to sequencing, ATAC seq and Fluorescence Lifetime Imaging coupled with FRET demonstrate MORC2's preference for open DNA binding over the repressed chromatin marker H3K9me3. *In vitro* single-molecule analysis of MORC2 and its variants elucidates that MORC2 imparts epigenetic silencing by DNA compaction driven by ATP hydrolysis. This activity is precisely regulated by extensive phosphorylation at its C-terminus.

Conclusions: Our findings provide direct evidence of how MORC2 cause chromatin remodeling and how it is regulated by phosphorylation, thereby, providing molecular basis of chromatin remodelling activities of the MORC family, contributing to our comprehension of epigenetic regulation.

BURNET INSTITUTE

ORAL PRESENTATION SESSION B

Enhancing parents' experiences of paediatric genomic testing in usual outpatient care: insights from a multi-perspective qualitative study

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Introduction: The availability of funded genomic tests in paediatrics is increasing as evidence about their ability to improve diagnosis and management of rare genetic conditions mounts. Funding criteria allow doctors outside specialised genetics services to order these tests, a change aiming to enhance patient access. Little is known about whether families' needs are being met as aspects of care shift to mainstream paediatric clinics or how care experiences may be enhanced.

Objective: To investigate what makes (or would make) for a good care experience of genomic testing delivered wholly or in part by paediatricians, from the perspectives of Australian parents and health professionals.

Methods and Results: An interpretive description qualitative study was undertaken. Interviews were conducted with a range of stakeholders to provide a richer understanding: parents (n = 24), paediatricians (n = 10), genetic counsellors (n = 8), and nurses (n = 2). Audio recordings were transcribed verbatim and analysed via inductive content analysis. Opportunities to enhance families' experiences across the testing process were identified. While genetic counsellors often expressed concerns about the quality of the consent process, some paediatricians reported spreading out information and testing discussions to help families make an informed decision – an approach parents supported. Parents highlighted key areas for improvement at the point of results disclosure, including communicating in advance how results will be returned and directing families to condition-specific information resources and psychosocial supports. The importance of follow-up support was also emphasised, with different ways of meeting this need (often described as unmet in genetic settings) outlined.

Conclusions: This study provides practical insights for paediatricians to support families navigating genomic testing. In addition, the study findings reveal potential quality indicators for health services. Developing robust, fit-for-purpose patient-centred measures will be crucial for evaluating and enhancing the care families receive in the genomic medicine era.

Harnessing CD19 CAR T Cell Therapy for Solid Tumour Treatment via a Novel Adaptor Approach

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Introduction: Chimeric antigen receptor (CAR) T cell therapy has revolutionised haematological cancer treatment but has shown limited success in solid tumours. It remains unclear whether the divergent treatment outcomes are attributable to distinct target antigens in blood versus solid malignancies.
Objective: To address the knowledge gap, we aim to perform a head-to-head comparison of CAR T cell efficacy against antigens from blood and solid cancers.

Methods and Results: To enable a fair comparison, we first generated human CARs with identical backbones against CD19 (a blood cancer antigen) or HER2 (a solid cancer antigen). We then engineered NALM6 leukaemia and MDA-MB-468 breast cancer cells to express either CD19 or HER2, creating paired antigen models within the same disease context. These human cancer cells were successfully engrafted in the mammary glands of NSG mice as solid tumours. Remarkably, CD19-CAR T cells eradicated all CD19$^+$ NALM6 and MDA-MB-468 solid tumour xenografts, while HER2-CAR T cells failed to control HER2$^+$ tumours. In comparing cell-to-cell interactions, CD19-CAR T cells demonstrated stronger binding to CD19$^+$ cancer cells, enhanced intracellular CAR signalling and higher cytotoxicity than observed with HER2-CAR T cells and HER2$^+$ cancer cells. The superior target engagement of CD19-CAR T cells *in vitro* correlated with enhanced CD19$^+$ solid tumour infiltration and clearance *in vivo*. To harness CD19-CAR T cells for solid cancer treatment, we developed a novel 'Adaptor'– a bispecific recombinant protein fusing the human CD19 extracellular domain to a HER2-specific single chain fragment variable (scFv). Excitingly, our Adaptor effectively redirected CD19-CAR T cells to suppress HER2$^+$ solid tumours in NSG mice.

Conclusions: Our findings highlight CD19 as an intrinsically superior antigen for CAR engagement and establish a promising Adaptor strategy to overcome barriers in solid cancer treatment, leveraging the clinical success of CD19-CAR T cell therapy.

On The Reproducibility and Reliability of Enrichment Analysis

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Introduction: Functional / gene set enrichment analysis involves identifying differentially regulated gene pathways from high-throughput profiling data. According to PubMed, it is one of the most used techniques in computational biology with ~ 33,358 articles with related keywords in 2023-2024. The results of enrichment analysis provide information on underlying biological processes and signaling pathways in a disease state. Despite its popularity, there are concerns around the reliability of these results.

Objective: Some critical issues related to lower reproducibility of enrichment studies include the lack of background correction in gene list analysis, lack of p-value correction when carrying out parallel tests, and a general lack of methodological details. These issues lead to statistically flawed results and studies that cannot be reproduced due to missing information. Our objective is to highlight this problem in the scientific community and work on rectifying problematic studies.

Methods and Results: In a survey done by our team, 151 enrichment articles with a Scimago Journal Rank (SJR) higher than 5 and published from 2020-2023 were checked from various high impact journals. It was found that 70% of articles did not mention the statistical tests used in their analysis, 83% articles did not specify background gene list, and ~40% articles did not use False Discovery Rate (FDR) values. Articles from respected journals like *Nature Communications, Nucleic Acid Research and Journal of Clinical Investigation* had high error rates for critical parameters. In this presentation, we will reveal the first batch of reproduction results, focusing on high-impact journal articles on single-cell RNA sequencing studies and discuss whether methodological errors have undermined their conclusions.

Conclusions: With our work, we aim to understand root causes of these problems in detail, devise solutions, develop tools and provide recommendations for performing rigorous enrichment analysis, with intentions to improve the quality of published bioinformatics research.

Evaluating the impact of COVID-19 vaccination strategies on infections and hospitalisations in Victoria in the context of non-seasonal epidemic waves

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Introduction: Despite COVID-19 having significant health impacts (16k hospitalisations, 2.5k deaths in Victoria, Australia in 2023) and an effective vaccine, booster vaccination rates have been low with the 3rd and 4th doses only reaching 50% and 25% coverage respectively. With waning vaccine immunity and ongoing waves caused by new variants, vaccination remains essential in controlling preventable infections and hospitalisations.

Objective: To assess the impact of different coronavirus disease 2019 (COVID-19) vaccination strategies on infections and hospitalisations in the context of non-seasonal epidemic waves.

Methods and Results: We used a dynamic compartmental model to compare COVID-19 infections and hospitalisations in Victoria, Australia, under the following vaccine scenarios: current vaccination rates uniformly throughout the year (~11% and 44% of 18-64 and 65+ year olds per annum); vaccine campaigns reaching similar coverage to influenza (~25% and 60% of 18-64 and 65+ year olds per annum), annually starting at the same time as the influenza vaccination rollout, August or December; doubling coverage for people under 65, maintaining current compliance with guidelines; and no further vaccination. The low baseline population level of recent COVID-19 vaccination means that any increase in coverage could reduce infection and hospitalisation incidence. Increasing COVID-19 vaccination coverage to match that of influenza vaccination with an annual vaccination campaign reduced the mean incidence of infections by 1–13% and that of hospitalisations by 3–14%, depending on the timing of vaccination campaigns with respect to the epidemic infections peak and assumptions about epidemic wave characteristics. Increasing coverage for people aged 65 years or older reduced hospitalisation incidence by 9–26% but required twice as many vaccine doses as the annual campaign strategies.

Conclusions: Annual COVID-19 vaccination campaigns at the same time as those for influenza vaccination could reduce the number of COVID-19-related hospitalisations, with lower logistical requirements than alternative approaches.

The powerhouse of fertility; a novel mitochondrial cause identified in two unrelated patients diagnosed with premature ovarian insufficiency

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Introduction: Premature ovarian insufficiency (POI) impacts ~1-3.7% of women and is characterized by absence or loss of ovarian function before the age of 40. The mitochondria are critical organelles that supply useable energy for cells, with many genes encoding mitochondrial proteins being implicated in human disease with broad aetiologies. Oocytes have a high energy demand and previous research has identified an association between reduced mitochondrial count/poor mitochondrial function and decreased reproductive potential. Next-generation sequencing (NGS) has allowed for the rapid detection of potentially causative variants in genes encoding mitochondrial proteins in patients presenting with POI. However, without functional validation, inaccurate variant curation has the potential to negatively inform patient care. This is pertinent for variants associated with mitochondrial disorders, whereby defective mitochondria have the potential to have multi-system effects.

Objective: To characterise variants in Mitofusin 1 (*MFN1*) as a potential novel cause of mitochondrial dysfunction and POI.

Methods and Results: We used whole exome sequencing and identified two unrelated patients with variants in *MFN1* who presented with clinical POI. We expressed tagged wildtype and mutant MFN1 in HeLa cells to investigate localization and mitochondrial network morphology via immunofluorescence. We also obtained patient-derived lymphoblasts and performed western blot, proteomic and mitochondrial morphology assays to determine the impact of identified variants. We identified a novel mitochondrial cause of POI, variants in

MFN1. We have observed that patient variants decrease mitochondrial fusion and proteomic analysis is consistent with western blot results demonstrating that variants destabilise MFN1 and contribute to combined oxidative phosphorylation deficiency.

Conclusions: This work identifies a novel human disease-associated gene, and a novel POI-associated gene in two unrelated individuals. It highlights the importance of mitochondrial dynamics in maintaining female reproductive potential and confirms that variants in genes encoding mitochondrial proteins should be interrogated further when identified in patients experiencing infertility.