HealtheX 2024

Celebrating Student Research

CONFERENCE PROGRAMME BOOKLET

FRIDAY, 6TH SEPTEMBER

UNIVERSITY OF AUCKLAND Waipapa Taumata Rau NEW ZEALAND

MEDICAL AND HEALTH SCIENCES

FMHS PGSA

Pacific Clinical Research NETWORK

in vitro technologies

MAURICE & PHYLLIS PAYKEL TRUST

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UNIVERSITY OF AUCKLAND Waipapa Taumata Rau NEW ZEALAND

LIGGINS INSTITUTE

Auckland Medical Research Foundation est. 1955

Message from the Deans and Directors

Tēnā koutou katoa

On behalf of Waipapa Taumata Rau | the University of Auckland, we are pleased to welcome participants and visitors to HealtheX 2024. This marks the 18th annual occasion that the Faculty of Medical and Health Sciences has had the privilege of hosting this celebration of student health research. HealtheX provides an opportunity for students from the Faculties of Science, Engineering, and Medical and Health Sciences, as well as the large-scale research institutes—Auckland Bioengineering and Liggins —to showcase their innovative research and demonstrate their research expertise

HealtheX provides a unique opportunity to showcase, in a single day, the diverse research initiatives and themes that have contributed to Waipapa Taumata Rau | the University of Auckland's ranking among the top 100 universities in the world. Of special note, Waipapa Taumata Rau has retained its position as one of the top universities worldwide for sustainability in 2024, ranked 5th in the world in the QR Sustainability rankings. HealtheX celebrates and highlights the depth of talent and dedication of our students. In so doing, HealtheX epitomizes many of the best parts of our strong, thriving research culture and emphasizes its role in improving health outcomes and sustainability for all people who live in Aotearoa New Zealand.

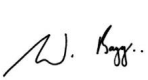
The research projects that are being presented at HealtheX in 2024 span a wide range of topics and activities, from a better understanding of the fundamentals of disease processes at the genetic and cellular levels to the application of population-based interventions and medical devices. The diversity of the research presented reflects the success of HealtheX in meeting the goals that are at the heart of the University of Auckland's strategic plan including those designed to encourage and develop professionalism in the distillation and communication of all health research.

We would like to acknowledge and thank the students and staff who collectively have ensured that HealtheX once again takes pride of place at the University of Auckland. Their efforts have ensured the success of HealtheX and reflect well the tremendous quality of the staff, students, medical and health research that is conducted across Waipapa Taumata Rau | the University of Auckland.

We would also like to acknowledge the long-standing support for HealtheX generously provided by the Auckland Medical Research Foundation and the Maurice and Phyllis Paykel Trust, as well as the support from newly established partnerships with external biomedical research-focused organizations. Without this support and encouragement, HealtheX would not have the impact and appeal it enjoys.

Finally, we encourage all participants to enjoy HealtheX 2024, which continues to be a celebration of health research excellence by your fellow students from the Faculties of Medical and Health Sciences, the Faculties of Science and Engineering, and the Auckland Bioengineering and Liggins Institutes.

Noho ora mai



Professor Warwick Bagg
Dean, Faculty of Medical and Health Sciences

Professor John Hosking
Dean, Faculty of Sciences

Professor Merryn Tawhai
Director, Auckland Bioengineering Institute

Professor Justin O'Sullivan
Director, Liggins Institute

On Behalf of the 2024 HealtheX Organising Committee

Tēnā koutou students, staff, and guests,

On behalf of the HealtheX 2024 organising committee we are honoured to welcome you to the 18th annual HealtheX Conference.

HealtheX is a student-organised and led conference designed to promote health-related research at Waipapa Taumata Rau | the University of Auckland. Founded by the FMHS PGSA in 2007, HealtheX has grown significantly and has evolved into a modern, reputable conference that reflects the excellence in student research here at Waipapa Taumata Rau.

The goal of HealtheX has always been to provide students with ample opportunities for presenting and networking, creating an environment where research can be freely discussed, new ideas can flourish, and lasting collaborations can be forged. HealtheX therefore promotes and inspires research excellence, and has become an annual celebration that is keenly anticipated and deeply embedded within the traditions of the Faculty of Medical and Health Sciences, the Liggins Institute, and the University as a whole.

As a conference organised by students, for students, the success of HealtheX 2024 is a testament to the commitment and hard work of the students and staff whose contribution continues to elevate HealtheX to greater heights. We thank our dedicated organising committee whose hard work and devotion over the past year has made this enjoyable and informative day possible.

We are also thankful for the supportive faculty academic and administrative staff for their invaluable mentorship and guidance. In particular, we would like to thank Bronwyn Staples for her continued assistance with marketing the conference, and Ian Sayer for his assistance in the technological aspects of the conference. We are grateful to all the staff and students who have given their time to help judge HealtheX 2024 and decide on the deserving winners.

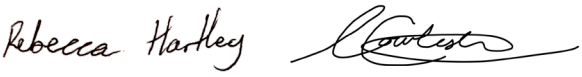
Last, but certainly not the least, the entire team of HealtheX 2024 is grateful for the trusted, continuous and generous support of the Auckland Medical Research Foundation, the Maurice and Phyllis Paykel Trust, FMHS PGSA, the Liggins Institute, and the Pacific Clinical Research Network. HealtheX is also grateful to the new collaborations with, and sponsorships by Mediray and InVitro Technologies.

We thank you all for your support, and we wish the participants the best for your presentation and future research endeavors.

Ngā mihi nui,

Rebecca Hartley and Issy Cowlishaw

HealtheX Co-Chairs 2024



HealtheX Site Map

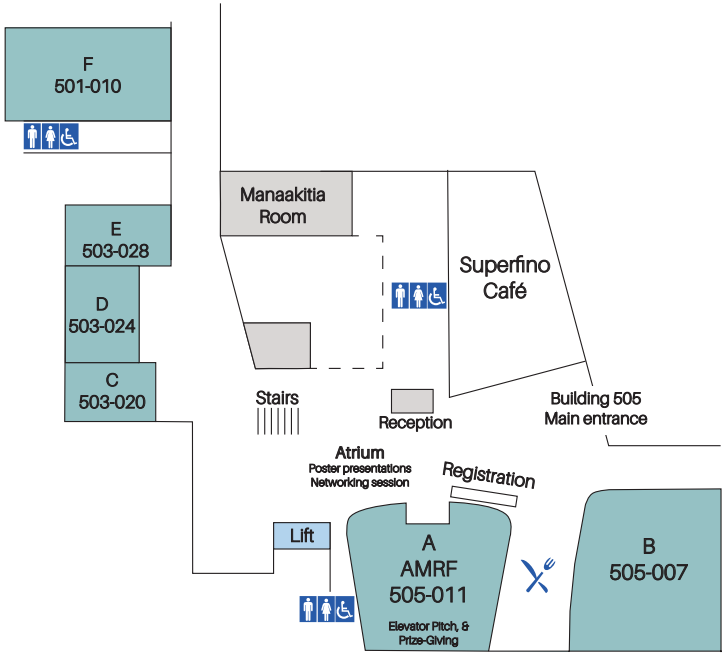
Registration - 8:30 am- 10:30 am
All judges, presenters, and invited guests are asked to register at the Registration Desk which can be found in the Grafton Atrium. This includes picking up ones' own name tag, other HealtheX items pertinent to ones' role (e.g., judging packs), and relevant HealtheX merchandise.

Lunch - 11:30 am - 13:00 pm
We cater for multiple dietary requirements for all registered judges, competitors, and invited guests. Please ensure your name tag is visible as you enter the main lunch area.

Poster Viewing - 12:15 pm - 13:15 pm
The posters of all applicants will be placed in the Grafton Atrium for the entirety of the day for viewing. However, the Poster Presenters will be asked to be present for questions from 12:15 pm - 13:15 pm.

Elevator Pitch Competition and Prize-Giving Ceremony, followed by Networking Session
Quick-fire presentations begin at 15:30 pm in the AMRF Auditorium Lecture Theatre (505-011), where 15 participants aim to summarise their message in a mere 3 minutes. This competition is the final competitive event preceding the Prize-Giving Ceremony where all participants are in the running for a share of over $17,000 in prize money.

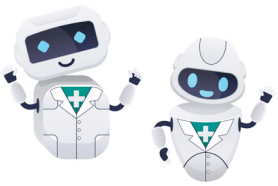
The day culminates in a catered Networking session for the entire Faculty research community to celebrate student research.



Conference Schedule

Date: Friday, 6th September
Time: 8:30 am - 6:00 pm
Location: Grafton Atrium, Grafton Campus, University of Auckland, Auckland 1023

Time	Programme					
8:30 am	Registration - Grafton Atrium					
8:55 am - 10:15 am	Oral Presentation Session 1					
	Room A 505-011 A1 - A5	Room B 505-007 B1 - B5	Room C 503-020 C1 - C4	Room D 503-024 D1 - D5	Room E 503-028 E1 - E4	Room F 501-010 F1 - F4
Break						
10:40 am - 12:00 pm	Oral Presentation Session 2					
	Room A 505-011 A6 - A10	Room B 505-007 B6 - B10	Room C 503-020 C5- C9	Room D 503-024 D6 - D10	Room E 503-028 E5 - E8	Room F 501-010 F5 - F9
11:30 am - 13:00 pm	Lunch for all Judges, Presenters, and Participants - Grafton Atrium					
12:15 pm - 13:15pm	Poster Viewing Session - Grafton Atrium					
13:25 pm - 15:00 pm	Oral Presentation Session 3					
	Room A 505-011 A11 - A13	Room B 505-007 B11- B16	Room C 503-020 C10 - C15	Room D 503-024 D11 - D14	Room E 503-028 E9 - E13	
Break						
15:30 pm - 18:30 pm	3-Minute Elevator Pitch Competition - AMRF Lecture Theatre (505-011)					
	Prize-Giving Ceremony - AMRF Lecture Theatre (505-011)					
	Networking Session - Grafton Atrium					
Event Closes						



Time	**Oral Presentations Room A -** 505-011
8:55 am	Introduction by Chairperson
9:00 am	A1 - Ashley Pereira — Supervisor: Prof. O'Grady, G Gastric Motility Responses to Heart Rate Variability Biofeedback
9:15 am	A2 - Hassan Shaaban — Supervisor: Dr. Calder, Sr Can We Measure Pathophysiology When Healthy Controls Experience Gastric Symptoms After Drinking to Maximal Satiety?
9:30 am	A3 - Bosco Yue — Supervisor: Prof. Douglas, R An investigation into the safety and anti-inflammatory effect of tofacitinib on sinonasal mucosa
9:45 am	A4 - Withdrawn
10:00 am	A5 - Baraa Abuharbid — Supervisor: Dr Marnewick, J Retrospective Audit of Thoracic Wall Injuries in the Bay of Plenty Region 2021-2023
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	A6 - Ariana Andrews — Supervisor: Dr Cormack, D How do we describe health equity? Concepts of health equity in New Zealand media discourse
11:00 am	A7 - Jingyuan Liang — Supervisor: Assoc Prof. Poppe, K Cardiovascular disease risk and preventive treatment in all New Zealanders without CVD aged 30-79 years
11:15 am	A8 - Francesca Pigatto — Supervisor: Prof. Waldie, K Cumulative risk of ACEs on depression symptoms in young people enrolled the GUINZ study
11:30 am	A9 - Courtney Brighouse — Supervisor: Dr. McBryde F Unlocking the Brain Drain in Hypertension and Diabetes
11:45 am	A10 - Withdrawn
12:15 pm	Break and Poster Viewing Session
1:25 pm	Introduction by Chairperson
1:30 pm	A11 - Yang Liu — Supervisor: Prof. Chamley, L Placental extracellular vesicles are a mechanistic link between preeclampsia and early cardiovascular mortality in women
1:45 pm	A12 - Radhika Sewram — Supervisor: Assoc Prof. Nosa, V Pasifika Women's Health and Wellbeing in Aotearoa New Zealand - A Scoping Review
2:00 pm	A13 - Eden Yin — Supervisor: Dr. Dieriks, V Global Insights into PINK1 Parkinson's Disease: A Meta-Analysis of Prevalence, Phenotypic Variability, and a-Synuclein Pathology
3:00 pm	Break
3:30 pm	3-Minute Elevator Pitch Competition - AMRF Lecture Theatre (505-011) Prize Giving Ceremony - AMRF Lecture Theatre (505-011) Networking Session - Grafton Atrium
6:30 pm	Event Closes

Time	Oral Presentations Room B - 505-007
8:55 am	Introduction by Chairperson
9:00 am	B1 - Rubina Bogati — Supervisor: Prof. Burholt, V Work or retire? What is later life like for ethnic minorities?
9:15 am	B2 - Sehar Moughal — Supervisor: Dr Eggleton, K Therapy framework for South Asian survivors of family violence – why, how and what?
9:30 am	B3 - Antonia Verstappen — Supervisor: Prof Poole, P Cultivating a primary care medical workforce for New Zealand: developing the General Practice Enhancement Model
9:45 am	B4 - Woroud Alzaher — Supervisor: Dr. Williams, S, Prof Stott, S Ageing well with cerebral palsy: experiences and adaptations through a healthy ageing lens
10:00 am	B5 - Mazyar Zarepour — Supervisor: Assoc Prof. O'Sullivan, M A Districting Model to Manage Age Residential Care Facilities for Transition to Home
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	B6 - Marguerite Sandleback — Supervisor: Dr. Astin, J Fishing for the origins of lymphatic vessels
11:00 am	B7 - Mejo Chiratteparambil Korah — Supervisor: Prof. Proft, T. Development of Vaccines against Gonococcal Disease using the PilVax Platform
11:15 am	B8 - Withdrawn
11:30 am	B9 - Linh Do — Supervisor: Assoc Prof. Misra, S HbA1c and white blood cells in diabetic macular oedema development: The systemic review and meta-analysis
11:45 am	B10-Danica Hamlin — Supervisor: Dr. Murray, H Characterising Cis Tau Pathology in Chronic Traumatic Encephalopathy
12:15 pm	Break and Poster Viewing Session
1:25 pm	Introduction by Chairperson
1:30 pm	B11 - Withdrawn
1:45 pm	B12 - Amanda Groenewald — Supervisor: Dr. Ward , M Cardiac Dysfunction Following Acute Exposure to Clozapine and Sodium Valproate
2:00 pm	B13 - Harrison Porritt — Supervisor: Assoc Prof. Malmstrom, J Hydrogels to help model stem cell derived cardiac disease models
2:15 pm	B14- Stian Thomson — Supervisor: Dr. Shanks, J Examining Vagal Regulation of Cardiac Function Using Directly Recorded Vagus Nerve Activity in Conscious Sheep
2:30 pm	B15-Sophie Piesse — Supervisor: Assoc Prof. Barrett, C Enduring impacts of placental extracellular vesicles on the maternal cardiovascular system in spontaneously hypertensive rats
2:45 pm	B16- Aatika Prasad — Supervisor: Dr Martini,N Adherence to iron deficiency treatment guidelines in heart failure patients
3:00 pm	Break
3:30 pm	3-Minute Elevator Pitch Competition - AMRF Lecture Theatre (505-011) Prize Giving Ceremony - AMRF Lecture Theatre (505-011) Networking Session - Grafton Atrium
6:30 pm	Event Closes

Time	Oral Presentations Room C - 503-020
8:55 am	Introduction by Chairperson
9:00 am	C1 - Jamie Hyde — Supervisor: Dr. Handley, R Huntington's disease as a whole-body syndrome? Investigating molecular mechanisms of liver pathogenesis in Huntington's disease
9:15 am	C2 - Stephanie Carr — Supervisor: Dr Singh-Bains, M Characterising microgliosis in the post-mortem human Huntington's disease neocerebellum
9:30 am	C3 - Khushi Sehajpal — Supervisor: Dr Singh-Bains, M Characterisation of the substantia nigra in post-mortem cases of X-linked Dystonia Parkinsonism
9:45 am	C4 - Withdrawn
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	C5 - Linh Nguyen — Supervisor: Prof. Connor, B Small molecule TrkB agonists enhance the generation of striatal neurons.
11:00 am	C6 - Brooke Hawker — Supervisor: Dr. McCaughey-Chapman, A Transforming Treats into Tools: Cuprizone-Peanut Butt er to Model Demyelination in Mice
11:15 am	C7 - Conor Nelson — Supervisor: Assoc Prof. Young, D An immunotherapeutic approach to modifying disease progression in the YAC128 mouse model of Huntington's Disease
11:30 am	C8 - Thai Nguyen — Supervisor: Assoc Prof. Young, D Functionality analysis of a novel molecular switch in YAC128 transgenic mouse model of Huntington's disease
11:45 am	C9 - Aimee Mills — Supervisor: Dr Mugisho, L Targeting Connexin Hemichannels and the Inflammasome pathway in an acute mouse model of Alzheimer's Disease
12:15 pm	Break and Poster Viewing Session
1:25 pm	Introduction by Chairperson
1:30 pm	C10 - Jean Yu Lim — Supervisor: Dr Smith, A Investigating the Role of Microglial Dysfunction in Alzheimer's Disease: Regulation of GPNMB Expression
1:45 pm	C11 - Jack Sloan — Supervisor: Prof. Mcbryde, F The Sympathetic Brain Drain
2:00 pm	C12 - Hannah Dexter — Supervisor: Assoc Prof. Dean, J Protective effects of intravenous apigenin infusion in a preterm fetal sheep model of hypoxic-ischemic enceph-alopathy
2:15 pm	C13- Sarah Gray — Supervisor: Dr. Jacobs, S Supporting Our Mental Health Nurses to Thrive at Work
2:30 pm	C14-Melanie Stowell — Supervisor: Dr. Dobson, R Digital tools to support mental health in later life: Scoping review of systematic reviews
2:45 pm	C15- Natalie Poša — Supervisor: Dr Stasiak,K Exploring the acceptability and safety of integrating AI capabilities into a youth mental wellbeing app
3:00 pm	Break
3:30 pm	3-Minute Elevator Pitch Competition - AMRF Lecture Theatre (505-011) Prize Giving Ceremony - AMRF Lecture Theatre (505-011) Networking Session - Grafton Atrium
6:30 pm	Event Closes

Time	Oral Presentations Room D - 503-024
8:55 am	Introduction by Chairperson
9:00 am	D1 - Afifa Safdar — Supervisor: Prof Stinear, C Biomarkers to target non-invasive brain stimulation in chronic stroke
9:15 am	D2 - Sachin Sood — Supervisor: Dr Sidhu, N Inadequate Neuraxial Anaesthesia During Caesarean Section: A Single-Institution Retrospective Cohort Study
9:30 am	D3 - Christopher Carson — Supervisor: Dr. Freestone, P Characterisation of Substantia Nigra pars Lateralis' Firing Patterns by Subthalamic Nucleus Stimulation
9:45 am	D4 - Briony Fanslow — Supervisor: Dr. Paynter J. Burden and seasonality of Influenza- and Human metapneumovirus-associated adult hospitalisations in Aotearoa New Zealand
10.00 am	D5 - Kelly Peterken — Supervisor: Dr Radcliff, F Investigating the addition of a novel TLR2 agonist to a S. aureus polyvalent protein vaccine
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	D6 - Ashok David Jose — Supervisor: Dr Thakur, S Development and evaluation of an oxygen microbubble hydrogel for sensitisation of cancer cells to radiotherapy
11:00 am	D7 - Yohanka Perera — Supervisor: Dr. Nolan, E Establishing 3D tumour models for breast cancer: a unique, New Zealand-specific tool for cancer research
11:15 am	D8 - Kamel Ahmed — Supervisor: Prof. Wu, Z Hyaluronic Acid-Functionalised pH-Responsive Liposomes for Targeted Chemotherapy Delivery to Breast Cancer Stem Cells
11:30 am	D9 - Claire Palma — Supervisor: Dr. Singleton, D PHD Inhibition Induces Antiproliferative Effects in Melanoma through HIF-1a Stabilisation
11:45 am	D10 - Olivia Hogan — Supervisor: Dr. Tomek, P Deciphering the mystery of arylformamidase' involvement in immunosuppressive kynurenine production in cancer
12:15 pm	Break and Poster Viewing Session
1:25 pm	Introduction by Chairperson
1:30 pm	D11 - Libby Lord — Supervisor: Distinguished Prof. Harding, J Intergenerational effects of antenatal corticosteroid exposure
1:45 pm	D12 - Michael Beacom — Supervisor: Prof. Bennet, L Non-linear quantitative EEG measures: Biomarkers for evolving fetal brain injury
2:00 pm	D13 - Tayla James — Supervisor: Assoc Prof James, J The role of placental macrophages in impaired placental vascular function in Fetal Growth Restriction
2:15 pm	D14 - Abbey Lissaman — Supervisor: Dr. Ponnampalam, A Stromal secrets – understanding endometrial stromal cell hormone responses and their dysregulation in endometriosis
3:00 pm	Break
3:30 pm	3-Minute Elevator Pitch Competition - AMRF Lecture Theatre (505-011) Prize Giving Ceremony - AMRF Lecture Theatre (505-011) Networking Session - Grafton Atrium
6:30 pm	Event Closes

Time	Oral Presentations Room E - 503-028
8:55 am	Introduction by Chairperson
9:00 am	E1 - Courtney Thorne — Supervisor: Assoc Prof. Lim, J Bovine lenses as a model for diabetic cataract: assessing metabolic changes in hyperglycaemia
9:15 am	E2 - Samuel James — Supervisor: Assoc Prof. Mellor, K Diabetic cardiomyopathy is characterised by dysregulated glycogen-autophagy and lysosomal glucose handling
9:30 am	E3 - Ibrahim Mohamed — Supervisor: Assoc Prof. Miles-Chan, J Evaluating Feijoa for Diabetes Prevention: FERDINAND study
9:45 am	E4 - Borson Wong — Supervisor: Assoc Prof. Mellor, K Targeting cardiac fructose metabolism in diabetic cardiomyopathy in mice
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	E5 - Santosh Bhujbal — Supervisor:Dr. Agarwal, P Formulation and characterization of transfersomes for ocular drug delivery
11:00 am	E6 - Nikhil Nair — Supervisor: Prof. Donaldson, P The role of Aquaporin 0 in the regulation of lens hydrostatic pressure
11:15 am	E7 - Crystal Tan — Supervisor: Dr Vorontsova, I Zebrafish Lens Anterior Suture Development: A Critical Piece in the Puzzle of Zebrafish Optical Development
11:30 am	E8 - Clare Gebbie — Supervisor: Prof. O'Sullivan, J Rapid Long Read Sequencing for the Diagnosis of Rare Disease
11:45 am	E9 - Anna Behling — Supervisor: Prof. O'Sullivan, J Matching bacterial strains to predict donor-recipient pairings in FMT
12:15 pm	Break and Poster Viewing Session
1:25 pm	Introduction by Chairperson
1:30 pm	E10 - Carina Donegan — Supervisor: Dr. Reynolds, L Set and setting the stage: Expectancies of individuals with MDD about to microdose LSD
1:45 pm	E11 - Ben Moloney — Supervisor: Dr Lin, J Developing neuroinflammation biomarkers to assess the antidepressant effects of naltrexone in major depressive disorder
2:00 pm	E12 - Dimitri Daldegan-Bueno — Supervisor: Dr. Muthukumaraswamy, S LSD microdosing in patients with major depressive disorder: results from an open-label trial.
2:15 pm	E13 - Katerina Gerasimenko — Supervisor: Prof. Tippett L Impacts of Friedreich's Ataxia on Well-being, Mood and Social Cognition
3:00 pm	Break
3:30 pm	3-Minute Elevator Pitch Competition - AMRF Lecture Theatre (505-011) Prize Giving Ceremony - AMRF Lecture Theatre (505-011) Networking Session - Grafton Atrium
6:30 pm	Event Closes

Time	Oral Presentations Room F - 501-010
8:55 am	Introduction by Chairperson
9:00 am	F1 - Xin Yi Lim — Supervisor: Prof. Barnes, J Pharmacovigilance and the natural health products (NHPs) industry: a scoping review.
9:15 am	F2 - Po-Yi Lue — Supervisor: Dr. Suzuki-Kerr, H Characterisation of sheep cochlea: translational platform for developing inner ear therapeutic
9:30 am	F3 - Saptorshi Gupta — Supervisor: Dr Thornley, S Global spatial-temporal trends in scabies prevalence (1990-2021): results from the Global Burden of Disease study
9:45 am	F4 - Estelle Miller — Supervisor: Dr Ponton, R Psychedelic Microdosing in Aotearoa
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	F5 - Catriona Miller — Supervisor: Prof. O'Sullivan, J Autism prediction using sex-dependent common variation
11:00 am	F6 -Andrew Holmes — Supervisor: Dr. Schierding, W Machine/Deep Learning to Identify Novel Clinical Risk Factors for Glaucoma
11:15 am	F7- Chaiquan Li — Supervisor: Assoc Prof. Poppe, K Using natural language processing and machine learning to categorise text-based cardiovascular death
11:30 am	F8 - Withdrawn
11:45 am	F9 - Enzo Allevard — Supervisor: Dr Choisne, J Tibia and fibula bones prediction from external shank skin shape in a paediatric population
12:15 pm	Break and Poster Viewing Session
3:00 pm	Break
3:30 pm	3-Minute Elevator Pitch Competition - AMRF Lecture Theatre (505-011) Prize Giving Ceremony - AMRF Lecture Theatre (505-011) Networking Session - Grafton Atrium
6:30 pm	Event Closes

Poster Session - Grafton Atrium	
P1 - Xin Yi Lim	Supervisor: Prof. Barnes, J
Consumers' views on pharmacovigilance for natural health products: preliminary findings from a qualitative interview study.	
P2 - Amelie Back	Supervisor: Dr. McCaughey-Chapman, A
Using Directly Reprogrammed Patient-Derived Oligodendrocytes to Model Huntington's Disease	
P3 - Jess Kelly	Supervisor: Prof. Connor, B
Novel Three-Dimensional Brain Organoids for Modelling Huntington's Disease.	
P4 - Harpinder Brar	Supervisor: Dr Sharma, M
Polymeric micelles for nose-to-brain delivery of Crizotinib-IR786 conjugate in the treatment of Glioblastoma	
P5 - Mikayla Chetty	Supervisor: Dr Smith, A
The effects of an impaired blood-brain barrier on microglial phenotype in Alzheimer's Disease	
P6 - Nathaniel Singleton	Supervisor: Dr O'Carroll, S
The Influence of Oxidative-Stress Induced Neuroinflammation on Bach2 Gene Expression in Rodent Glial Cells	
P7 - Kaya Girdlestone	Supervisor: Dr O'Carroll, S
Targeting hypoxia-ischemia damage in astrocytes via kinase inhibition in a model of spinal cord injury.	
P8 - Angeline van Kuilenburg	Supervisor: Assoc Prof. Dean, J
Assessment of the developing white matter in the neonatal rat using advanced magnetic resonance imaging	
P9 - Catriona Miller	Supervisors: Prof. O'Sullivan, J
Linking causal ADHD genes to co-occurring conditions	
P10 - Hailey Yoon	Supervisor: Dr. Grimsey, N
The Role of Cannabinoid Receptor 2 in Interferon-γ Stimulated Human Macrophage Function	
P11 - Malak Alshakhouri	Supervisor: Dr Sumner, M
Investigating the Neurosteroid Withdrawal Hypothesis of Catamenial Epilepsy in Humans using Visually Induced Gamma Oscillations	
P12 - Liam Zhang	Supervisor: Dr. Ward, M
Comparison of Human Atrial Tissue Composition between Diabetic and Non-Diabetic Patients	
P13 - Dilsha Gimhani	Supervisor: Assoc Prof. Ramchandra. R
The Abundance and Morphology of the Cardiac Lymphatic Vasculature in Sheep with HFpEF	
P14 - Simone Watkins	Supervisor: Prof. Bloomfield, F
Factors Associated with Critical Congenital Heart Disease Mortality: A National Cohort Study	
P15 - Ben Buttle	Supervisor: Dr Sheppard, H.
Generating T-cells for Cancer Immunotherapy Using Advanced Gene Editing Tools	
P16 - Janneke Grundemann	Supervisors: Dr. Nolan, E
Friend or Foe: Deconstructing cancer-immune interactions using patient-derived tumour models	
P17 -Sophia O'Brien-Gortner	Supervisor: Assoc Prof. Hay, M
Evaluation of new DNA-dependent protein kinase inhibitors as radiosensitisers of head and neck cancer cells	
P18 -Queenie Young	Supervisor: Assoc Prof. Jamieson, S
Tackling Resistance to HER2-Targeted Antibody-Drug Conjugates in Breast Cancer	

Poster Session - Grafton Atrium	
P19 - Ashton Machado	Supervisor: Prof. Helsby, N
Assessing dihydropyrimidine dehydrogenase dimer formation as a technique to understanding missing factors within 5-fluoro-uracil-related toxicity.	
P20 - Ben Watkin	Supervisor: Dr Rustenhoven, J
Novel Generation of iPSC-Derived Lymphatic Endothelial Cells for Functional Assays	
P21 - Xini Puah	Supervisor: Dr. Kalev, M
A Novel Synthetic Hydrogel for Studying Megakaryocytic Differentiation and Bone Marrow Fibrosis	
P22 - Leilei Xu	Supervisor: Dr. Poulsen, R
Phenotypic difference of osteoblasts isolated from macroscopically normal or osteoarthritic zones in hip versus knee	
P23 -Greer Pugh	Supervisor: Dr. Fisher, J
Understanding standing… Exploring vascular properties in Postural Orthostatic Tachycardia Syndrome (POTS)	
P24 - Antalya Stevens	Supervisor: Prof. Broadbent, E
Embodiment in Health Communication: Harnessing Patient Posture to Optimise Recall of Health Information	
P25 - Genevieve Boom	Supervisor: Dr Cree, L
Developing a SERS surface for analysis of small extracellular vesicles	
P26 - Janice Yeoman	Supervisor: Assoc Prof. Misra, S
Optometrists' and ophthalmologists' views on the utility of scleral shell prostheses for disfigured eyes	
P27 - Aleisha Carter	Supervisor: Prof. Helsby, N
Characterising the effect of Proton Pump Inhibitors on the Cellular Uptake of Pyrimidine Nucleosides.	
P28 - Emily Caldelari-Hume	Supervisor: Assoc Prof. Wiles, S
Investigating the consequences of experimental evolution of the mouse enteropathogen Citrobacter rodentium using deletion mutants	
P29 -Kate Pennycuick	Supervisor: Assoc Prof. Lott, S
RNase HI as a drug target in Neisseria gonorrhoeae	
P30 -Ishana Ratti	Supervisor: Dr. Dawes, S
Investigating the role of the CobC domain in promoting RNase HI function in Mycobacterium tuberculosis	
P31 -Saptorshi Gupta	Supervisor: Dr Thornley, S
Prevalence and determinants of scabies: a global systematic review and meta-analysis	
P32 -Angelina Soh	Supervisor: Assoc Prof. Dean, J
Effects of targeting hyaluronidase enzymes following hypoxic-ischemic brain injury in the preterm fetal sheep	
P33 -Claire O'Shea	Supervisor: Assoc Prof. Ramke, J
Have services for diabetes, eye, hearing, foot health been integrated for adults? A scoping review.	
P34 -Audrey Zhu	Supervisor: Dr Roberts, R
Bandpass filtering changes the correlations between age and Blood Oxygen Level-Dependent (BOLD) variability	
P35 -Zara Collins	Supervisor: Assoc Prof. James, J
Characterisation of the placental glycocalyx throughout gestation and in fetal growth restriction	

Poster Session - Grafton Atrium	
P36 - Grace Donaldson	Supervisor: Dr Cree, L
Development of a Non-Invasive Embryo Quality Evaluation Tool for Equine Embryos	
P37 - Tram Bui	Supervisor: Dr. Toldi, G
The impact of short-chain fatty acids on Tregs and T cell proliferation in neonates	
P38 - Ayamita Paul	Supervisor: Dr. Toldi, G
Optimisation of T cell Isolation from Human Milk	
P39 -Elisa Weiss	Supervisor: Dr. Musson, D
The Impact of Western-Style Parental Diet on Offspring Metabolic Health: Initial Parental Phenotype	
P40 - Flora Lam	Supervisor: Assoc Prof. Davidson, J
Neuroprotective effects of progesterone given before hypoxia ischemia in near-term fetal sheep	
P41 - Anja Bronnert	Supervisor: Prof. Bloomfield, F
Vitamins for preterm infants	
P42 - Anmol Sandhu	Supervisor: Prof. Sherwin, T
Evaluating Barrier Function in Differentiated Human Umbilical Vein Endothelial Cells for Corneal Endothelial Cell Therapy	
P43 - Lilia Delgado Paramo	Supervisor: Prof. Bloomfield, F
Does exposure to the smell and taste of milk accelerate feeding in preterm infants?	
P44- Dansoa Tabi-Amponsah	Supervisor: Prof. Dalbeth, N
Evaluating gout remission definitions in a randomized controlled trial: Nurse-led versus usual-care.	

3-Minute Elevator Pitch Competition - AMRF Lecture Theatre (505-011)	
EP1 - Yevetta Xiang	Supervisor: Dr. Hall, C
Exploring how the liver circadian clock regulates the host response to infection	
EP2 - Cristal Salatas	Supervisors: Prof. Bloomfield, F
Investigating and mapping the factors associated with preterm birth in New Zealand: cross-sectional geospatial study	
EP3 - Megan Kemp	Supervisor: Prof. Harrison J
Determining the optimal approach to initiating lithium in acute mania: A clinical pharmacokinetic approach	
EP4 - Duy Nguyen	Supervisor: Prof. Bohlander, S
Mutational analysis of the gene DDX41 in myelodysplastic syndromes and acute myeloid leukaemia	
EP5 - Jonathan Zong	Supervisor: Dr. Forsyth, A
Investigating EEG-Derived Biomarkers of Major Depressive Disorder: Lempel-Ziv Complexity, Spectral Power and Peak Alpha Frequency	
EP6 - Meiliana Meiliana	Supervisor: Distinguished Prof. Harding, J.
Minimum reporting set for measures of nutrition and growth in preterm studies: A Delphi study	
EP7 - Suci Hermita	Supervisor: Dr. Ramzan, F
Kawakawa and Its Antidiabetic Effects: A Mechanistic Approach	
EP8 - Mariam Alhilali	Supervisor: Prof. Bohlander, S
Optimising MRD-Seq: an improved method for measurable residual disease detection in acute myeloid leukaemia	
EP9 - Holly Wilson	Supervisor: Assoc Prof Chan, A
If they had actually listened to me Identifying patients at risk of hospital readmissions	
EP10 - Muna Dhakal	Supervisor: Assoc Prof.Young, D
Reducing the construction load: Nurr1 variants as switch for viral vector therapy for Parkinson's disease	
EP11 - Mary Spring	Supervisor: Assoc Prof. James, J
The impact of fetal sex on placental vascular development and function in fetal growth restriction.	
EP12 - Michael Ng	Supervisor: Prof Connor, B
The role of Hap1 and Rhes in mediating selective striatal cell loss in Huntington's Disease.	
Followed by the Prize-Giving Ceremony - AMRF Lecture Theatre (505-011) Networking Session - Grafton Atrium	

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Jess Kelly, 2023 HealtheX winner says:

"This award means a lot for several reasons. Firstly, it is amazing recognition of my capability in the research field and my ability to communicate the work I am so passionate about to other people, including those not in my field. This is extremely validating and rewarding. Secondly, this travel grant is going to make it possible for me to attend the International Society for Stem Cell Research Conference in Hamburg, Germany, in 2024, to present a poster on my work. This will be my first international conference and is a great stage to be able to share my work and network with others in my field from all over the world. Without this award, this travel would be extremely challenging to fund, and so I am very grateful to AMRF."

Julia Plank, 2022 HealtheX winner says:

"I am honoured to receive this award from AMRF. The standard of presentations at HealtheX is always very high so I am really pleased that my presentation struck a chord with the audience. Doing a PhD is a long and arduous journey so it means a lot to have this affirmation from AMRF. Moreover, I am very grateful to receive this funding so that I can present my results at an international conference in my final year of my PhD."

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HealtheX greatly appreciate the assistance of Faculty of Medical and Health Sciences, Liggins Institute, Mediray, Pacific Clinical Research Network, FMHS Postgraduate Student Association and In Vitro Technologies in the funding and staging of HealtheX 2024

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HealtheX would not be possible without the help of all our generous supporters, mentors, volunteers

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Celebrating Student Research

FRIDAY, 6TH SEPTEMBER

ABSTRACTS

Oral Presentation Room A

9:00 : Ashley Pereira

Gastric Motility Responses to Heart Rate Variability Biofeedback

Pereira A[1], Varghese C[1], Xu W[1], Fu L[1], Law M[1,2], Wallace I[1,2], Gharibans A[1,2,3], Calder S[1,2,3], O'Grady G[1,2,3]

[1] Department of Surgery, The University of Auckland, [2] Alimetry Ltd, Auckland, [3] Auckland Bioengineering Institute, The University of Auckland.

Background: Functional Gastrointestinal Disorders (FGIDs), also known as Disorders of Gut-Brain Interaction (DGBIs), lack identifiable physiological causes, posing significant diagnostic and treatment challenges. Dysregulation of the autonomic nervous system (ANS) is hypothesised to influence FGID incidence. Heart rate variability biofeedback (HRVB), a non-invasive therapy, uses real-time feedback to enhance heart rate oscillations and improve ANS regulation. This pilot study examines whether HRVB can improve gut function and alleviate FGID symptoms by enhancing ANS regulation. **Objectives**: The primary objective is to assess HRVB's impact on gastric function in patients with functional dyspepsia or chronic nausea and vomiting syndrome. Secondary objectives include evaluating changes in gastric symptoms, psychological well-being, and quality of life. **Methods**: Patients with functional dyspepsia or chronic nausea and vomiting syndrome practice HRVB daily for six weeks. A systematic scoping review defined optimal HRVB protocols. Changes in gastric function are assessed using Body-Surface Gastric Mapping (BSGM). Secondary outcomes are measured through validated symptom tracking, psychological assessments, and quality of life questionnaires. **Results**: The scoping review identified 4 relevant articles out of 1013 screened, with 2 studies showing HRVB efficacy on gastrointestinal symptoms after more than 6 weeks of therapy. These findings informed the study design. Approved by the Health and Disability Ethics Committees (HDEC), this clinical pilot study is currently collecting data, expected to complete by September 2024. **Discussion**: This study explores the link between ANS regulation and FGIDs, aiming to provide evidence that HRVB can improve gastric function, symptoms, and overall well-being in affected patients.

Main Supervisor: Professor Greg O'Grady

9:15 : Hassan Shaaban

Can We Measure Pathophysiology When Healthy Controls Experience Gastric Symptoms After Drinking to Maximal Satiety?

Shaaban H[1, 2], Varghese C[1, 2], Schamberg G[1, 2], Wallace I[2], Law M[2], Andrews C[4], Gharibans A[1, 2, 3], O'Grady G[1, 2, 3], Calder S[1, 2]

[1]Department of Surgery, University of Auckland, New Zealand, [2]Alimetry Ltd, Auckland, New Zealand, [3]Auckland Bioengineering Institute, University of Auckland, New Zealand, [4]Department of Gastroenterology, University of Calgary, Canada

Background: Chronic gastroduodenal symptoms afflict >10% of the global population, imposing significant personal, social and economic burdens. The underlying mechanisms for disorders of gut-brain interactions (DGBIs) remain elusive. Suggested plausibility criteria for uncovering putative pathophysiological mechanisms in DGBIs include the ability to induce symptoms in healthy controls by provoking transient pathophysiological responses. **Objectives:** To induce gastric distention causing transient gastric myoelectrical abnormalities that correlate with symptomology in healthy controls, measured via Gastric Alimetry® (GA). **Methods:** 20 healthy controls completed a body surface gastric mapping (BSGM) test using GA, which non-invasively measures gastric myoelectrical activity (via spectral outputs) and symptomatology. A standardised liquid nutrient drink test (LNDT) was simultaneously administered, consuming 30ml/min of Ensure® until maximally satiated. **Results:** Preliminary findings: 65% of the healthy controls had transient spectral abnormalities that correlated with the severity of symptoms (qualitative). Increased principal gastric frequency was associated with both increased upper gut pain (β = 0.76, 95% CI 0.04-1.49, *p = 0.039*) and increased total symptom burden during the drink period *(β = 7.65, 95% CI 0.01-15.29 p = 0.05)*. A subgroup of subjects showed induced gastric dysrhythmias that correlated with symptoms (β = -9.41, 95% CI -16-91–1.9, *p = 0.016*). **Discussion:** GA measured LNDT-induced gastric pathophysiology that correlated with symptoms, likely associated with gastric distension. These findings support GA's ability to detect putative pathophysiology in DGBIs. This can improve DGBIs stratification, allow for targeted therapy, and reduce the patient and the healthcare system burden.

Primary Supervisor: Dr. Calder, S

9:30 : Bosco Yue

An investigation into the safety and anti-inflammatory effect of tofacitinib on sinonasal mucosa

Yue B[1], Hale S[1], Broderick D[1], Biswas K[1], Kim R[1], Douglas R[1]

[1] Department of Surgery, University of Auckland

Background: Chronic rhinosinusitis (CRS) affects 10% of the global population. It is characterised by chronic mucosal inflammation of the nasal cavity and paranasal sinuses. Some CRS patients respond poorly to corticosteroid-based agents. The Janus kinase (JAK) inhibitor tofacitinib may be an effective topical treatment due to its regulatory effect on proinflammatory cytokine signalling. **Objectives:** To determine tissue viability, epithelial structural changes and genetic expression of proinflammatory cytokines after the topical application of tofacitinib onto sinonasal mucosa. **Methods:** Sinonasal mucosa was obtained from 10 patients during sinus surgery (6 CRS, 4 non-CRS). Tissue samples were cut into standardised tissue samples using a 3mm biopsy punch. These samples were incubated in either control media, fluticasone 0.005 mg/mL, or tofacitinib 0.1 mg/mL for twenty-four hours. A resazurin viability assay, histological assessment, and quantitative polymerase chain reaction assay for JAK-related gene expression were performed at baseline and after incubation. **Results:** Treatment groups showed no difference in tissue viability or epithelial structure after incubation. Suppression of the JAK-related regulatory genes SOCS1 ($p=0.0298$) and SOCS3 ($p=0.0047$), and the downregulation of the Th2-differentiation-related gene GATA3 ($p=0.0077$) were observed following tofacitinib exposure to CRS tissue. **Discussion:** Our results demonstrate topical tofacitinib maintains tissue viability, epithelial structure, and inhibits JAK-mediated inflammatory signalling in sinonasal mucosal tissue. This suggests tofacitinib's potential as a safe and effective topical therapeutic agent for CRS. To establish its safety profile further, investigations into tofacitinib's effects on epithelial ciliary function are warranted.

Primary Supervisor: Prof. Richard Douglas

9:45 : Withdrawn

10:00 : Baraa Abuharbid

Retrospective Audit of Thoracic Wall Injuries in the Bay of Plenty Region 2021-2023

Abuharbid B[1], Marnewick J[2,3], Shannon S[2,3]

[1]Department of Medicine, University of Auckland, [2]Tauranga Hospital, [3]Midland Trauma Service

Background: Trauma is the leading cause of death and disability in people under 45 years worldwide. In Aotearoa, nearly 60% of major trauma patients sustained thoracic wall injuries (TWI) in the past six years. Over 1500 TWIs were recorded in the Bay of Plenty region across 2020 and 2021. The high avoidable complication and readmission rates indicated potential management inadequacies, prompting introduction of a new management protocol in Nov-2022. This protocol incorporates relevant patient background and TWI details to generate a score that guides subsequent analgesia, care setting, and established a new patient follow-up service. **Objectives:** To evaluate TWI prevalence and management in the Bay of Plenty and assess the efficacy of the new management protocol. **Methods:** Patient data from Jan-2021 to Nov-2023 was gathered retrospectively and divided into pre-protocol (Jan-2021 to Nov-2022) and post-protocol (Nov-2022 to Nov-2023) cohorts. This data included TWI type and severity, anticoagulation use, chronic lung disease status, admitted hospital, ICU contact, length of stay, pain management (basic or advanced), and readmission rates. **Results:** Across 868 total patients, 657 presented during the pre-protocol period, and 211 post-protocol. Post-protocol, complications decreased by 59%, and hospital re-admissions within two weeks of injury halved, relative to the pre-protocol cohort. Advanced pain management was offered to 51% of post-protocol patients, and 66 patients were referred to the new follow-up service. **Discussion:** This audit has found improved TWI outcomes following new protocol implementation, reducing pain severity and hospital re-presentations, thereby alleviating the individual and societal burden of TWIs.

Primary Supervisor: Mr. Marnewick, J

10:45 : Ariana Andrews

How do we describe health equity? Concepts of health equity in New Zealand media discourse

Andrews A[1], Cormack D[1]
[1]Te Kupenga Hauora Māori

Background: Health equity holds relevance for Māori health and the health of other marginalised and oppressed groups. Despite the rising prominence of health equity discourse, its frequent appearance in government documents and its corresponding impetus for action, Māori health inequities persist. **Objectives:** To understand how health equity was conceptualised in news articles published in New Zealand media during the first Covid-19 lockdown. Implications for Māori health advancement and the elimination of health inequities will also be considered. **Methods:** Research was informed by Kaupapa Māori and Black Feminist theories and conducted using critical discourse analysis. News articles published between 25 March and 27 April 2020 were collected from the Newztext Plus database using search terms related to health, equity and Covid-19. **Results:** Of the 454 articles identified, 95 were duplicates and 319 did not have a strong focus on health equity. The 40 remaining articles were included in analysis. Much of the discourse focused on the avoidable nature of health inequities and sought to compel action to prevent future inequities. When health inequities were situated as the result of structural factors, focus often remained on proximal factors such as housing and poverty, with infrequent discussion of foundational causes such as racism and colonialism. **Discussion:** Conceptualisations of health equity inform the types of measures that will be implemented to address inequities and their urgency, resourcing, and implementation. Discourses that shift focus away from foundational causes of inequities can lead to responses that may reduce inequities but are unlikely to eliminate them.

Primary Supervisor: Dr. Cormack, D

11:00 : Jingyuan Liang

Cardiovascular disease risk and preventive treatment in all New Zealanders without CVD aged 30-79 years

Liang J[1], Jackson R[1], Wells S[1], Choi Y[1], Li C[1], Poppe K[1,2]
[1]School of Population Health, [2]School of Medicine

Background: Cardiovascular disease (CVD) risk assessment is recommended by New Zealand national guidelines to reduce the burden of CVD by identifying high-risk individuals for targeted prevention. **Objectives:** To quantify predicted CVD risk and preventive medication treatment by risk categories and determine whether there are risk management gaps. **Methods:** De-identified individual-level linkage of national administrative health datasets included almost every New Zealander (2,660,771) without CVD, heart failure, or severe renal disease, aged 30-79 years in 2023. Five-year CVD risk was calculated using sex-ethnic-specific risk prediction equations derived from demographics, disease history and medications, and was categorised using nationally recommended cut-offs: low (<5%), moderate (5-14%) and high (≥15%). **Results:** Five-year CVD risk increased with age and was higher in men than women. The median (IQR) 5-year CVD risk was 1.2% (0.4-3.7%) in women and 2.6% (1.1-6.6%) in men. Among women, 81%, 17% and 2% were categorised at low-, moderate- and high-risk, respectively, and corresponding figures for men were 68%, 26% and 6%. Māori had approximately twice the proportion with CVD risk ≥15% as Europeans (7% vs 4%). Among those with high-CVD-risk, only 38% of women and 37% of men were receiving recommended dual blood pressure- and lipid-lowering medications. **Discussion:** About 4% of the total national primary prevention population (7% of Māori) aged 30-79 years had a 5-year CVD risk of ≥15% in 2023. Over 60% of high-risk-individuals were not receiving the recommended combination blood pressure- and lipid-lowering treatment, suggesting a substantial and inequitable CVD risk and risk management gap in clinical practice.

Primary Supervisor: Assoc Prof. Poppe K

11:15 : Francesca Pigatto

Cumulative risk of ACEs on depression symptoms in young people growing up *in New Zealand*

Pigatto F[1], Grant C[2,3], Marks E[1], Walker C[1], Fletcher B[4], Waldie K[5]

[1]School of Population Health, The University of Auckland, [2]Department of Paediatrics: Child & Youth Health, School of Medicine, The University of Auckland, [3]General Paediatrics, Starship Children's Hospital, [4]Social and Community Health, The University of Auckland, [5]School of Psychology, The University of Auckland

Background*:* The prevalence of depression in young people has increased markedly over the last decade. Identifying adverse childhood experiences (ACEs) associated with depression may help refine early interventions reducing such condition. **Objectives**: Develop a predictive model to identify young people at increased risk for depression symptoms. **Methods:** The study included 4563 participants from the Growing Up in New Zealand (*GUiNZ)* longitudinal study who completed a questionnaire on depression symptoms at age 12 years (Centre for Epidemiological Studies Depression Scale for Children (CESD-10). A Cumulative Risk (CR) score was created to assess the combined effect of multiple ACEs on depression symptoms. The CR score was calculated by combining ACEs identified at ages 4.5 and eight years that were significantly associated with depression symptoms. Three categories were created, and their association with depression symptoms at age 12 years was investigated in univariable level and multivariable analyses, controlling for multiple covariates. **Results***:* Overall, 31.6% (*n*=1443) of our sample did not report any ACEs (no risk CR), 53.8% (*n*=2455) were exposed to one or two ACEs (low CR score), and 14.6% (*n*=655) to three or more ACEs (high CR). In the adjusted analysis, exposure to the low and the high CR scores was associated with higher depression scores (B 1.16, p <.0001; and 2.35, p <.0001, respectively) compared to no ACEs. **Discussion:** The CR score is a useful approach to identify a subgroup of young people at increased risk for depression symptoms. Interventions addressing several ACEs should be evaluated to help prevent depression.

Primary Supervisor: Prof Karen Waldie

11:30 : Courtney Brighouse

Unlocking the Brain Drain in Hypertension and Diabetes

Brighouse C.[1], Emans T. [1], Scadeng M.[2], McBryde F.[1]

[1]Department of Physiology, [2]Department of Anatomy and Medical Imaging

Background: 10-20% of New Zealanders are affected by diabetes and hypertension, frequently occurring together ("glucotension") - 75% of diabetic patients also have hypertension. A common symptom of hypertension and diabetes is inflammation in the brain blood vessels, which is believed to impair the glymphatic "brain cleaning" system and contribute to symptoms of cognitive impairment or "brain fog" in patients. **Objectives**: We hypothesise diabetes and hypertension impair the brains' glymphatic waste clearance, due to increased cerebral vascular inflammation. We propose to test whether treatment with the drug lumacaftor, which reduces cerebrovascular inflammation, can rescue glymphatic and cognitive function. **Methods:** We assessed effects of lumacaftor treatment (2mg/kg/day intraperitoneally) on cognitive function (Barnes Maze) and glymphatic influx (cisterna magna infusion of florescent tracers) in a rat model of normotension (n=9), hypertension (n= 10) and combined diabetes and hypertension (=glucotension, n=15). After perfusion fixation, coronal whole brain sections (50µm) were taken between +1.5 to –2.0 from bregma, mounted, imaged and analysed using ImageJ. Cognitive function (learning and memory) was assessed using the Barnes Maze. **Results:** Glymphatic intensity [mean $\pm$ SD] was highest in normotensives (221 $\pm$ 15), reduced in hypertensives (151 $\pm$ 9) and profoundly reduced in glucotension (126 $\pm$ 12). An ANOVA produced p-values of 0.016 and 0.002 respectively. Outcomes for cognitive function and lumacaftor treatment to be confirmed. **Discussion:** In rats, we confirmed glymphatic influx is profoundly impaired in glucotension. Further results will determine whether lumacaftor treatment can improve glymphatic and/or cognitive function. We believe these are translational for future human studies.

Primary Supervisor: Dr. McBryde F.

11:45 : Withdrawn

13:30 : Yang Liu

Placental extracellular vesicles are a mechanistic link between preeclampsia and early cardiovascular mortality in women

Liu Y [1], Lau S [1], Piesse S [2], Barrett C [2], Chamley L[1]

[1] Department of Obstetrics, Gynecology & Reproductive Science, [2] Department of Physiology

Background: Preeclampsia (PE) is a human pregnancy-specific hypertensive disorder with long-term implications for cardiovascular health. The mechanism(s) by which preeclampsia leads to this increased cardiovascular risk is unknown. Extracellular vesicles (EVs) are small, membrane-bound particles released by cells that facilitate cell-to-cell communication. The placenta extrudes vast quantities of EVs into the maternal blood throughout pregnancy. In preeclampsia, there is a twenty-fold increase in the number of placental EVs compared with normotensive pregnancy. **Objectives:** To determine whether preeclamptic placental EVs induce permanent dysfunction in the cardiovascular system that may explain the increased risk of future cardiovascular disease after preeclampsia. **Methods:** We obtained EVs from early-onset (EOPE, n=7) and late-onset (LOPE, n =7) PE placentae. Placental EVs or vehicle control were injected five times over ten days during pregnancy into Wistar rats. We measured blood pressure non-invasively monthly and performed echocardiography quarterly for one year postpartum. **Results:** EOPE and LOPE EVs caused significant elevations in systolic blood pressure from 3 months postpartum, approximately 20 mmHg higher than baseline ($p<0.05$). The difference in pressure was greatest 6 months-postpartum in the LOPE group (around 30 mmHg higher than baseline, $p<0.01$) and 9 months-postpartum in the EOPE group (around 30 mmHg higher than baseline, $p<0.05$), respectively. **Discussion:** EOPE and LOPE EVs can cause high blood pressure many months after administration during pregnancy in Wistar rats. This increased blood pressure may contribute to arterial damage and increased cardiac workload. The findings underscore the importance of vigilant postpartum care and monitoring in women who have experienced preeclampsia.

Primary Supervisor: Prof. Chamley, L

13:45 : Radhika Sewram

Pasifika Women's Health and Wellbeing in Aotearoa New Zealand - A Scoping Review

Sewram R[1], Nosa V[1]

[1]Department of Pacific Health, School of Population Health

Background: As a minority group, Pasifika women in Aotearoa face discrimination and inequitable health outcomes. Literature on their health and wellbeing is varied and disjoint. This project served to highlight recommendations, gaps, and areas of need. One of the review's major focal points was equity and unpacking its impact on health and wellbeing. **Objectives:** To collate existing research to i) identify determinants of health (DOH) that impact Pasifika women, ii) discuss key issues, iii) examine barriers and enablers to accessing and utilising healthcare services, and iv) identify interventions and programmes. **Methods:** A scoping review was conducted using PRISMA guidelines, with database searches identifying 1,128 pieces of literature published in the past ten years. These were screened and 60 chosen for review. Results were stratified by disease category, and findings were discussed in alignment with the objectives. **Results:** Longstanding structural and systemic inequities in DOH and healthcare access resulted in inequitable outcomes. Despite significant improvements over time, substantial gaps remain. There exist social, financial, socioeconomic and cultural barriers. Interventional programs worked best when they were culturally-responsive, co-designed, and co-conducted with Pasifika women. **Discussion:** A prominent theme was the influence of culture throughout the health continuum from DOH to systems and processes to outcomes. There are gaps in research on illicit drug use and other lifestyle conditions, and a strong need for disaggregated data. An understanding and appreciation of the role that Pasifika women play within their families and communities is key to bridging cultural gaps and fulfilling their right to health.

Primary Supervisor: A/Prof Nosa, V

14:00 : Eden Yin

Global Insights into *PINK1* Parkinson's Disease: A Meta-Analysis of Prevalence, Phenotypic Variability, and α-Synuclein Pathology

Eden Paige Yin[1, 2] , Birger Victor Dieriks[1, 2]
[1]Department of Anatomy and Medical Imaging, [2]Centre for Brain Research

Background: PTEN-induced kinase 1 (*PINK1*) Parkinson's disease (PD) is often dismissed as a rare autosomal recessive form of PD lacking classically observed α-synuclein pathology. This inaccurate simplification reflects a lack of extensive study in the affected ethnic populations. **Objectives:** We conducted a meta-analysis of the global prevalence and characteristics of *PINK1*-mutated PD. **Methods:** Databases were extensively searched, identifying 111 studies of 650 individuals (229 with a potentially pathogenic mutation and sex and/or age at onset data). **Results**: *PINK1* PD is more common than expected with regional 'hotspots' in Polynesia, Europe, and Africa. Mutation rates range from 1-9% of all early-onset PD cases, with the specific p.L347P mutation affecting 1:1300 West Polynesians. 87.5% of postmortem *PINK1* cases show α-synuclein pathology typical in idiopathic PD (ages of death 39-93 years). Homozygote *PINK1*-PD has a distinct phenotype, responsive to levodopa pharmacotherapy, with early onset (35.03±1.08 years) predominantly affecting lower limbs. *PINK1*-PD heterozygotes exhibit an 'intermediate' phenotype, with onset age (41.60±1.63 years) significantly later than *PINK1* homozygotes (p=0.00032) though earlier than idiopathic PD (>65 years). We suggest phenotype severity is determined by the mutation's zygosity and pathogenicity, pushing a proportion of individuals over a disease threshold. *PINK1*-PD females exhibit earlier onset compared to males (34.89±1.42 years vs. 38.52±0.43 years, p=0.038), especially in homozygosity (p=0.049) and with mutations in the first half of *PINK1*'s kinase region (p=0.030). **Discussion:** We challenge conventional views on *PINK1*, revealing distinct phenotypes influenced by zygosity, sex and a role for a-synuclein pathology, urging for increased recognition of this not-so-rare disease.

Primary Supervisor: Dr. Dieriks, V

Oral Presentation Room B

9:00 : Rubina Bogati

Work or retire? What is later life like for ethnic minorities?

Bogati R[1], Alpass F[2], Burholt V[1], Parsons J[1]

[1]Faculty of Medical and Health Sciences, University of Auckland, [2]School of Psychology, Massey University

Background: Our society is ageing and increasing in diversity, which presents unique opportunities and challenges for policymakers, employers, and individuals. To promote economic sustainability, older people are encouraged to continue working. However, the decision to work later in life is influenced by various factors that can vary among ethnic groups. There is a significant gap in knowledge on later life work among ethnic minority groups. **Objectives:** To develop a model of later-life work based on the evidence available thus far about the later-life work experience of older workers from minority ethnic backgrounds and to emphasise the need for timely research on the later-life work decisions of ethnic minority older workers. **Methods:** This 'critical review' integrates and interprets existing literature globally on later life work among different minority ethnic groups. **Results:** A model for later life work is developed, which shows that working in later life is influenced by complex interactions among individual, familial, community, and societal factors that unfold over time. **Discussion:** The model developed serves as a starting point for further theoretical and empirical work in this area. There is a need to understand the work decisions of ethnic minority workers to develop effective support systems and policies, addressing ethnic inequalities and maximising the potential of an ageing workforce.

Primary Supervisor: Professor Burholt, V

9:15 : Sehar Moughal

Therapy framework for South Asian survivors of family violence – why, how and what?

Moughal S [1,2], Eggleton K[1], Gavey N[2]

[1]Department of General Practice and Primary Care, [2]Department of Psychology

Background: Migrants from Asian communities who experience family violence are less likely to seek help due to various contextual factors, including inappropriate and inaccessible services. Due to cultural differences in assessment and treatment, people from Asian communities are labelled as 'less likely to engage' in Eurocentric ways of 'therapy'. Clinicians with limited understanding of their client's cultural norms and values may struggle to build rapport. This may result in an incorrect or incomplete treatment, causing more harm. **Objectives:** To design a therapy framework for migrant South Asian women who have experienced family violence. **Methods:** The study comprised three parts: 1) An integrative literature review was conducted to identify existing therapeutic modalities for Asian women who have experienced family violence. 2) Clinicians supporting Asian women who have experienced family violence were interviewed. A constant comparison method was used to identify themes for Parts 1 and 2 (deductive and inductive). A theme map was created of the therapy framework for trial. **Results:** A literature review showed that most modalities were grounded in Eurocentric knowing. The interventions primarily focused on changing the thought patterns of participants and 'letting go' of negative emotions and feelings. In comparison, the interviewees (professionals) focused on strength-based goals, using fused versions of existing modalities, including Eastern storytelling as a way of knowing. **Discussion:** There were noticeable differences in the literature (research) and clinician (praxis) when supporting Asian women who have experienced family violence. Results from both were used to create a unique therapy framework for this population.

Primary Supervisor: Dr. Eggleton, K

9:30 : Antonia Verstappen

Cultivating a primary care medical workforce for New Zealand: developing the General Practice Enhancement Model

Verstappen, A[1,2], Poole, P [1], Webster, C [2]
[1]School of Medicine, [2]Centre for Medical and Health Sciences Education

Background: The shortage of General Practitioners (GPs) in New Zealand is well-documented. However, we have little recent knowledge about the career specialty intentions of recent medical graduates, and the factors that predict or motivate their choice of a GP career. **Objectives:** To identify influential or predictive factors associated with an interest in GP career choice for doctors five years post-graduation, and to show how combining quantitative and qualitative data may allow the development of a whole-of-system model to enhance career choice in GP. **Methods:** An iterative model was developed by layering longitudinal quantitative analyses with insights from qualitative interviews. This allowed for the development of the General Practice Enhancement Model that suggests tailored workforce interventions at specified timepoints along the training pathway. **Results:** Combining quantitative and qualitative data allows for a better understanding of the intentions underlying career choices, in this case, a GP career. In addition to demographic factors, these include positive experiences with GP, interactions with mentors, and concerns about workload. A whole-of-system model has been created using final results. This model may allow for the aggregation of marginal gains to supply graduates that better suit community health needs. **Discussion:** Longitudinal data that tracks the same student throughout their training and into the workforce is critical to identify where system changes may be made. The overlay of qualitative and quantitative data has helped to clarify where gains may be made and confirms the need for a systemic approach to building priority health workforces such as General Practice.

Primary Supervisors: Prof. Poole, P.; Assoc. Prof. Webster, C.

9:45 : Woroud Alzaher

Ageing well with cerebral palsy: experiences and adaptations through a healthy ageing lens

Alzaher W [1], Williams SA [1,2], Stott S [3,4], Hogan A [5,6]

[1]Liggins Institute, University of Auckland, New Zealand, [2]School of Allied Health, Curtin University, Australia. [3]Department of Surgery, University of Auckland, New Zealand, [4]Department of Surgery, Starship Hospital, New Zealand, [5]New Zealand Cerebral Palsy Society, New Zealand, [6]Adult with cerebral palsy

Background: Cerebral palsy (CP), the most common childhood onset physical disability, is a lifelong condition with no current cure. Adults with CP are at an increased risk of preventable chronic conditions and can experience early ageing. Despite this, information and advice about ageing well with CP is strikingly scarce. The World Health Organisation's Healthy Ageing (WHO-HA) model focuses on sustaining functional ability, considering both intrinsic capacity and environmental factors. Though the WHO-HA model has never been applied to CP, it appears highly relevant to persons with CP who routinely adapt their environment to increase functional ability and facilitate societal participation. **Objectives:** Evaluate the ageing experiences and health priorities for adults with CP in New Zealand (NZ), and the applicability of the WHO-HA model. **Methods:** Semi-structured interviews with adults (>30years) with CP were analysed thematically. **Results:** Early analysis of completed participant interviews (n=12, 5 females, median age 43 (31-79 years), 10 NZ European, Gross Motor Function Classification Scale I-IV) highlights functional mobility changes during their 20's and 30's. Helpful adaptations to these early and evolving changes, included utilising better suited equipment (e.g. change from walking frame to wheelchair), carefully apportioned use of their energy reserves throughout their day and employed carer support. Abilities for social connection, such as ways to communicate, and healthcare professionals knowledgeable about CP were identified as vital in healthy ageing. **Discussion:** Adults with CP face both typical ageing changes and changes specific to CP. Social connections, environmental adaptations and holistic healthcare are key supports for healthy ageing.

Joint primary supervisors: Dr Williams S, Prof Stott S.

10:00 : Mazyar Zarepour

A Districting Model to Manage Age Residential Care Facilities for Transition to Home

Zarepour M[1], O'Sullivan M[1], Walker C[1], Parsons M[2]
[1]Department of Engineering Science, University of Auckland, [2]School of Health, University of Waikato

Background: The districting problem addressed involves grouping small geographic areas into larger clusters to optimize healthcare delivery for elderly patients transitioning to home (T2H) in Waikato, New Zealand. By assigning patients to Aged Residential Care (ARC) facilities, the model aims to enhance long-term planning and resource allocation. **Objectives:** The research aims to partition Waikato into districts, assigning each district to an ARC facility. The goals are to ensure patients are assigned to the nearest ARC, minimize overflow, and manage patient flow efficiently, particularly during the COVID-19 pandemic. This model also aims to simulate workload and predict future demands for strategic planning. **Methods:** Using 4.5 years of historical data on patient admissions and discharges from older person health wards, the model clusters area units into six districts, each centred around an ARC. An optimization model, implemented in Python and solved with the PULP CBC CMD solver, considers integrity, balancing, and contiguity criteria. **Results:** The model successfully generated districts, ensuring no ARC facility experienced overflow during the COVID-19 pandemic. Simulations of daily occupancy trends provided insights into workload patterns, helping to visualize seasonal demands and estimate future resource needs. **Discussion:** The districting model supports effective long-term planning for patient assignment and resource management in Waikato. By simulating demands, policymakers can manage costs and develop appropriate funding models, ultimately improving service quality for elderly patients during their T2H journey. The model's output was implemented in practice and a0s a result no overflow happened in ARC facilities during Covid-19.

Primary Supervisor: Associate Prof. O'Sullivan, M

10:45 : Marguerite Sandleback

Fishing for the origins of lymphatic vessels.

Sandleback M[1], Chen W [1], Herbert C [1], Hall C [1], Astin J [1]

[1] Department of Molecular Medicine and Pathology

Background: Lymphatic vessels are an essential component of the cardiovascular system, and their dysregulation causes conditions such as lymphoedema, impaired wound healing and tumour metastasis. For 120 years, lymphatics were proposed to be derived solely from veins, but recent evidence indicates that lymphatic progenitors arise from both veins and mesoderm. In mice, evidence suggests that the craniofacial lymphatics arise from the cardiopharyngeal mesoderm; a mesodermal compartment that also gives rise to the heart and facial muscles. Recently, our laboratory provided the first live imaging-based evidence of a non-venous lymphatic progenitor using transparent zebrafish embryos. This places us in a unique position to confirm the non-venous, cardiophayrngeal origin of lymphatic vessels. **Objectives:** Use live imaging and genetic approaches to confirm the cardiopharyngeal origin of the craniofacial lymphatics. **Methods:** A *tbx1:EGFP* reporter was crossed to various vascular reporters to determine the contribution of the cardiopharyngeal lineage to the facial lymphatics using live imaging. The gene *tbx1* is expressed in the cardiopharyngeal mesoderm and its lineages. It is also required for the proliferation of a subset of this lineage. CRISPR-Cas9 knockdown of *tbx1* was performed and larvae were examined for cardiopharyngeal and lymphatic defects. **Results:** Expression of the *tbx1:EGFP* reporter was found in the non-venous facial lymphatic progenitor. The *tbx1* knockdown larvae have both cardiopharyngeal and lymphatic defects. **Discussion:** This study provides the first live imaging-based evidence for the cardiopharyngeal origin of lymphatic vessels. Understanding the lineage behind lymphatic development will help develop novel therapies to treat lymphatic diseases.

Primary Supervisor: Dr. Astin, J

11:00 : Mejo Chiratteparambil Korah

Development of Vaccines against Gonococcal Disease using the PilVax Platform

Chiratteparambil Korah M[1,2], Tsai C[1,2], Proft T[1,2]

[1]School of Medical Sciences, University of Auckland, [2]Maurice Wilkins Centre for Molecular Biodiscovery

Background: Gonorrhoea is a sexually transmitted disease with a high prevalence across the world. There is currently no licenced vaccine against gonorrhoea, but vaccine development is a top priority, particularly with the rise of antimicrobial resistance (AMR). **Objectives:** To develop a mucosal vaccine against *Neisseria gonorrhoeae* using the Pilvax platform for presentation of selected peptides. **Methods:** Selected peptides from the *Neisseria gonorrhoeae* multidrug transporter system E (MtrE), Transferrin binding protein A (TbpA), and a peptidomimetic of lipooligosaccharide have previously raised interest as potential vaccine targets for gonorrhoea. Those peptides were bioengineered into different exposed loop regions of the backbone pilus protein of *Streptococcus pyogenes* and expressed in the food-grade bacterium *Lactococcus lactis*. BALB/c mice will be immunized intranasally with the modified *L. lactis*, and antibody responses (serum IgA/IgG) and IgA from multiple mucosal sites will be evaluated. In-house generated peptide proteins fused with either thioredoxin or glutathione-S-transferase will be used as a control in *in vivo* studies and ELISA. Furthermore, serum bactericidal assay (SBA) and a mouse vaginal tract infection model will be employed to test for vaccine efficacy. **Results:** The selected peptides from *N. gonorrhoeae* were successfully cloned into the loop regions of the pilus backbone protein, and expression in *L. lactis* was confirmed by Western blot and flow cytometry. **Discussion:** Pilus expression was confirmed by Western blot, and flow cytometry indicated that inserting gonococcal epitopes did not disturb the pilus assembly. Hence, PilVax is a promising novel vaccine platform that can elicit mucosal immunity against bioengineered peptides.

Primary supervisor: Prof. Proft T

11:15 : Withdrawn

11:30 : Linh Do

HbA1c and white blood cells in diabetic macular oedema development: The systemic review and meta-analysis

Do L[1], Kuo CY-J[1], Misra S[1] and Mugisho OO[1]

[1]Department of Ophthalmology

Background: Diabetic macular oedema (DMO) is the leading cause of vision loss in patients with type 2 diabetes mellitus (T2DM). Chronic hyperglycaemia and inflammation are key factors in DMO, prompting recent studies to investigate the association between glycated haemoglobin (HbA1c) and systemic inflammatory markers (white blood cells - WBC) with DMO development. However, results remain inconsistent. **Objectives:** To investigate the association between HbA1c and WBC counts with DMO development in T2DM patients. **Methods:** A comprehensive literature search on PubMed and EMBASE up to May 2024 was conducted, including studies investigating HbA1c and WBC counts in patients with and without DMO. Standardized mean differences (SMD) and odds ratios (OR) 95%CI were calculated. A random-effect model was used to pool data. Statistical analysis was performed using R. **Results:** Pooled results showed that higher HbA1c levels may increase the risk of DMO (SMD = 0.29, 95%CI: 0.17 to 0.41; OR = 1.32, 95%CI: 1.19 to 1.48). Eager's test indicated a significant publication bias among studies reporting HbA1c as OR 95%CI. Regarding WBC counts, the meta-analysis suggested a significant association between lymphocytes and DMO (SMD = -0.24, 95%CI: -0.45 to -0.03). **Discussion**: This study suggested that both HbA1c and WBC counts may contribute to DMO development, highlighting the impact of glycemic control and systemic inflammation and supporting the development of effective screening programs for DMO prevention. Due to significant publication bias among studies investigating HbA1c as OR 95% CI, further research is needed to clarify the independent role of HbA1c in DMO development.

Primary Supervisor: Associate Professor. Misra, S

11:45 : Danica Hamlin

Characterizing Cis Tau Pathology in Chronic Traumatic Encephalopathy

Hamlin D[1], Osterman C[1], Curtis M[1], Murray H[1].

[1]Department of Anatomy and Medical Imaging, Centre for Brain Research

Background: Tau protein is a hallmark pathology of both Alzheimer's Disease (AD) and Chronic Traumatic Encephalopathy (CTE), a neurodegenerative disease associated with repetitive traumatic brain injuries (TBI). Several modifications to tau occur during disease causing aggregation and formation of lesions around damaged blood vessels in CTE. The earliest modification is a shift from the healthy trans to the pathological cis conformation of tau. With phosphorylated-cis-tau (cis-ptau) being detected in postmortem human brain tissue as early as eight hours following severe TBI. O**bjectives:** We sought to establish whether the cis conformation of phosphorylated tau is a feature of the lesions observed in CTE; this included studying the relationship between cis-tau and other pathological tau species as well as with various cell types. **Methods:** Using multiplexed fluorescent immunohistochemistry, we labelled postmortem human brain tissue with antibodies targeting various tau epitopes and cell markers. We compared CTE pathology to both neurologically normal and AD cases to establish differences in both non-pathological and mixed tauopathy states. **Results:** Cis-ptau co-labelled with AT8, AT180, and 4R tau. All of which are abundant within the CTE lesion area. We also found cis-ptau within astrocytes located at the subpial boarder; as well as co-labelling with markers of glial reactivity in this region. This is consistent with aging related tau astrogliopathy. **Discussion:** Our data supports the idea that cis-ptau is the earliest pathological variation of tau associated with traumatic brain injury and neurotrauma associated pathology. Investigating this early tau modification provides insights into the mechanisms linking TBI and neurodegeneration.

Primary Supervisor: Dr. Murray, H

13:30 : Withdrawn

13:45 : Amanda Groenewald

Cardiac Dysfunction Following Acute Exposure to Clozapine and Sodium Valproate

Groenewald A[1], Power A[1], Burns K[2], Tingle M[2], Ward M-L[1]
[1]Department of Physiology, [2]Department of Pharmacology and Clinical Pharmacology

Background: Clozapine (CLZ) is the only drug recommended for treatment-resistant schizophrenia. Unfortunately, CLZ is associated with cardiotoxicities. While the mechanism behind this is not known, concomitant sodium valproate (VPA) treatment is a well-established risk factor in its development. Preliminary evidence suggests that reactive oxygen species (ROS) are produced by the metabolism of CLZ within the heart, which may cause mitochondrial dysfunction and impair Ca^{2+} cycling in cardiomyocytes, impairing contractile function. VPA administration is thought to exacerbate these CLZ-related effects. **Objective:** To investigate the acute effects of CLZ and VPA exposure on isolated cardiac tissue function. **Methods:** Atrial tissue samples from consenting patients undergoing routine cardiac surgery were obtained. Small bundles of permeabilised cardiac fibres were micro-dissected and used to investigate the acute effects of CLZ and VPA on mitochondrial O_2 consumption and ROS production. Experiments to assess contractile function and Ca^{2+} cycling during acute CLZ and VPA exposure were conducted in isolated cardiac muscle preparations (trabeculae). **Results:** CLZ and VPA decreased mitochondrial O_2 consumption, both alone and in combination. However, no detectable change in mitochondrial ROS production was observed. Both CLZ and VPA impaired Ca^{2+} release and stress production in isolated cardiac trabeculae. **Discussion:** This investigation provides evidence for the acute effects of both CLZ and VPA on human cardiac mitochondria. These findings also suggest that VPA alone may have cardiotoxic effects. Overall, CLZ and VPA were demonstrated to cause acute dysfunction in cardiac bioenergetics and Ca^{2+} cycling, with profound effects on contractile function.

Primary Supervisor: Dr. Ward, M-L

14:00 : Harrison Porritt

Hydrogels to help model stem cell derived cardiac disease models

Porritt H.[1], Winbo A.[2], Taberner A.[3], Malmstrom J.[1]
[1]Department of Chemical and Materials Engineering, [2]Department of Physiology, [3]Auckland Bioengineering Institute

Background: The persistence of Cardiac scar tissue is a major cause for heart failure. Scar tissue stabilises the heart right after a heart attack, but causes contractility and distensibility issues, once the patient is recovered. Scar tissue is caused by the differentiation of cardiac fibroblasts into the more active myofibroblast. One factor that continues this state well after patient recovery has occurred, is tissue stiffness, through mechanotransduction pathways. Accurate cardiac models derived from stem cells that reciprocate disease hallmarks could be utilised for patient specific rapid drug testing. **Objectives:** To create stem cell derived models in 3D that mimic the boundary region between healthy, and fibrotic cardiac tissue. **Methods:** These models are created by encapsulating stem cell derived cardiomyocytes and cardiac fibroblasts in stiffness patterned hydrogels **Results:** It was demonstrated that stiffness patterned hydrogels can be controlled over the range of 10 microns from healthy stiffnesses (<10 kPa) to fibrotic stiffnesses (>50 kPa). Hydrogels are also able to control fibroblast differentiation, based on hydrogel stiffness alone, and can also maintain populations of beating cardiomyocytes. **Discussion:** These results suggest that this protocol for stiffness patterned hydrogels can be used to create disease models of cardiac tissue for patient specific rapid drug testing models.

Primary Supervisor: Assoc. Prof Malmstrom, J.

14:15 : Stian Thomson

Examining Vagal Regulation of Cardiac Function Using Directly Recorded Vagus Nerve Activity in Conscious Sheep

Thomson S[1], Shanks J [1], Ramchandra R [1]
[1]Department of Physiology

Background: The vagus nerve provides parasympathetic innervation to the heart, modulating cardiac function by decreasing heart rate and regulating cardiac output and coronary blood flow. Vagal dysfunction plays a role in numerous cardiovascular diseases. Previously, vagal nerve activity has predominantly been investigated using indirect methods such as pharmacological blockade, limiting our understanding of cardiac parasympathetic regulation under physiological conditions. **Objectives:** To directly record nerve activity from the cardiac vagal branch and investigate how changes in nerve activity (CVNA) affect cardiac function. **Methods:** CVNA, cardiac output (CO), coronary blood flow (CoBF) and heart rate (HR) were recorded from conscious sheep (n = 7). CVNA in each cardiac cycle was measured, and haemodynamic changes in the subsequent cardiac cycles were averaged. Atropine (0.8 mg/kg/min) was then administered to block the action of acetylcholine, the primary vagal neurotransmitter, and investigate the changes in the CVNA-haemodynamic response (n = 5). **Results:** Cardiac cycles containing high levels of CVNA were associated with a subsequent increase in CO (0.14 ± 0.06 L/min, p = 0.038), which was absent following cycles containing low CVNA. An increase in CoBF was observed following cardiac cycles with low CVNA (0.8 ± 0.30mL/min, p = 0.011). These changes were attenuated in the presence of atropine. **Discussion:** This study demonstrates some of the first direct recordings of CVNA in a large animal model. Additionally, the study demonstrated that a rise in CVNA within a cardiac cycle increased cardiac output and that this response was likely acetylcholine-mediated.

Primary Supervisor: Dr Shanks, J

14:30 : Sophie Piesse

Enduring impacts of placental extracellular vesicles on the maternal cardiovascular system in spontaneously hypertensive rats

Piesse S[1], Lau, S-Y[2], Liu Y[2], Chamley L[2], Groom K[3], Oyston C[2] and Barrett C[1]

[1]Department of Physiology, [2]Department of Obstetrics, Gynaecology and Reproductive Sciences, [3]Liggins Institute

Background: Preeclampsia is a pregnancy disorder triggered by placental dysfunction. Traditionally characterised by maternal hypertension and proteinuria that resolves postpartum, recent studies indicate a 4x greater lifetime risk of cardiovascular disease following affected pregnancies. Placental extracellular vesicles (EVs) from preeclamptic pregnancies may provide the key link between the placenta and adverse maternal cardiovascular changes occurring during pregnancy and long-term postpartum. **Objectives:** To identify the effects of placental EVs during pregnancy and long-term postpartum on the maternal cardiovascular system. **Methods:** EVs isolated from human placental explants were injected into pregnant spontaneously hypertensive rats (SHRs) via a tail vein. SHRs received either vehicle control (n=11), or EVs from normotensive (n=10), late-onset preeclamptic (n=10) or early-onset preeclamptic (n=10) placentae. Non-invasive blood pressure and echocardiography were performed pre-pregnancy, day 20.5 of pregnancy, and monthly until 12 months postpartum. Wire myography assessed vasoactivity of third-order mesenteric vessels 12 months postpartum. **Results:** Early-onset EVs increased ejection fraction above the normotensive group during pregnancy and up to one month postpartum *(p=0.0436).* Nine months postpartum, systolic blood pressure was significantly higher in the early-onset group compared to the normotensive group (*p=0.0413*). This trend was consistent from pregnancy through to 12 months postpartum. By 12 months postpartum, mesenteric arteries from the early-onset group were more responsive to the vasoconstrictor phenylephrine than the normotensive group (*p=0.0079*) and less responsive to the vasodilator acetylcholine (*p=0.0004*). **Discussion:** Compared with normotensive placental EVs, early-onset preeclamptic EVs demonstrate life-long impacts on the cardiovascular system in female SHRs, facilitating hypertension, vasoconstriction and altered cardiovascular function.

Primary supervisor: Associate Professor Barrett, C

14:45 : Aatika Prasad

Adherence to iron deficiency screening and treatment guidelines in patients with heart failure

Prasad, Aatika[1], Martini, Nataly[2], Mohammed, Mohammed [2]

[1]Faculty of Medical and Health Sciences, [2]School of Pharmacy

Background: Iron deficiency (ID) is prevalent in heart failure (HF), impacting quality of life and could worsen the condition. Both international and national guidelines recommend routine screenings for ID and anaemia, however only a mere fraction of these patients are being screened and treated in real-world practice. **Objectives:** Identify which proportion of 2021 HFrEF (Heart Failure with Reduced Ejection Fraction) patients diagnosed with ID received iron supplementation in primary care and secondary care. Specifically, identifying the formulation of iron received and the dates these were received. **Methods:** Retrospective analysis of adult patients with HFrEF using a sample of patients admitted to Auckland City Hospital in 2021. Data collected from Testsafe to capture primary healthcare scene. **Results:** Adult HFrEF patients are under screened and undertreated for ID in primary care. **Discussion:** It is assumed that there will be a large proportion of HFrEF patients that are under screened, undertreated or treated with oral iron rather than intravenous (IV) iron in primary care in 2021, despite international guidelines suggesting IV iron for all HFrEF patients who meet the definition for ID. Thus indicating a poorer quality of life and increased chance of mortality for HF patients with ID, merely due to funding issues for Ferinject which outline that HF patients with ID do not qualify for IV iron.

Primary Supervisor: Dr. Martini, N

Oral Presentation Room C

9:00 : Jamie Hyde

Huntington's disease as a whole-body syndrome? Investigating molecular mechanisms of liver pathogenesis in Huntington's disease

Hyde J[1], Handley R[1], Jiang A[2], Snell R[1]

[1]School of Biological Sciences, [2]Center for Genomic Medicine, Massachusetts Central Hospital.

Background: Huntington's disease (HD) is a neurodegenerative condition characterised by progressive neurological and motor symptoms and caused by an expanded CAG repeat in the huntingtin (*HTT)* gene. Despite extensive efforts, largely focusing on mechanisms within the brain, no viable disease-modifying therapy has been produced yet. Our laboratory has identified elevated levels of the metabolite urea in post-mortem brain tissue from HD patients and a sheep model of HD. Urea and its precursor, ammonia, are neurotoxic and implicated in other neurological conditions. The primary site of urea/ammonia metabolism is the liver. **Objectives:** To investigate altered urea/ammonia metabolism as a pathogenic mechanism and potential therapeutic target in HD by exploring molecular effects of mutant HTT in liver. **Methods:** Liver tissue from our sheep model of HD will undergo targeted biochemical analysis for metabolites/enzymes involved in urea/ammonia processing. Direct molecular effects of *HTT* in the liver will also be investigated by a) expressing mutant HTT, and b) knocking down endogenous HTT in the HepaRG human liver cell line. Resulting cell lines will be analysed for eight metabolites/enzymes involved in urea/ammonia metabolism and transcriptomic changes using RNA-seq. **Results:** Preliminary evidence suggests knock-in of mutant *HTT* and knockdown of endogenous *HTT* alter urea/ammonia concentrations. Gene expression of urea cycle enzymes is also altered in transgenic HD sheep liver tissue. **Discussion:** Urea/ammonia metabolism appears altered in the HD liver. Accumulation of these metabolites may exacerbate neurodegeneration. Further characterisation of these biochemical changes will validate this as a potential pathogenic mechanism and therapeutic target.

Primary Supervisor: Dr. Handley, R

9:15 : Stephanie Carr

Characterising microgliosis in the post-mortem human Huntington's disease neocerebellum

Carr S[1], Tan A[1], Faull R[1], Singh-Bains M[1]

[1]Centre for Brain Research, Department of Anatomy with Medical Imaging.

Background: Huntington's disease (HD) is an inheritable neurodegenerative disease that manifests in mid-life with motor, mood, and cognitive symptoms. There are no disease-modifying treatments, with patients facing progressive deterioration and premature death. Historically considered a disease affecting basal ganglia neurons, studies from our laboratory report neuronal loss in areas including the cortex and cerebellum. Furthermore, studies report the involvement of non-neuronal glial cells including astrocytes and microglia, which contribute to inflammation and pathology. Our lab has found significant loss of Purkinje neurons and evidence of increased astrocytic activation in the human cerebellum of HD cases with a predominantly motor symptom presentation. This implicates cerebellar neurons and glia in HD pathogenesis and symptomatology, justifying further investigation into cerebellar microglia. **Objectives:** To characterise microgliosis in the HD human cerebellum. **Methods:** Free-floating immunofluorescence is being conducted on post-mortem human cerebellum tissue from 15 HD and 8 neurologically normal control cases to investigate immunoreactivity patterns of microglial markers IBA-1, HLA-DR, and TMEM119. **Results:** Preliminary results demonstrate immunoreactivity of all markers in 4/4 HD cases investigated to date, with data collection for all cases on-going for subsequent quantitative analysis of cell number and protein expression. **Discussion:** These results implicate microglial reactivity in the cerebellum of a subset of HD cases. Completion of the dataset will enable comparison of immunoreactivity patterns between control and HD cases of mood and motor symptomatology, as well as other clinicopathological features, to further characterise the non-neuronal contribution of HD cerebellar pathology.

Primary Supervisor: Dr. Singh-Bains, M

9:30 : Khushi Sehajpal

Characterisation of the substantia nigra in post-mortem cases of X-linked Dystonia Parkinsonism

Sehajpal K [1,2], Tan A [1,2], Arasaratnam C [1,2], Faull R, [1,2] Singh-Bains M [1,2]

[1] Department of Anatomy and Medical Imaging, [2] Centre for Brain Research

Background: X-linked Dystonia Parkinsonism (XDP) is a genetically inherited, rare, X-linked recessive neurodegenerative movement disorder clinically characterised by the presence of dystonia and parkinsonism. Previous research implicates spiny projection neuron (SPN) loss in the striatum to underlie the core of XDP pathophysiology. The substantia nigra (SN) is a critical component of the basal ganglia network, which both receives striatal output and influences striatal activity. Given the SN is also widely implicated in Parkinson's disease, a condition which shares partial symptomatology in XDP, investigating nigral changes in the XDP human brain is essential to elucidate pathological mechanisms of disease to guide therapeutic strategies. **Objectives:** We aimed to characterise the SN of 12 XDP post-mortem cases and 4 neurologically normal cases. **Methods:** Free-floating histological and fluorescence immunohistochemical staining was performed using antibodies targeting a range of known nigral markers. Semi-quantitative high-throughput analysis was performed to assess changes in protein expression, cell number and size. **Results:** We report a significant 67.59% reduction in the number of tyrosine hydroxylase^{+} dopaminergic neurons *($p = 0.0280$),* and an 80.28% reduction in the DARPP-32 (SPN marker) expression *($p = 0.0022$)* which also correlated with disease duration *($p = 0.0477$)* in the XDP SN. We also report a 61.76% reduction in SPN marker substance P *($p = 0.0077$)* which correlated with disease duration *($p = 0.0457$),* and a 48.28% reduction in enkephalin (SPN marker) immunolabelling *($p = 0.0077$).* **Discussion:** Together, these findings are the first to point towards significant dopaminergic dysfunction and dysregulation of both nigrostriatal and striatonigral connectivity in the XDP brain, which may contribute towards the neuropathological signature of XDP and has consequences for the development of meaningful patient therapeutics.

Primary Supervisor: Dr. Singh-Bains, M

9:45 : Withdrawn

10:45 : Linh Nguyen

Small molecule TrkB agonists enhance the generation of striatal neurons.

Nguyen L[1], McCaughey-Chapman A[1], Raos B[2], Svirskis D[2], Connor B[1]

[1]Department of Pharmacology, [2] School of Pharmacy

Background: Brain-derived neurotrophic factor (BDNF) binds to the high affinity tropomyosin-related kinase B (TrkB) receptor to mediate neuronal survival and maturation and provide neuroprotection. Activating the BDNF-TrkB pathway has significant potential for the treatment of several neurological diseases and injuries including Huntington's disease. Exogenous BDNF or monoclonal antibody agonists as therapeutic agents have potential limitations for therapeutic use. To overcome this, two BDNF small molecule mimetics LM22A-4 and 7,8- dihydroxyflavone (7,8-DHF) with specific affinity for the TrkB receptor were developed and are potential candidates for treating Huntington's disease (HD). **Objectives:** BDNF provides neurotrophic support for medium spiny striatal neurons (MSNs) that are selectively lost in HD. This study investigated the ability for LM22A-4 or 7,8-DHF to support the generation of MSNs from directly reprogrammed human induced striatal precursor cells (hiSNPs). **Methods:** Human dermal fibroblasts were reprogrammed into hiSNPs by transfecting with lipid nanoparticle *SOX2* and *PAX6* mRNA. During differentiation, cells were treated with either 1nM BDNF, LM22A-4 (5µM, 10µM and 20µM) or 7,8-DHF (5µM, 10µM and 20µM), then fixed for immunocytochemistry and Sholl analysis or collected for ELISA. **Results:** Treatment of hiSNPs with LM22A-4 and 7,8-DHF increased the number of DARPP32+ MSNs compared to treatment with BDNF. However, neither LM22A-4 or 7,8-DHF increased neurite length compared to BDNF. Phosphorylation of the TrkB receptor following LM22A-4 or 7,8-DHF treatment was confirmed by ELISA analysis. **Discussion:** This research demonstrates small molecule TrkB agonists can promote the generation of MSNs from hiSNPs suggesting these compounds have potential for the treatment of Huntington's disease.

Primary Supervisor: Prof. Connor, B

11:00 : Brooke Hawker

Transforming Treats into Tools: Cuprizone-Peanut Butter to Model Demyelination in Mice

Hawker B[1], Chiddicks E[1], Connor B[1], McCaughey-Chapman A [1]
[1]Department of Pharmacology & Clinical Pharmacology

Background: The cuprizone (CPZ) mouse model of demyelination is a well-established model of Multiple sclerosis (MS), inducing central nervous system (CNS) demyelination within 6 weeks. Typically, CPZ is mixed into ground rodent chow, however, its bitter taste reduces food intake, causing severe weight loss and variability in daily CPZ consumption. This leads to inconsistent demyelination, complicating disease comparison between animals. To address this, we propose mixing CPZ into peanut butter (CPZ-PB) as a novel method of CPZ delivery. **Objectives:** To assess the use of CPZ-PB to standardize daily dosing and minimise weight loss while maintaining effective demyelination in comparison to CPZ administration through chow (CPZ-Chow). **Methods:** 30 male, C57BL6/J mice were divided into control, CPZ-PB or CPZ-Chow groups (n = 10 per group) and received daily CPZ treatment for 6 weeks. Weight was recorded daily, behavioural testing via the dynamic plantar aesthesiometer (DPA) was conducted at 0, 3 and 6 weeks, and demyelination of the brain and spinal cord was confirmed at 6 weeks via immunohistochemical (IHC) analysis of myelin proteins. **Results:** CPZ-PB animals consumed a consistent daily dose of CPZ for 6 weeks without experiencing significant weight loss. DPA analysis revealed increased sensitivity to mechanical allodynia with CPZ treatment, which was greater in CPZ-PB animals at 6 weeks ($p=0.000305$). IHC analysis confirmed comparable levels of demyelination in the brain and spinal cord of both CPZ-PB and CPZ-Chow animals. **Discussion:** This study introduces a novel CPZ-intoxication methodology that alleviates welfare concerns and provides a more reliable model for MS research.

Primary Supervisor: Dr McCaughey-Chapman, A

11:15 : Conor Nelson

An immunotherapeutic approach to modifying disease progression in the YAC128 mouse model of Huntington's Disease

Nelson C[1], Wu A [1], Young D [1]
[1]Department of Pharmacology and Clinical Pharmacology and Centre for Brain Research

Background: N-methyl-D-aspartate receptor (NMDAR) dysfunction is observed in a variety of neurodegenerative diseases. One characteristic change of this dysfunction is a negative shift in the ratio of pro-survival to pro-death NMDAR signalling in the central nervous system. A novel antibody-based therapy produced by our lab targeting the NMDAR GluN1 subunit has previously been found to differentially modulate NMDARs to favour pro-survival signalling. As NMDAR activity is implicated in the aggregation of mutant huntingtin protein, we hypothesise that a shift in NMDAR signalling could modify the progression of Huntington's Disease. **Objectives:** This study aims to investigate the viability of GluN1 antibodies as a therapy using the transgenic YAC128 mouse model of Huntington's disease. **Methods:** YAC128 mice were treated with control or GluN1 IgG antibodies. Motor function was assessed via the accelerating rotarod and open-field tests. Analysis of aggregate formation and striatal volume changes were assessed via immunohistochemistry, and NMDAR signalling pathway activation via Western Blot. **Results:** Preliminary results from our pilot study suggested a treatment-dependent preservation of striatal volume in YAC128 mice at 12 months of age and a reduction in the motor deficits typically observed in 7-month-old mice. Further studies to validate the results of this pilot have been completed, and analysis is underway. **Discussion:** Our results showing improvements in motor function and long-term reduction in neuropathology in this model are promising early signs for therapeutic effectiveness.

Primary Supervisor: Assoc Prof. Young, D

11:30 : Thai Nguyen

Functionality analysis of a novel molecular switch in YAC128 transgenic mouse model of Huntington's disease

Nguyen T[1], Young D[1], Mouravlev A[1]

[1] Department of Pharmacology

Background: Gene therapy has a great potential in treating various diseases, but the current strategies typically employ an overexpression of therapeutic gene. This approach is rather problematic due to potential toxicity caused by a lack of regulation at tissue and/or cell level, which severely limits laboratory - clinical translation. To address this problem, we have developed a novel molecular switch that relies on stress-induced activation of protease to selectively regulate therapeutic gene expression in at-risk cells only. Huntington's disease (HD) is a late onset, single gene mutation neurodegenerative disorder with calpain acting as a key protease in its pathogenesis. It is therefore an ideal disease model to evaluate our system. **Objectives:** To examine the functionality of our gene switch *in vivo* using the YAC128 transgenic mouse model of HD. **Methods:** Subgroups of 2-month old YAC128 and wild-type (WT) littermate controls received a bilateral adeno-associated virus (AAV) vector infusion into the striatum. Mice were euthanised at 2 months following vector infusion and the brains prepared for immunohistochemistry (IHC) and western blot. **Results:** Calpain was confirmed to be upregulated in YAC128 mice striatum compared to WT, and calpain activity was also confirmed to drive the functionality of our system. The expression of mutant Huntingtin proteins (mHTTs) were drastically reduced in mice injected with our cassette. **Discussion:** This study demonstrated that our molecular switch successfully utilised upregulated calpain activity to initiate the transcription of transgene, which led to a timelier and more specific response to alleviate cell stress caused by accumulation of mHTTS.

Primary Supervisor: Assoc Prof Young, D

11:45 : Aimee Mills

Targeting Connexin Hemichannels and the Inflammasome pathway in an acute mouse model of Alzheimer's Disease

Mills A[1,2], Acosta M[3], Green C[2], Danesh-Meyer H[2], Kwakowsky A[1,4], Mugisho O [1, 2]
[1]Centre for Brain Research, Faculty of Medical and Health Sciences, University of Auckland, [2]Department of Ophthalmology and Aotearoa national eye centre, University of Auckland, [3]School of Visual Sciences, University of Auckland, [4]Pharmacology and Therapeutics, University of Galway, Ireland

Background: Pathologically opened connexin hemichannels can establish a self-propagating inflammasome activation loop that may contribute to Alzheimer's disease (AD) pathogenesis. **Objectives:** This project investigated the effect of connexin hemichannel blockade in mice with acute onset of AD characteristics such as neurodegeneration induced by aggregated amyloid beta 1-42 (Aβ1-42), neuroinflammation, and memory deficits. **Methods**: One day after intrahippocampal injection of Aβ1-42, mice (n=9) were administered connexin hemichannel blocker, Tonabersat, in peanut butter for 16 days before tissue collection. Aβ1-42- and vehicle-injected mice (n=8 each) received peanut butter pellet only, while Naïve controls received no pellet or Tonabersat only (n=8 each). Fluorescent immunohistochemistry and densitometry analysis were used to quantify the response of astrocytes, microglia, and neurons as well as expression of inflammasome-associated proteins. **Results:** In the hippocampus, Aβ1-42 induced an elevated microglial response compared to naïve mice (*p=0.0150) and a reduction in neuron area compared to vehicle-injected controls (*p=0.0185). Mice treated with Tonabersat following Aβ1-42 injection showed a reduced microglial response compared to untreated (*p=0.0430). Tonabersat also prevented the decrease in neuron area caused by Aβ1-42 (*P=0.0493). **Discussion:** This data demonstrates the ability of connexin hemichannel blockade to modulate the inflammatory response of microglia to Aβ1-42 and result in a neuroprotective outcome. This highlights connexin hemichannels as a potential therapeutic target for inflammasome-related neurodegenerative diseases such as AD.

Primary Supervisor: Dr. Mugisho, O

13:30 : Jean Yu Lim

Investigating the Role of Microglial Dysfunction in Alzheimer's Disease: Regulation of GPNMB Expression

Yu Lim J[1,2], Smith AM[1,2], Park TI-H[1,2], Dragunow M[1,2]

[1]Centre for Brain Research, [2]Department of Pharmacology and Clinical Pharmacology

Background: Alzheimer's Disease (AD) is a neurodegenerative disorder characterised by cognitive and memory impairments. Although AD research has historically been neuro-centric, increasing evidence supports the importance of microglia in AD. Microglia are the resident immune cells of the brain, and their dysfunction contributes to AD pathogenesis and progression. Previous transcriptomic studies revealed glycoprotein NMB (GPNMB) as a gene highly upregulated in AD human microglia, but its precise function and how its expression is regulated is unknown. Microphthalmia-associated transcription factor (MITF) has been hypothesised to regulate GPNMB expression in response to cytokines, nutrient status, and AD pathology. **Objectives:** To determine whether GPNMB expression is regulated by MITF in human microglia. **Methods:** Human induced pluripotent stem cell (iPSC)-derived microglia were exposed to conditions hypothesised to alter MITF transcriptional activity: nutrient depletion, cytokine stimulation, and amyloid beta protein. Direct knock-down of MITF was achieved using RNA interference. GPNMB protein levels were assessed using immunocytochemistry. **Results:** Preliminary data indicates that MITF and GPNMB expression is increased in response to nutrient depletion and cytokines (one-way ANOVA, $p<0.001$), and their expression is highly correlated. Ongoing work with MITF knock-down aims to provide direct evidence that MITF is required to upregulate GPNMB expression. **Discussion:** Preliminary evidence suggests that MITF regulates GPNMB expression in human microglia in response to nutrient status and cytokine signalling. Understanding the role of GPNMB in microglia may provide novel targets for rationalised therapeutic intervention in AD.

Primary Supervisor: Dr. Smith, A. M.

13:45 : Jack Sloan

The Sympathetic Brain Drain

Sloan J.[1], McBryde F.[1],

[1]Department of Physiology

Background: The glymphatic system is a waste disposal system unique to the brain, which harnesses the bulk flow of cerebrospinal fluid (CSF) to flush out metabolic waste. CSF is thought to be driven along paravascular pathways by vascular pulsatility, but how glymphatic flow is regulated remains unclear. **Objectives:** We will test our hypothesis that a key regulator of glymphatic flow is cerebral vascular tone, which we believe is modulated via the sympathetic nerves innervating the cerebral vasculature. **Methods:** We have separately examined the impact of electrical stimulation of the *extrinsic* and the *intrinsic* sympathetic innervation of the cerebral vasculature. The extrinsic sympathetic nerves were activated via the cervical sympathetic trunk, located on the side of the neck, which primarily controls superficial cerebral vessels. The intrinsic sympathetic nerves were activated via unilateral stimulation of the locus coeruleus (LC), which innervates the cerebral microvasculature, using stereo-tactically placed bipolar electrodes. During stimulation, a fluorescent dye mix was injected into the CSF reservoir of the cisterna magna and allowed to diffuse into the brain via perivascular pathways. These tracer-infused brains were then fixed, cryo-sectioned and imaged. Fluorescence intensity was compared between the left (non-stimulated) and right (stimulated) hemispheres to assess glymphatic function. **Results:** We found that activation of the extrinsic sympathetic nerves had no significant effect on glymphatic flow ($p=0.479$). Ongoing studies will examine the effect of the intrinsic sympathetic nerves. **Discussion:** Our findings will provide important context for the regulation of the glymphatic system and may have relevance to variety of neurodegenerative diseases.

Primary Supervisor: Dr F McBryde

14:00 : Hannah Dexter

Protective effects of systemic apigenin infusion in a preterm fetal sheep model of hypoxic-ischemic encephalopathy

Dexter H[1], Cho KHT[1], Lear B[1] & Dean JM[1]
[1]Department of Physiology

Background: Hypoxic-ischaemic (HI) brain injury has devastating consequences on the neurological outcome of premature infants. There is growing appreciation that inhibiting the hyaluronidase family of extracellular remodelling enzymes following HI may afford neuroprotection. Apigenin, a natural bioactive flavonoid, is a potent inhibitor of hyaluronidase enzymes and has been recently shown to modulate outcomes after perinatal HI. **Objectives:** In the present study, we examined therapeutic potential of intravenous apigenin infusion following a severe HI insult in the clinically relevant preterm fetal sheep model of preterm brain injury. **Methods:** Fetal sheep at 0.7-gestation (term ~145-days) received sham asphyxia (n=9) or asphyxia induced by umbilical cord occlusion for 25 minutes. Immediately after occlusion, fetuses received either a continuous intravenous infusion of saline (n = 9) or apigenin (n=4) for 24h. After 72 hours recovery *in utero*, ewes were euthanised. **Results:** Apigenin significantly reduced the number and burden of post-asphyxial seizures over the 72 hour recovery period (vs. asphyxia-vehicle; P=0.03). In animals that developed seizures, apigenin was associated with earlier seizure cessation (vs. asphyxia-vehicle; P=0.048). Histologically, apigenin increased neuronal survival in the CA1-4 regions of the hippocampus (vs. asphyxia-vehicle; P=0.04), but did not change the number of oligodendrocytes within the periventricular and intragyral white matter (P>0.05). No changes were observed in astroglial and microglial numbers in both white matter regions (P>0.05). **Discussion:** This suggests targeting hyaluronidase enzymes via apigenin improves electrophysiological recovery and confers partial neuroprotection in selected regions. Further analysis of physiological and histological data are required to fully assess its therapeutic potential.

Primary Supervisor: A/Prof Justin Dean

14:15 : Sarah Gray

Supporting Our Mental Health Nurses to Thrive at Work

Gray S[1], Jacobs S[1], Parke R[1]
[1]School of Nursing

Background: The thriving of mental health nurses not only promotes retention in this hard-to-staff specialty, but also impacts on care provision for tangata whaiora. Organisational support, including strong collaboration between kaimahi and leadership, is essential to ensure thriving. At present, there is not a clear strategy for collaboration to support mental health nurses to thrive at work. **Objectives:** To develop a framework for services providers to support mental health nurses to thrive at work. **Methods:** An anonymous questionnaire was distributed to all mental health nurses (including leadership) at participating Te Whatu Ora localities, identifying what mental health nurses perceive they need to thrive at work, and barriers and enablers to collaboration with leadership. Focus groups at each locality will review, develop, and refine findings. Working groups will then co-design processes for collaboration and support initiatives. A framework for collaboration will be developed, informed by findings from each stage. **Results:** Questionnaire responses indicated kaimahi want the resources and support to provide high quality care. Successful collaboration may be aided by strong interpersonal engagement, belief that change is possible, and practical implementation. Success may be hindered by resourcing issues and interpersonal clashes. **Discussion:** This questionnaire and focus groups (to be held in July 2024) will inform and guide collaboration between kaimahi and leadership in pursuit of supporting mental health nurses to thrive. The subsequent framework can inform other locality processes in New Zealand and internationally as part of a wider research programme to support nurses to thrive at work.

Primary Supervisor: Dr. Jacobs, S

14:30 : Melanie Stowell

Digital tools to support mental health in later life: Scoping review of systematic reviews

Stowell M[1], Dobson R[1,2], Bunkley N[1], McCool J[1], Nosa V[1], Whittaker R[1,2]

[1] School of Population Health, University of Auckland, [2] Institute for Innovation and Improvement, Te Whatu Ora Waitematā, Auckland, New Zealand

Background: Older people are often overlooked in the development of digital health interventions, including those designed to support mental health. In an era of population ageing, a strained mental health system and increasing implementation of digital health services, it is crucial to understand the mechanisms needed to circumvent a growing 'digital divide' among older adults needing mental health support. **Objectives:** To clarify our understanding of the components involved in existing digital tools to promote mental health and how these have been tailored to meet the needs and preferences of older adults. **Methods:** A scoping review of systematic reviews is currently underway. Searches were conducted in five databases (MEDLINE, Embase, PsycINFO, Web of Science, and Cochrane Library). Reviews were eligible if they reported on studies in which a digital health intervention was developed and tested with community-dwelling older adults (aged 65+ years) to support their mental health. Included papers will be appraised using a modified Critical Appraisal Skills Programme (CASP) checklist for systematic reviews. Evidence will be extracted and summarised in a narrative synthesis. **Results:** Fourteen systematic reviews are being included for appraisal and analysis. The presentation will discuss key characteristics of included systematic reviews and will highlight relevant study methods (e.g. co-design and recruitment of priority subgroups), outcomes (e.g. acceptability and engagement), and evidence gaps. **Discussion:** Older people's needs and preferences must be considered in the development and implementation of digital mental health services. Implications for policy and practice will be discussed and future directions for research considered.

Primary Supervisor: Dr Dobson, R

14:45 : Natalie Poša

Exploring the acceptability and safety of integrating AI capabilities into a youth mental wellbeing app

Poša N[1], Dixon H[1], Kang A[1], Holt-Quick C[2], Stasiak K[1]
[1]Department of Psychological Medicine, [2]Kekeno Tech

Background: Digital health chatbots are at risk of being overtaken by artificial intelligence (AI) tools with better understanding and conversational capabilities. There is a lack of research exploring the opinions of young people and mental health professionals regarding the use of AI in mental wellbeing chatbots. **Objectives:** To investigate the acceptability and safety of integrating AI into Headstrong, an Aotearoa-based mental wellbeing app for rangatahi, from the perspective of young people and mental health professionals. **Methods:** Semi-structured, in-person interviews were conducted with rangatahi (aged 16-24) and mental health professionals. Each interview was recorded, transcribed with the help of WhisperAI, and analysed using thematic analysis supported by NVivo. **Results:** Sixteen young people (10 females, 5 males, 1 non-binary; average age = 17.81 (*SD* = 2.24)) and eight mental health professionals were interviewed. A majority of the young people preferred the AI-supported version of the chatbot, whereas health professionals' views were more divided. Reasons for this preference included higher perceived levels of empathy and understanding for the AI version of the chatbot. Key concerns surrounding the use of AI included privacy breaches, unsafe advice, an overreliance on digital wellbeing tools and Western-centric views of wellbeing. Participants noted the benefit of instant access to free, youth-appropriate mental health support without stigma. **Discussion:** This study provides preliminary support for the use of generative AI in youth mental wellbeing apps. Concerns and benefits highlighted by participants offer important insight for integrating AI into existing digital health tools for young people.

Primary Supervisor: Dr. Stasiak, K

Oral Presentation Room D

9:00 : AFIFA SAFDAR

Biomarkers to target non-invasive brain stimulation in chronic stroke

Safdar A[1,2], Jordan H[1,2], Byblow W[2,3], Stinear C[1,2]
[1]Department of Medicine, Faculty of Medical and Health Sciences, [2]Centre for Brain Research, [3]Movement Neuroscience Laboratory, Department of Exercise Sciences

Background: Non-invasive brain stimulation (NIBS) techniques have predominantly been used to suppress the contralesional primary motor cortex (cM1) in stroke patients to improve their paretic upper limb performance. However, recent studies have shown that suppressing the cM1 may be detrimental in stroke patients with severe upper limb impairment with absent motor evoked potentials (MEPs). **Objective:** To identify the effects of cM1 facilitation using NIBS on paretic hand performance in chronic stroke patients stratified according to presence (MEP+) and absence (MEP-) of MEP biomarker. **Methods:** In this double-blinded study, facilitatory intermittent theta burst stimulation (iTBS) and sham iTBS were applied to cM1 of 19 chronic stroke participants in two separate sessions in randomized order. Repeated squeeze and release (RSR) of a handgrip dynamometer was used to assess total force released and squeezed with the paretic hand before and after the application of real and sham iTBS. **Results:** After the application of real iTBS, the total force released and total force squeezed with the paretic hand was significantly higher compared to baseline in 9 MEP- participants ($p = 0.047$ and $p = 0.048$, respectively). The application of sham iTBS in 9 MEP- participants and real and sham iTBS in 10 MEP+ participants did not affect paretic hand grip performance (all $p > 0.87$). **Discussion:** The facilitation of cM1 is beneficial for paretic hand grip performance in MEP- but not MEP+ chronic stroke patients. The consideration of the MEP status of chronic stroke patients might enable the targeted application of NIBS techniques.

Primary Supervisor: Prof. Stinear C

9:15 : Sachin Sood

Inadequate Neuraxial Anaesthesia During Caesarean Section: A Single-Institution Retrospective Cohort Study

Sood S[1], Sidhu N[1], Chiang D[1]
[1]School of Medicine

Background: Caesarean section is commonly performed under neuraxial anaesthesia, which can sometimes be inadequate, leading to discomfort and adverse outcomes. The incidence and risk factors of inadequate neuraxial anaesthesia in New Zealand, particularly among Māori and Pasifika populations, are not well documented. **Objectives:** This study aimed to determine the incidence of inadequate neuraxial anaesthesia during caesarean sections in New Zealand and identify associated risk factors, focusing on anaesthesia type, case acuity, and patient demographics, including ethnicity. **Methods:** A retrospective cohort study analysed 3,062 caesarean sections in Waitematā from August 2021 to December 2022. Data included patient demographics, anaesthesia type, and outcomes. Inadequate neuraxial anaesthesia was defined as the need for repeat or supplemental anaesthesia and conversion to general anaesthesia. Statistical analyses assessed associations between variables and anaesthesia inadequacy. **Results:** The incidence of inadequate neuraxial anaesthesia was 8.07% (247/3,062). Epidural anaesthesia had the highest inadequacy rate at 11.80%, followed by combined spinal-epidural at 10.28%, and spinal anaesthesia at 5.86%. Inadequate anaesthesia was significantly associated with emergency cases ($p = 0.002$) and varied by anaesthesia mode ($p < 0.001$). There was no significant variation by ethnicity ($p = 0.381$). **Discussion:** The study found an 8.07% incidence of inadequate neuraxial anaesthesia during caesarean sections, with higher rates in emergency cases and those using epidural anaesthesia. These findings highlight the need for improved anaesthetic techniques and protocols, particularly in emergency settings. The study provides a benchmark for New Zealand and underscores the importance of further research to reduce inadequate anaesthesia rates and GA conversions.

Primary Supervisor: Dr. Sidhu, N

9:30 : Christopher Carson

Characterisation of Substantia Nigra pars Lateralis' Firing Patterns by Subthalamic Nucleus Stimulation

Carson C[1], Todd K[2], Freestone P[1]

[1]Department of Physiology, Faculty of Medical and Health Sciences, University of Auckland, New Zealand,
[2]Faculty of Physiology, Anatomy and Genetics, Oxford University, United Kingdom

Background: Compared to the motor symptoms of Basal Ganglia diseases, such as Parkinson's, the less easily recognised non-motor symptoms have more poorly characterised pathophysiologies. Because the substantia nigra pars lateralis (SNl) specifically terminates in the tail striatum (TS), which receives sensory information, its dysfunction contributes to non-motor symptoms. The main target of deep brain stimulation (DBS) used in Parkinson's treatment is the subthalamic nucleus (STN). This has recently been shown to regulate dopamine release in the TS by directly modulating SNl firing. Little is known about this pathway. **Objectives:** To characterise, using electrophysiological techniques, the firing patterns of rat SNl dopamine-neurons through STN-stimulation to better understand the non-motor basal ganglia pathways. **Methods:** In vivo insertion in rats (urethane anaesthetised) of a bipolar-electrode into STN and multielectrode-array into SNl. Neurons were identified from depth, spontaneous firing frequency and action potential shape/duration. STN stimulated with 1mA, 10-150Hz, 0.1ms-pulse, 2s-train and output recorded with OpenEphys electrophysiology platform. Characterisation algorithms programmed in MATLAB. **Results:** Preliminary results show 130Hz stimulation raised SNl firing frequency 2.2±0.4x above its 8.5±4.5Hz baseline (no effect <60Hz). Basal frequency with its coefficient-of-variation, and, following STN-stimulation, peak firing frequency and timing of response need further investigation. **Discussion:** SNl firing patterns show distinctive characteristics from other substantia nigra neurons. Only high-frequency STN stimulation excited SNl dopamine-neurons, consistent with only high-frequency DBS treatment of Parkinson's being effective. This possibly indicates a dopamine-neuron excitation mechanism for DBS. Understanding SNl dopamine-neuron firing patterns helps elucidate non-motor symptom pathogenesis, previously often unrecognised or viewed as untreatable.

Primary Supervisor: Dr. Freestone, P

9:45 : Briony Fanslow

Burden and seasonality of Influenza- and Human metapneumovirus-associated adult hospitalisations in Aotearoa New Zealand

Fanslow B[1, 2], Aminisani N[2], Huang S[2], Wood T[2], McIntyre P[3], Petousis-Harris H[1], Paynter J[1,3], and The SHIVERS Investigation Team

[1] Department of General Practice and Primary Health Care, University of Auckland, [2]Institute of Environmental Science and Research, Otago University, [3]The Immunisation Advisory Centre

Background: Prior research using Auckland's hospital-based acute respiratory illness (ARI) surveillance platform found hospitalisation rates for human metapneumovirus (HMPV), an influenza-like virus, were 3–6 times higher for Māori and Pasifika across socio-economic groups during 2012–2015. Because the COVID-19 pandemic altered viral circulation patterns, updated burden estimates are needed to inform introduction strategies for HMPV vaccines (in late-stage development). **Objectives:** Evaluate 2012–2023 epidemiological patterns in HMPV and influenza hospitalisations to inform adult vaccination policies and compare post-pandemic re-emergence. **Methods:** Annual ARI hospitalisation rates for patients ≥20 years of age were used to calculate overall and demographic-specific incidence. Non-testing rates were controlled using imputation. Incidence rate ratios (IRRs) were computed using Poisson regression. **Results:** Among 36,201 hospitalisations during 2012–2023, the rate per 100,000 residents was 12.9 (95% CI:12.2–13.0) for HMPV and 57.7 (95% CI:56.1–59.2) for influenza. IRRs were highest for older adults; HMPV 18.6 (95% CI:14.7–23.5) and influenza 13.4 (95% CI:12.2–14.9), comparing ≥80-year-olds with 20–49-year-olds. Age-adjusted HMPV IRRs remained higher for Māori (2.0, CI:1.5–2.5) and Pasifika (3.4, CI:2.9–4.0), relative to European/other (similar for influenza). Both viruses' seasonal epidemics peaked high and early in 2022 (post-pandemic), then later in 2023 (typical for HMPV, atypical for influenza). **Discussion:** Although HMPV rates were much lower than influenza, HMPV burden may prove higher if tail-end ascertainment for later-peaking epidemics (also seen for influenza post-COVID-19) were improved through longer-lasting surveillance. IRRs from available data identify older-adults, Māori, and Pasifika as priority-groups for HMPV vaccination and therapeutics.

Primary Supervisor: Dr Paynter, J

10:00 : Kelly Peterken

Investigating the addition of a novel TLR2 agonist to a *S. aureus* polyvalent protein vaccine

Peterken K[1,4], Clow F[1], Cameron A[2,4], Kavianinia I[3,4], Langley R[1], Brimble M[2,4], Dunbar R[3,4], Fraser J[1], Radcliff F[1,4]

[1]Department of Molecular Medicine and Pathology, [2]School of Chemical Sciences, [3]School of Biological Sciences, [4]Maurice Wilkins Centre

Background: *Staphylococcus aureus* is an opportunistic human pathogen that causes a range of diseases. Emergence of multi-drug resistant strains and diminishing antibiotic options prompts the need for alternate treatments such as vaccines. Our group is developing a polyvalent vaccine targeting three highly conserved proteins. Animal models investigating other pathogens show that agonists, like those targeting Toll-like receptors (TLRs), can improve vaccine efficacy. TLR2 signalling pathway activation is important in controlling *S. aureus* infections. Therefore, we elected to test combining a potent TLR2 agonist with our vaccine. **Objectives:** This study investigates whether combining a novel TLR2 agonist with our polyprotein vaccine will improve protection against *S. aureus*. **Methods:** The vaccine efficacy was tested using a mouse vaccine challenge model and *S. aureus* burden was recovered from tissues. Antibody titres were measured via enzyme-linked immunoabsorbent assays (ELISA), and their neutralising capability was analysed by ELISA-based assays. A cytometric bead array was used to investigate cytokine production in splenocyte supernatant. **Results:** Our studies show that TLR2 agonist addition improves both antibody titres and their neutralisation activity. This combination significantly reduces *S. aureus* burden in the liver compared to Adju-Phos alone (P <0.001) and TLR2 agonist without the protein vaccine (P = 0.018). The splenocyte supernatant of these mice showed significantly more production of IFN-γ, TNF, and IL-6 cytokines following stimulation with the vaccine polyprotein. **Discussion:** Our results suggest that combining a novel TLR2 ligand with our polyprotein vaccine enhances immunogenicity, improves *S. aureus* protection in an infection model and warrants further investigation.

Primary Supervisor: Dr. Radcliff, F

10:45 : Ashok David Jose

Development and evaluation of an oxygen microbubble hydrogel for sensitisation of cancer cells to radiotherapy

Jose A D[1], Chong C HN[1], Jaiswal J[2], Wu Z[1], Thakur S S[1]
[1] School of Pharmacy, [2] Auckland Cancer Society Research Center

Background: There is mounting evidence that reoxygenating tumours can improve their sensitivity to conventional cancer therapies. While oxygenated microbubbles (OMB) have shown promise for this application, they suffer from poor stability and rapid clearance from the tumour site. Incorporating OMB in an injectable hydrogel depot may achieve prolonged oxygenation of the tumour microenvironment. **Objectives:** To formulate OMB dispersed in a temperature sensitive hydrogel for intratumoural administration. **Methods:** OMB were generated by first preparing a liposomal mixture which was dispersed in a thermosensitive poloxamer hydrogel, pressurised with oxygen in a gas-tight vial and vortexed to achieve the formulation. OMB size distribution, hydrogel rheology, formulation injectability, oxygen loading and release, and the formulation impact on efficacy of radiotherapy against a colon cancer cell line (HCT116) were evaluated. **Results:** DSPC:DSPE-PEG2000 liposomes (94:6 molar ratio) dispersed in a poloxamer 407: poloxamer 188 (21:6.5% w/w) hydrogel generated OMB predominantly sized <1 µm. Formulations were within the established limits of injectability (F<38N) at room temperature and gelled near physiological temperatures, demonstrating both greater oxygen loading and prolonged oxygen release compared to OMB alone. The formulation co-treatment enhanced radiotherapy significantly, reducing clonogenic survival rates in HCT116 cells by 78% in hypoxic conditions and by 68% in normoxic conditions ($p<0.0001$ in both cases). **Discussion:** Reoxygenation with a newly developed OMB hydrogel formulation effectively sensitised HCT116 to radiotherapy *in vitro*. Ongoing studies are exploring the importance of reoxygenation rate and extent for optimal tumour sensitisation.

Primary Supervisor: Dr. Thakur S S

11:00 : Yohanka Perera

Establishing 3D tumour models for breast cancer: a unique, New Zealand-specific tool for cancer research

Perera Y[1], Jamieson S[1,2], Nolan E[1]

[1]Auckland Cancer Society Research Centre, [2]Department of Pharmacology and Clinical Pharmacology

Background: Breast cancer is the most common malignancy among New Zealand (NZ) women, with Māori and Pasifika patients experiencing alarmingly worse outcomes. Human epidermal growth factor receptor-2 (HER2) positive and triple negative breast cancer (TNBC) are aggressive tumour subtypes with poor prognoses. Clinically relevant, advanced tumour models are urgently required improve our understanding of disease biology and drug resistance. **Objectives:** To establish and validate two NZ-specific tumour models: patient-derived tumour organoids (three-dimensional 'mini-tumours') and tumour explants (freshly resected tumour pieces cultured on sponges) and investigate how drug sensitivity can be modified by intrinsic and extrinsic tumour factors. **Methods:** Breast tumour organoids and explants are being generated from treatment-naïve primary tumour tissues donated by consenting patients post-surgery. Following characterization, their response against targeted therapy and/or chemotherapy is measured using the Cell Titre-Glo® 3D cell viability assay. To explore factors that influence inter-patient variability in drug response, tumour heterogeneity will be evaluated using immunohistochemistry and transcriptomics. The effect of cellular interactions within the tumour microenvironment will be studied using multiplex imaging and organoid co-cultures. **Results:** To date, a collection of organoids (n=5) and explants (n=2) have been generated. Subsequent characterization and drug response profiling have been performed for n=1 HER2+ organoid line and n=1 TNBC organoid line. Additionally, preliminary experiments indicate possible pro-tumorigenic effects of mature adipocytes on patient drug sensitivity to T-DM1. **Discussion:** The use of tumour organoids and explants as advanced cancer models has exciting potential to improve patient outcomes by supporting pre-clinical drug discovery and personalized cancer therapy.

Primary Supervisor: Dr. Nolan, E

11:15 : Kamel Ahmed

Hyaluronic Acid-Functionalised pH-Responsive Liposomes for Targeted Chemotherapy Delivery to Breast Cancer Stem Cells

Ahmed K[1], Nolan E[2], Shelling A[3], Wu Z[1]

[1] School of Pharmacy, [2]Auckland Cancer Society Research Centre, [3]Department of Obstetrics, Gynaecology and Reproductive Sciences, and Centre for Cancer Research,

Background: Cancer stem cells (CSC) contribute to drug resistance and cancer metastasis, reducing patient outcomes. Synergistic drug combinations targeting multiple pathways have shown promise in overcoming resistance and metastasis in cancer therapy. Moreover, pH-sensitive liposomal (pSL) delivery systems can potentially enhance intracellular drug delivery and maximise drug efficacy. **Objectives:** This study aimed to develop pH-sensitive liposomes functionalised with hyaluronic acid (HA-pSL), loaded with doxorubicin (DOX), and a CSC inhibitor, BUF for targeting HER2+ breast cancer, particularly CSCs. **Methods**: Different pSL formulations (DOX-HA-pSL and BUF-pSL) and their corresponding non-pSL were prepared using the ethanol injection method. The liposomes were characterised in terms of morphology, size, and pH-responsiveness. Cytotoxicity was evaluated in 2D cell lines and 3D spheroids which were formed using the hanging drop technique. **Results**: All liposomal formulations showed a spherical nanosised particle (< 150 nm). HA-pSL loaded with 80% DOX showed minimal leakage at pH 7.4 and rapid drug release at the endosomal pH (pH 5). The combination therapy of DOX-HA-pSL and Buf-pSL displayed greater cytotoxicity against BT474 (Half maximal inhibitory concentration IC_{50} 0.189 µM DOX) and HCC1954 (IC_{50} 0.058 µM DOX) cancer cells with lower IC_{50} than the free DOX and corresponding non-pSL formulations. Treatment with HA-pSL combination formulations led to the dissociation of the BT474 and HCC1954 multicellular spheroids (250 µm), confirming the CSC-eliminating efficiency of the formulation. **Discussion**: Co-delivery of DOX and Buf via pSL demonstrates enhanced intracellular delivery and cellular release through endosomal escape, maximising the synergistic cytotoxic effects to HER2+ cancer cells including CSCs.

Primary Supervisor: Prof. Zimei Wu

11:30 : Claire Palma

PHD Inhibition Induces Antiproliferative Effects in Melanoma through HIF-1α Stabilisation

Palma C[1], Jamieson S[1,2], Lee TW[1], Singleton D[1,3]

[1]Auckland Cancer Society Research Centre, [2]Department of Pharmacology and Clinical Pharmacology, [3]Department of Molecular Medicine and Pathology

Background: *EGLN1*, the gene encoding the prolyl hydroxylase domain protein 2 (PHD2) enzyme, is a significant gene dependency in melanoma and has been identified as a druggable target. Recently, the PHD inhibitors Roxadustat and Daprodustat have been developed for treating anemia in patients with chronic kidney disease. **Objective**: This study aims to determine the sensitivity of melanoma cell lines to PHD inhibitors and whether the anticancer effect is mediated by HIF-1α stabilisation. **Methods**: Melanoma cells with known *EGLN1* dependency were transduced with CRISPR-Cas9 lentiviral vectors and subjected to single-cell cloning. *HIF1A* knockout (KO) models were generated and validated through Western blotting. The effect of PHD inhibitors on both wild-type (WT) and *HIF1A* KO cells was assessed using thymidine incorporation assays and comparative proliferation assays. Further validation was conducted by knocking out *EGLN1* to compare genetic with pharmacological dependence. **Results**: Significantly higher IC_{50} values were observed *HIF1A* KO compared to WT cells ($P<0.05$, $n=3$) upon Roxadustat, but not Daprodustat, treatment. Longer-term assays showed 30-70% inhibition in WT cell proliferation and 0-10% inhibition in *HIF1A* KO cells at pharmacologically achievable concentrations of Roxadustat (10-20 µM) and Daprodustat (1-2 µM). Additionally, *EGLN1* KO cells exhibited a significant decrease in growth compared to *HIF1A* KO and control cells. **Discussion**: These findings indicate that melanoma cell lines are sensitive to PHD inhibition, and the antiproliferative effects are mediated by HIF-1α. These preliminary results support further investigation into the potential of PHD inhibition as a novel anti-melanoma strategy, either alone or in combination with existing therapies.

Primary Supervisor: Dr. Singleton, D

11:45 : Olivia Hogan

Deciphering the mystery of arylformamidase' involvement in immunosuppressive kynurenine production in cancer

Hogan O[1], Wang Y[1], Leung E[1], Tomek P[1]
[1] Auckland Cancer Society Research Centre

Background: Stopping cancers from producing an immunosuppressive tryptophan metabolite called kynurenine holds great potential for sensitising patients to curative immunotherapies. We hypothesised that the arylformamidase enzyme, historically assumed to control kynurenine production, could become a drug target for stopping kynurenine formation. However, our data challenge arylformamidase's essentiality as arylformamidase-knockout liver cancer cells still produce kynurenine. But this result cannot be recapitulated in protein lysates, thus confounding interpretation. This discrepancy likely arises due to non-physiological doses of kynurenine's precursor N-formyl-kynurenine used in the protein lysate assay. **Objectives:** To clarify arylformamidase's involvement in kynurenine production, I aim to develop an assay that mimics enzymatic formation of N-formyl-kynurenine by tryptophan-metabolising enzyme indoleamine-2,3-dixzoygenase 1 (IDO1). **Methods:** Protein lysates were incubated at 37°C either with a mix of IDO1, tryptophan and activating co-factors, or N-formyl-kynurenine to test functionality of individual metabolic steps. Measuring stability of metabolites in blank solutions tested reliability of the assay, and inhibitors of IDO1 (NLG-919) or kynurenine-producing enzymes (diazinon) tested enzymatic source of metabolism. Metabolites were quantified by liquid chromatography. **Results:** Neither 6-hour incubation nor activating co-factors substantially degraded any metabolite (12.2% ± 21.0% change relative to control). Protein lysates from 2 liver cancer lines and mouse liver produced kynurenine from both N-formyl-kynurenine and tryptophan at 24 ± 6.0 µM/hour (13 to 33.5 µM/hour range) mimicking that of living cells (15.6 ± 7.1 µM/hour), and the metabolism was essentially terminated by pharmacological inhibition. **Discussion:** This new physiologically relevant assay will help clarifying arylformamidase's essentiality for kynurenine production in cancer and beyond.

Primary Supervisor: Dr. Tomek, P

13:30 : Libby Lord

Intergenerational effects of antenatal corticosteroid exposure

Lord L[1], Gamble G[1], Harding J[1], Walters A[1], May R[1] for the ANCHOR Study Group.
[1]Liggins Institute

Background: Antenatal corticosteroids are given to women at risk of preterm birth to reduce rates of poor newborn health outcomes, including respiratory distress syndrome. However, there is concern surrounding potential adverse effects on subsequent generations. Animal studies have demonstrated endocrine and metabolic changes in those exposed to corticosteroids *in utero* (F1) and in the second generation (F2). **Objectives:** To assess the effects of parental antenatal corticosteroid exposure on health outcomes of the second generation (F2) of Auckland Steroid Trial (AST) participants**. Methods:** In the AST, women expected to birth between 24- and 36-weeks' gestation (F0) were randomised to corticosteroid or placebo injections. When F1 participants were 50 years of age, they and their children (F2) were followed up with a self-report questionnaire and data linkage. The primary outcome for the F2 analysis was body mass index (BMI) z-score. Secondary outcomes included respiratory, neurodevelopmental, cardiovascular, mental and general health, and social outcomes. **Results:** Of the 214 F2 participants followed up, 145 had BMI data available. Mean BMI z-score was 0.53 (standard deviation 1.4), the proportion of overweight or obesity was 48/145 (33%) and obesity 24/145 (17%). Neurodevelopmental conditions were present in 27/214 (13%), mental health conditions in 57/214 (27%), respiratory conditions in 87/214 (41%) and prediabetes in 2/214 (0.9%). Comparison between groups is ongoing. **Discussion:** Demonstrating intergenerational safety will continue to promote the use of antenatal corticosteroids, an effective neonatal treatment. If impacts of antenatal corticosteroids are seen in the second generation, this may provide an opportunity for monitoring and intervention.

Primary Supervisor: Distinguished Professor Harding, J

13:45 : Michael Beacom

Non-linear quantitative EEG measures: Biomarkers for evolving fetal brain injury

Beacom MJ[1], King VJ[1], Lear CA[1], Dhillon SK[1], Gunn AJ[1], Bennet L[1]
[1]Department of Physiology

Background: Hypoxia-ischemia (HI) is a significant contributor to perinatal brain injury. Early identification and treatment during pregnancy may improve neural outcomes. Traditional quantitative electroencephalogram (EEG) metrics, like spectral analysis, have shown limited ability to discriminate between injury severities. **Objectives:** This study investigates the potential of non-linear EEG analysis for improved detection. **Methods:** Instrumented preterm fetal sheep received complete umbilical cord occlusion (UCO) to induce HI. Fetal sheep randomly received either control (n=9), 15 minutes (n=9), or 25 minutes-UCO (n=9). Physiological and blood-gas parameters were recorded for 21 days post-UCO before fetal brains were collected. Quantitative EEG metrics included spectral band analysis and non-linear measures: sample-entropy (SampEn), slope entropy (SlopEn) and Permutation Entropy (PermEn).**Results:** Altered spectral and non-linear EEG marked the first 6h for both groups but with no initial differences between HI severities. Thereafter, only the Severe HI group showed persistent suppression of specific spectral bands (total, delta, theta) until experiments end. By contrast, most entropy measures revealed persistent changes until 21 days of recovery (decreased SampEn, increased SlopEn and PermEn) in both groups with greater magnitude of change in severe HI until 9 days of recovery, before recovering towards mild HI levels. **Conclusions:** This study demonstrates that the severity of HI injury was associated with persistent changes in entropy measures even after mild HI, suggesting that non-linear EEG analysis is a promising long-term biomarker for assessing HI injury severity and phases of injury. These approaches may reveal subtle changes in EEG activity missed by traditional spectral methods.

Primary Supervisor: Professor Bennet, L

14:00 : Tayla James

The role of placental macrophages in impaired placental vascular function in Fetal Growth Restriction

James TJ[1], Boss AL[1], James JL[1]
[1]Department of Obstetrics and Gynaecology

Background: The placenta is a fetal organ essential for exchange. It has a branched villous structure, within which an extensive network of blood vessels enable efficient oxygen and nutrient delivery to the fetus. Impaired placental vascular development is associated with the pregnancy disorder fetal growth restriction (FGR). Placental macrophages, termed Hofbauer cells, are thought to support placental vascular development. However, limited and conflicting data exists describing Hofbauer cell abundance in FGR placentae, and differences in Hofbauer cell phenotype have not been examined. **Objectives:** This PhD work aims to utilise advances in recent understanding of Hofbauer markers and high-spectrum flow cytometry to better characterise Hofbauer cells in term and FGR placentae and identify potential pro-angiogenic subpopulations of interest. **Methods:** FGR and gestation-matched normal placentae (n=10/group) will be enzymatically digested, and villous core cells analysed using a 19-colour flow cytometry panel to characterise Hofbauer populations present. The functional capacity of sorted Hofbauer cells to promote angiogenesis via paracrine mechanisms will be assessed via cytokine bead array. **Results:** Data collection is underway to identify differences in the prevalence of pro-angiogenic macrophage subpopulations in FGR placentae, possibly providing mechanistic clues to the vascular impairment of this disorder. Further investigation of the secretome of subpopulations identified will help us understand which subpopulations may confer greatest functional importance. **Discussion:** This work seeks to provide a better understanding of how Hofbauer cells may contribute to vascular development and how this may go wrong in FGR, potentially allowing therapeutic targeting of the cause of placental dysfunction in FGR.

Primary Supervisor: A/P. James, J

14:15 : Abbey Lissaman

Stromal secrets – understanding endometrial stromal cell hormone responses and their dysregulation in endometriosis

Lissaman A[1], Cree L[2], Girling J[3], Ponnampalam A[1,4]

[1]Department of Physiology, [2]Department of Obstetrics and Gynaecology, [3]Department of Anatomy, [4]Pūtahi Manawa Healthy Hearts for Aotearoa New Zealand Centre of Research Excellence

Background: The endometrial stroma has important supportive and regulatory effects on endometrial epithelial cells throughout the menstrual cycle. Research on endometrial stromal cells themselves primarily focuses on preparation for embryo implantation. Little is known about the regulation of cycling steroid hormones and their receptors in stromal cells in the healthy non-pregnant uterus, let alone in conditions like endometriosis. **Objectives:** Characterise and compare endometrial and endometriotic stromal cells to determine differences in hormonal responses and regulation of steroid hormone receptors. **Methods:** Endometrial and endometriotic stromal cells were treated for 21 days with control, estrogen, or combined estrogen and progesterone with or without estrogen priming. Proliferation curves were determined using AlamarBlue. Steroid hormone receptor expression was determined using PCR and western blotting. **Results:** Baseline estrogen receptor alpha, progesterone receptor, and androgen receptor expressions were elevated in endometriosis compared to normal endometrial cells (135%, 55%, and 60% increase, respectively). Growth patterns for each cell line were unchanged in response to different hormone treatments. However, the proliferation of endometriosis cells remained significantly lower than normal stromal cells at multiple time points over a 21-day period with control (Day 5 p=0.0214, Day 10 p=0.0083) and estrogen treatment (Day 10 p=0.0464). **Discussion:** Hormonal treatment did not influence growth patterns of endometrial stromal cells as reported for epithelial cells. Endometriotic stromal cells grew at reduced rates compared to normal endometrial stromal cells and exhibited altered steroid hormone receptor expression. Further work will investigate if hormonal treatments differentially influence transcriptional responses of endometrial and endometriotic stromal cells.

Primary Supervisor: Dr. Ponnampalam, A

Oral Presentation Room E

9:00 : Courtney Thorne

Bovine lenses as a model for diabetic cataract: assessing metabolic changes in hyperglycaemia

Thorne C[1,2], Guo G [1,2], Grey A[1,2], Donaldson P[1,2], Lim J[1,2]

[1]Department of Physiology, [2]Aotearoa New Zealand National Eye Centre

Background: Diabetic cataract results from cortical cell swelling that causes light scatter. This is linked to osmotic and oxidative stress from the conversion of glucose to sorbitol and fructose by the polyol pathway, but the exact mechanism is unclear as a suitable animal model is lacking. **Objectives:** To assess the suitability of bovine lenses to study hyperglycemic polyol metabolism and its effects on volume regulation and oxidative stress. **Methods:** Expression of volume regulatory proteins was compared in bovine and human lenses by Western blotting. Gas chromatography-mass spectrometry (GCMS) measured polyol metabolites in bovine lenses incubated in 50mM (high) glucose to mimic hyperglycaemia. Oxidative stress was examined by comparing levels of the antioxidant glutathione and the lipid peroxidation marker Malondialdehyde (MDA). **Results:** Bovine and human lenses express similar volume regulatory proteins. High glucose incubation significantly increased levels of glucose (300-fold increase $p<0.001$), sorbitol (24-fold increase $p=0.003$), fructose (11-fold increase $p=0.004$) and MDA (1.6-fold increase $p<0.001$), and significantly decreased levels of reduced glutathione (1.4-fold decrease $p=0.01$) in the outer cortex at 24hrs compared to control lenses. **Discussion:** Our findings confirm that high glucose incubation mimics metabolic changes observed in human diabetic cataracts, suggesting this bovine model may be useful to study hyperglycaemia-induced oxidative stress and its effect on volume regulation in diabetic lenses. Future work will utilize inhibitors of the polyol pathway to assess the individual impact of glucose, sorbitol and fructose on oxidative stress markers, and determine how these changes affect the function of key proteins involved in cell volume regulation.

Primary Supervisor: Assoc. Prof. Lim, J

9:15 : Samuel James

Diabetic cardiomyopathy is characterised by dysregulated glycogen-autophagy and lysosomal glucose handling

James S [1], Koutsifeli P [1], Annandale M [1], Bell J [2,3], Weeks K [3], Delbridge L [3], Mellor K [1,3].

[1]Department of Physiology, [2]La Trobe University, Melbourne, [3]University of Melbourne, Melbourne.

Background: Diabetic heart disease is characterised by functional and metabolic disturbance. We have previously shown that diabetes is associated with cardiac glycogen accumulation and impaired glycogen-autophagy ('glycophagy'). The mechanisms of lysosomal glycogen and glucose handling remain elusive. **Objectives:** This study investigated the role of potential lysosomal glucose transporters, Spns1 and Glut8, in diabetic animal models and isolated cardiomyocytes. **Methods:** Cardiac Spns1 and Glut8 expression was measured using qPCR in streptozotocin-induced type 1 diabetic rats (T1D) and high fat diet-induced type 2 diabetic mice (T2D). Neonatal rat ventricular myocytes (NRVMs) were transfected with siRNA to induce Spns1 and Glut8 knockdown. NRVMs were cultured in normal (5mM) or high (30mM) glucose for 24 hours. Gene knockdown was confirmed by qPCR, glycogen content measured enzymatically and protein expression measured by western blot. **Results:** T1D rats exhibited 3.9-fold increased cardiac glycogen coincident with reduced cardiac Spns1 and Glut8 mRNA. In contrast, cardiac Spns1 mRNA was increased in T2D mice. High glucose induced a 22% increase in glycogen and downregulation of Spns1 in NRVMs. SiRNA knockdown of Spns1 and Glut8 did not alter cellular glycogen content or protein expression of glycogen synthase and phosphorylase. **Discussion:** This study is the first to demonstrate that cardiac Spns1 is differentially regulated by T1D and T2D in vivo, and cardiomyocyte Spns1 and Glut8 are responsive to high glucose in vitro. Investigation into the effect of Spns1 and Glut8 knockdown on lysosomal glycogen is underway. Lysosomal glucose transport may be instrumental in cardiomyocyte glucotoxicity in diabetes, warranting further investigation.

Primary Supervisor: A/Prof Mellor, K

9:30 : Ibrahim Mohamed

Evaluating Feijoa for Diabetes Prevention: FERDINAND study

Mohamed, I[1,2], Miles-Chan, J[1,2], Sequeira-Bisson, I[1,2]
[1]Human Nutrition Unit, School of Biological Sciences, [2]High-Value Nutrition National Science Challenge

Background: Low energy diets (LEDs) are effective for body weight loss, with consequent improvement of type 2 diabetes (T2D) biomarkers. In prior clinical studies, whole fruit powdered feijoa, rich in polyphenol and abscisic acid, has shown similar improvements in body weight and T2D biomarkers. However, longer-term human studies, combined with LEDs, have not yet been undertaken. **Objective:** The 6-month FERDINAND study primarily investigated whole fruit feijoa powder on fasting plasma glucose (FPG) and body weight, in a multiethnic cohort with overweight and prediabetes. **Methods:** In this double-blinded, randomised control trial, 97 participants consumed 2.3 grams/day of feijoa or placebo intervention powder. Participants underwent LED-induced weight loss in the first 2 months and weight loss maintenance in the following 4 months. Participants received best practice diet advice, delivered by registered dieticians. Absolute FPG and body weight were measured at 4 timepoints; baseline and months 2, 4 and 6. **Results:** For body weight, no significant interaction was observed between time and intervention powder (P=0.178). However, this interaction approached significance for FPG (P=0.054). Within the feijoa group, FPG was lower than baseline at all timepoints. Within the placebo group, FPG was significantly lower than baseline at months 2 and 4, but not at month 6. **Discussion:** These preliminary findings indicate that daily consumption of whole fruit feijoa powder may elicit improvements on FPG in a multiethnic population with prediabetes. Further statistical analyses to include other T2D biomarkers is being conducted, to better understand the role of feijoa powder in T2D prevention.

Primary Supervisor: Assoc. Prof. Miles-Chan, J; Dr. Sequeira-Bisson, I

9:45 : Borson Wong

Targeting cardiac fructose metabolism in diabetic cardiomyopathy in mice

Wong B[1], D'Souza RF[1], Annandale M[1], Li X[1], James S[1], Weeks K[2], Delbridge LMD[2], Mellor KM[1]

[1]Department of Physiology, [2]Department of Anatomy and Physiology, The University of Melbourne, Australia

Background: Diabetic cardiomyopathy is characterised by impaired heart relaxation and filling (diastolic dysfunction). Cardiac and circulating fructose is elevated in diabetic patients. In diabetic rodents, it has been reported that fructose metabolism is elevated in cardiomyocytes. Our preliminary study showed that cardiac fructose knockdown improved diastolic heart function in diabetic mice. Fructose interventions may be an effective treatment strategy for diabetic heart disease. **Objectives:** To evaluate the effects of fructose intervention on cardiac function in diabetic mice. **Methods:** Male C57BL/6J mice (8 week old) were fed a high-fat, high-sugar diet for 15 weeks to induce diabetes. Mice were treated with an inhibitor (50mg/kg) or vehicle (20mg/kg methylcellulose) via daily oral gavage for 4 weeks. Body weight, blood glucose, glucose tolerance, and cardiac function (echocardiography) were evaluated. **Results:** Diabetic mice exhibited obesity, hyperglycemia, hyperinsulinemia, glucose intolerance and diastolic dysfunction (32% increase in E/e', $p<0.0001$) with preserved ejection fraction. Treatment induced full rescue of E/e' and hyperinsulinemia with 15% weight loss in diabetic mice. Treatment also elicited significant reductions in plasma triglycerides and fatty acids in both control and diabetic mice. Plasma glucose and glucose tolerance were unaffected by fructose intervention. **Discussion:** These findings provide the first evidence that a fructose intervention attenuates diastolic dysfunction in diabetic mice. Functional rescue was associated with weight loss and hyperinsulinemia reversal. This preclinical study suggests that fructose metabolism may provide a novel therapeutic avenue for treating heart complications in diabetic patients.

Primary Supervisor: A/Prof. Mellor, K

10:45 : Santosh Bhujbal

Formulation and characterization of transfersomes for ocular drug delivery

Santosh B[1], Ilva D. R[1], Priyanka A[1]

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Background: Delivering hydrophobic drugs across ocular-tissues remains a challenge due to the complex structure of the eye. Transfersomes (TFS) have previously been shown to efficiently deliver hydrophobic drugs across the stratum-corneum of the skin and can potentially also facilitate ocular drug delivery. **Objective**: This study investigated the ability of TFS to enhance ocular-penetration of tonabersat, a hydrophobic inflammasome inhibitor. **Methods:** TFS were prepared using Phospholipon 90G, Tween 80, and tonabersat at a ratio of 9:1:0.5 by the thin-film-hydration technique. Vesicle size, polydispersity index, and zeta potential were measured using a Zetasizer Nano ZS. The morphology was evaluated by transmission electron microscopy and the tonabersat content was determined by HPLC. Conjunctival and corneal tolerability was tested using Hen's Egg Chorioallantoic Membrane (HET-CAM) and bovine corneal opacity and permeability (BCOP) tests. Finally, ocular penetration into the conjunctiva, eyelid, cornea, and sclera-choroid was evaluated using an ex-vivo porcine whole-eye model. **Results:** TFS were spherical unilamellar structures of 125.50±0.66 nm with an entrapment efficiency of 81.57±8.34%. No conjunctival or corneal irritation was observed for either formulation using HET-CAM and BCOP assays, respectively. In ex-vivo penetration experiments, TFS exhibited a significant improvement in tonabersat penetration ($p<0.05$) in all ocular tissues, with the Cmax of the TFS formulation in the conjunctiva, eyelid, cornea, and sclera-choroid was 72.58±4.12µg/g, 49.64±4.00µg/g, 15.59±1.53µg/g and 2.93±0.33µg/g respectively, while the Cmax of the MCT formulation was only 5.51±0.48µg/g, 3.79±1.1µg/g, 2.39±0.31µg/g, and 0.13±0.13µg/g respectively. **Discussion**: TFS eyedrops offer a promising approach for improving ocular bioavailability, permeability and therapeutic potential of poorly soluble tonabersat.

Primary Supervisors: A/P Rupenthal, I and Dr. Agarwal, P

11:00 : Nikhil Nair

The role of Aquaporin 0 in the regulation of lens hydrostatic pressure

Nair N[1], Vorontsova I[1], Petrova R[1], Chen Y[1], Donaldson P[1]
[1]Department of Physiology

Background: Our sense of sight is critically dependent on the lens' ability to correctly focus light onto the retina, and with age, detrimental changes to lens physiology manifest as cataract. Lens homeostasis relies on water transport via aquaporins (AQPs), a family of water channels, of which AQP0 is the most abundant in the lens. AQP0 is a multifunctional and highly modified protein, and its complexity makes it difficult to study. Zebrafish provide an opportunity to genetically dissect the study of these functions, as they have two orthologues for AQP0 that have subfunctionalised. **Objectives**: To use the advantages of the zebrafish model to test relative contributions of *Aqp0a* and *Aqp0b* to whole lens water transport, assessed by measuring lens hydrostatic pressure. **Methods**: A manometer based microelectrode system was used test hydrostatic pressure at different depths in lenses by advancing a microelectrode towards the lens centre. **Results:** WT zebrafish lenses revealed a hydrostatic pressure gradient that is similar to that observed in the mammalian lens. The maximum pressure developed as a function of zebrafish development. *Aqp0* null mutant lenses showed disruption in their hydrostatic pressure. **Discussion**: The conservation of hydrostatic pressure between mammals and zebrafish strengthens the use of this new model to study the roles of water transport in lens homeostasis. Future studies will test for lens AQP0 as a potential target for the development of novel therapeutic approaches to prevent or treat cataract.

Primary Supervisor: Prof. Donaldson, P

11:15 : Crystal Tan

Zebrafish Lens Anterior Suture Development: A Critical Piece in the Puzzle of Zebrafish Optical Development

Tan C[1], Safrina O[2], Schilling T.F[2], Donaldson P.J[1], Vorontsova I[1]

[1]Department of Physiology, [2]Department of Developmental and Cell Biology, University of California, Irvine, United States

Background: Myopia affects a third of the global population and is projected to impact half by 2050. Zebrafish has emerged as a novel, powerful model to study mechanisms of eye growth and for drug discovery. However, understanding of the interplay between anterior suture anatomy, lens nucleus centralisation (a requirement for normal zebrafish optical development), and refractive properties are lacking, hindering discoveries of mechanisms leading to myopia. **Objectives:** To characterise the normal phenotypic variability of anterior lens suture morphology throughout zebrafish development. **Methods:** Micro-dissected lenses from zebrafish of six developmental stages (from 6 days post-fertilisation to 1 year old) were fixed and labelled with the nuclear stain, DAPI, and filamented-actin stain, Phalloidin-488, labelling lens cell membranes. Confocal optical slices of anterior sutures were captured in wholemount lenses. The length of anterior sutures was measured by ImageJ. **Results:** The anterior lens suture in zebrafish consistently shifts from a point-suture at larval stages to a line-suture in late juvenile stages. Length of the line anterior suture increases with development. **Discussion:** This is the first study to identify the increasing complexity of the anterior zebrafish lens suture, similar to that seen in other species. The transition from a point to a line coincides with the same developmental stage as completion of lens nucleus centralisation, and maturation of lens refractive properties. This indicates a coordination between lens anatomy and optics to achieve a functional optical system throughout zebrafish development, laying the foundation for future work into pathological molecular mechanisms underpinning myopia.

Primary Supervisor: Dr. Vorontsova, I

11:30 : Clare Gebbie

Rapid Long Read Sequencing for the Diagnosis of Rare Disease

Gebbie C[1], Nyaga D[1], Tsai P[1], Phua H H[1,2], Rong J[1], Yap P[3], Le Quesne Stabej P[1,2], Farrow S[1], Toldi G[1,4], Thorstensen E[1], Stark Z[5,6], Lunke S[5,6], Gamet K[3], Van Dyk J[1], Greenslade M[7], O'Sullivan J[1]

[1]Liggins Institute, [2]Molecular Medicine and Pathology, [3]Genetic Health Service New Zealand-Northern Hub, Te Toka Tumai, Auckland, [4]Starship Child Health, Te Whatu Ora Te Toka Tumai, Auckland, [5]Victoria Clinical Genetic Services, Murdoch Children's Research Institute, Parkville, Melbourne, [6]Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Melbourne, [7]LabPLUS, Auckland District Health Board

Background: Rare disorders are overrepresented in neonatal care and are a significant cause of infant mortality. These disorders can be both genetic or epigenetic in origin, meaning rapid sequencing of native DNA with base modifications intact may help improve diagnostic rates and potentially reduce the number of iterative and invasive genetic tests often needed to gain a diagnosis. **Objectives:** We have established an acute care clinical sequencing pipeline based on long-read whole genome sequencing (LRS) of parents and infants. **Methods:** This pipeline integrates the PromethION P2 system (Oxford Nanopore Technologies) with a Bayesian AI-based clinical decision support tool (Fabric GEM™ software). **Results:** We present results for the first ten families processed through the pipeline validation phase. Clinically relevant variants were identified in six out of ten cases. One case was clinically resolved as non-genetic, with three remaining genetically unresolved. We have characterised 14 known clinically relevant differentially methylated regions (DMRs) associated with nine key imprinted disorders for the three unresolved cases. We are developing bioinformatic tools to characterise DMRs across the whole genome, both known and unknown, focusing on genes identified through the phenotype ontology of the infant. **Discussion:** Rapid LRS could help to end the diagnostic odyssey for patients as it offers new avenues for studying how the genome, epigenome and environment interact in the context of human disease, as well as the potential for identifying DNA modifications as therapeutic targets.

Primary Supervisor: Professor. O'Sullivan, J

11:45 : Anna Behling

Matching bacterial strains to predict donor-recipient pairings in FMT

Behling A[1], Portlock T[1], Ho D[1], Wilson B[1], Vatanen T[1,2,3], O'Sullivan J[1,4,5,6,7]

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Background: Faecal microbiota transplantation (FMT) aims to treat gut-related conditions, such as ulcerative colitis (UC), through the restoration of dysbiotic intestinal microbiota. This restoration may be facilitated by the long-term retention (engraftment) of donor bacterial strains. Understanding differences in bacterial community engraftment from each donor is crucial for enhancing treatment effectiveness. We hypothesised that donor strain engraftment analysis could be used to predict FMT donor-recipient pairings. **Objectives:** 1) Identify donor-matching strains in FMT recipients following treatment to predict donor-recipient pairings in a multi-donor FMT trial for UC (FOCUS trial). 2) Determine structural and functional features of donor microbiomes with high engraftment efficiency. **Methods:** FMT donor and recipient strains were profiled using StrainPhlAn. Donor-recipient pairings were predicted by identifying novel donor-matching strains in a recipient's post-FMT sample that were absent prior to treatment. Engraftment efficiency was calculated as the proportion of donor strains detected through strain engraftment analysis in their respective true recipients. **Results:** Strain engraftment analysis correctly predicted some donor-recipient pairings (F1 = 0.56). FMT donor recall (true positive rate) ranged from 0-83% and was strongly correlated with engraftment efficiency (Pearson correlation = 0.81, $p < 0.001$). **Discussion:** To understand the factors underlying efficient microbial engraftment, microbiome diversity (α and β), species relative abundances and gene function profiles of donors with high- and low-engraftment efficiency will be compared. We suggest the performance of strain engraftment analysis in predicting FMT donor-recipient pairings is limited by microbiome sequencing depth. Therefore, future work could assess this approach using studies with higher sequencing depth.

Primary Supervisor: Prof. O'Sullivan, J

13:30 : Carina Donegan

Set and setting the stage: Expectancies of individuals with MDD about to undertake LSD microdosing

Donegan C[1], Daldegan-Bueno D[2], Sumner R[2], Menkes D[3], Evans W[4], Hoeh N[1], Sundram F[1], Reynolds L[1], Ponton R[2], Smith T[6], Allen N [7], Forsyth A[2], Muthukumaraswamy S [2]

[1]Department of Psychological Medicine, [2]School of Pharmacy, [3]Department of Psychological Medicine Waikato, University of Auckland [4]Mana Health, [5]School of Population Health, [6]Te Whatu Ora, [7]Faculty of Engineering

Background: Expectancy in antidepressant clinical trials is crucial but often overlooked. Participant expectations about treatment efficacy can potentially enhance the placebo effect and outcome of antidepressants. Similarly, in psychedelic therapy, "set and setting" can shape outcomes, with expectancy being a critical component of "set". Understanding these expectancies can optimise therapeutic approaches to microdosing. **Objectives:** This study examined expectancy in a clinical trial of Lysergic Acid-diethylamide (LSD) microdosing for depression. **Methods:** Twenty-one individuals aged 21-65 with Major Depressive Disorder microdosed LSD twice weekly for 8 weeks. Before starting, they completed a semi-structured interview on their expectancies for the trial. Transcribed interviews underwent qualitative content analysis, analyzed alongside Credibility/Expectancy Questionnaire (CEQ) scores. **Results:** Five themes were identified: motivation, influence, expected effects, mechanism and hope. Motivations included treatment failure (14/21), long-term depression (6/21), psychedelic interest (7/21), alternative treatment for others (3/21) and professional recommendations (2/21). Influences were media (11/21) and social circles (5/21). Participants expected consciousness change (5/21), subtle effects (9/21) or no expectations (12/21). They believed microdosing would work through neural rewiring (11/21), changing thought patterns (6/21) or were unsure (6/21). Regarding hope, some were optimistic (7/21), cautious (7/21), or just excited about the research (7/21). CEQ scores: mean credibility 19.43 (SD= 3.54) and mean expectancy: 15.43 (SD= 4.03). The mean hope score was 6.67 (SD: 1.77) out of 10. **Discussion:** Participants held positive expectations about microdosing, shaped by predominantly positive media coverage. They viewed microdosing as credible, approaching it with moderate hope. These insights illuminate how psychological factors influence microdosing outcomes.

Primary Supervisors: Dr. Reynolds, L & AP. Muthukumaraswamy, S.

13:45 : Ben Moloney

Developing neuroinflammation biomarkers to assess the antidepressant effects of naltrexone in major depressive disorder

Moloney B[1], Forsyth A [1], Morgan C[1], Dell' Acqua F[2], Sumner R[1], Hoeh N[3], Sundram[3], Muthukumaraswamy S[1], Lin J[1]

[1]Department of Pharmacy, [2] Department of Forensic and Neurodevelopmental Sciences at Kings College London, [3]Department of Psychological Medicine

Background: Current treatments for major depressive disorder (MDD) are ineffective in approximately one-third of patients. Increased inflammation may reflect an MDD sub-type which would benefit from adjunctive anti-inflammatory treatment such as low-dose naltrexone (LDN). However, there is a lack of validated tools to assess treatment effects for neuroinflammation. **Objectives:** To determine if magnetic resonance imaging (MRI) and spectroscopy (MRS) markers sensitive to neuroinflammation in brain regions known to be impacted by inflammation in MDD (anterior cingulate gyrus (ACG) and insula) are different between patients with low C-reactive protein (CRP), those with high CRP, and healthy controls. **Methods:** Participants with moderate MDD and CRP≤1mg/L (n=18) or CRP≥3mg/L (n=7) and healthy controls (n=13) were recruited. MRS and diffusion-weighted MRI data were collected to evaluate local brain temperature, metabolites and diffusion metrics. **Results:** Low-CRP MDD exhibited significantly higher temperature and free-water fraction in the ACG than controls, p=0.016 and p=0.011. High-CRP MDD showed significantly higher myo-inositol/creatine ratio in the right insula compared to low-CRP MDD, p=0.014. **Discussion:** MRI/MRS-measured neuroinflammation may occur in MDD without elevations in serum CRP. These markers will be tested after the MDD participants have been administered LDN to determine their sensitivity to treatment effect.

Primary Supervisor: Dr. Lin, J

14:00 : Dimitri Daldegan-Bueno

LSD microdosing in patients with major depressive disorder: results from an open-label trial.

Daldegan-Bueno D[1], Donegan C[2], Sumner R[1], Forsyth A[1], Evans W[3], Alshakhouri M[1], Reynolds L[2], Ponton R[1], Smith T[4], Roop P[5], Hoeh N[2], Allen N[5], Sundram F[2], Menkes D[6], Muthukumaraswamy S[1]

[1]School of Pharmacy, [2]Department of Psychological Medicine, [3]Mana Health (Auckland), [4]Te Whatu Ora (Auckland), [5]Faculty of Engineering, [6]Department of Psychological Medicine

Background: Major depressive disorder (MDD) affects approximately 5% of the global population and presents significant treatment challenges such as slow onset, variable tolerability, and partial efficacy. Classic psychedelics have shown promise in treating various mental health disorders. **Objectives:** To investigate the feasibility and tolerability of an 8-week regimen of LSD microdosing in people with MDD. **Methods:** Participants with MDD took 16 doses of a titratable formulation of LSD. The first dose (8 µg) was given in the laboratory, with the remaining doses taken at home twice a week, titratable between 4–20 µg. Tolerability was evaluated as participants withdrawing from the trial due to adverse events, and feasibility by the clinic visits attended. Depression severity was measured using the Montgomery-Åsberg Depression Rating Scale (MADRS); other mental health measures were also collected. Safety measures included adverse events, blood laboratory tests, electrocardiogram (ECG), and echocardiograms. **Results:** Nineteen participants (male n = 15, 79%) received the intervention. There were no serious or severe adverse events or clinically significant alterations on laboratory safety assessments. One participant withdrew due to experiencing anxiety when dosing. Participants attended all scheduled visits. MADRS scores were reduced by 60% at the end of the intervention and sustained up to three months post-treatment. Anxiety, rumination, and stress scores also reduced (40-59%). **Discussion:** There was good compliance, and the intervention was well tolerated. Results provide preliminary evidence supporting the safety and feasibility of using LSD microdosing in treating moderate depression and underscore the need for further randomised controlled trials.

Primary Supervisor: Dr. Muthukumaraswamy, S.

14:15 : Katerina Gerasimenko

Impacts of Friedreich's Ataxia on Well-being, Mood and Social Cognition

Gerasimenko, K [1], Rodrigues, M [2,3], Collins, J [3] , Roxburgh, R [2,3,4], Tippett, L [1,4]

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Background: Friedreich's ataxia (FRDA) is an autosomal recessive neurodegenerative condition with onset typically between ages 5 and 15, affecting balance, speech, vision, hearing, muscle control, and heart function. Research on cognition, particularly social cognition, and emotional wellbeing in FRDA is limited. Studies exploring depression have yielded inconsistent findings. **Objectives:** To investigate in FRDA participants (i) social cognition and executive functioning; (ii) impacts of FRDA on mood and well-being and (iii) impacts of low mood on social and executive function. **Methods:** Sixteen individuals with FRDA (aged 20-72) enrolled on Pūnaha Io the New Zealand Neurogenetic Registry & Biobank and 26 age, gender, and education-matched healthy controls participated. Measures assessed facial emotion recognition, theory of mind, verbal fluency, processing speed, inhibition of automatic responses, as well as depression, anxiety, irritability and well-being. Between-group differences were examined with parametric (*t*-test, ANOVA) and non-parametric analyses (Mann-Whitney *U*) as appropriate**. Results:** The FRDA group had significantly poorer performance on the ability to infer the mental states of others, verbal fluency, and processing speed, but no difference in emotion recognition ability or inhibition. They also reported significantly lower mood and well-being than the matched control group. There were no significant associations between mood and social cognition or executive function. **Discussion:** This group of FRDA participants did not show previously reported executive impairments, but did show impairments in theory of mind and lowered mood. Targeted interventions to improve quality of life, social functioning, and overall well-being in FRDA individuals may enhance quality of life.

Primary Supervisor: Prof. Tippett, L

Oral Presentation Room F

9:00 : Xin Yi Lim

Pharmacovigilance and the natural health products (NHPs) industry: a scoping review.

Lim XY [1], Ram S [1], Scahill S [1], Barnes J [1]
[1]School of Pharmacy

Background: Pharmacovigilance involves safety monitoring for medicinal products, including natural health products (NHPs). While the pharmaceutical industry's role in pharmacovigilance for medicines is well established, the NHP industry's contributions remain under-explored. **Objectives:** This scoping review aimed to map global and local literature describing the NHP industry's contributions to pharmacovigilance for NHPs. **Methods:** Using pre-defined keyword and MeSH search strategies, relevant articles were identified from seven international electronic journal databases. In addition, the Medsafe (New Zealand medicines regulator) website was screened to identify gray-literature. **Results:** Thirty-one articles describing the involvement of the NHPs industry in pharmacovigilance were included. Of these, approximately half (n=16) had at least one author from the NHPs industry. The remaining articles involved contributions from the industry through funding, investigational product sponsorship, and/or research data through submitted spontaneous reports to pharmacovigilance databases. Seven articles described industry involvement with active surveillance, usually undertaken in non-community settings, such as medical centres/clinics. Of 61 gray-literature articles relating to New Zealand, 18 described industry engagement, predominantly involving Medsafe requesting product recalls due to adulteration of specific NHPs with unapproved medicines. **Discussion:** The NHPs industry contributes mainly through the collection of spontaneous reports relating to their (manufacturers') products. Active surveillance undertaken by NHP manufacturers rarely involves community users, revealing a gap in safety monitoring among many NHPs users. Local literature describing the NHP industry's contribution to pharmacovigilance is limited. Future studies should explore the potential for the NHPs industry to take a proactive role in pharmacovigilance, including through surveillance methods within community settings.

Primary Supervisor: Prof. Barnes, J

9:15 : Po-Yi Lue

Characterisation of sheep cochlea: translational platform for developing inner ear therapeutic

Lue P.Y.[1,2], Telang R.S. [1,2], Oliver M.H.[3,4], Neeff M.[5,6], Thorne P.R. [1,2,7], Suzuki-Kerr H. [1,2]

[1]Department of Physiology, [2]Eisdell Moore Centre, [3]Liggins Institute, [4]Ngapouri Research Farm Laboratory, [5]Te Whatu Ora, [6] School of Medicine, [7]Department of Audiology.

Background Hearing loss affects 1.5 billion people worldwide; a large proportion of this is caused by sensorineural hearing loss (SNHL). Currently, there are no effective pharmaceutical therapies to prevent or reverse pathologies of SNHL. The translational challenge from preclinical studies in rodent models to clinical studies is the anatomical features of cochlea, which makes therapeutic administration and monitoring of its effect difficult. **Objectives:** This study aims to establish an anatomical baseline in sheep cochlea and assess the feasibility of using sheep as a translational animal model for SNHL research. **Methods**: Cochleae from adult New Zealand Romney sheep were used in this study. Spiral ganglion neuron (SGN) count (n=4) and differentiation (n=3) were assessed by serial-cryosection with haematoxylin and eosin staining and peripherin immunofluorescence labelling, respectively. Cochlear hair cell density was counted by whole mount preparation with phalloidin labelling (n=3). Micro-computerized tomography was used to assess the bony labyrinth structures (n=4). **Results:** Sheep cochleae have 18867±3201 SGNs with a density of 6.0±0.9 cells/0.01 mm^2, and 5.3%±0.4% of them are type II SGN. Cochlear hair cell density is 429.6±29.5 cells/mm basilar membrane. Bony labyrinth volume is 56.6±16.6 µl with 7.2±0.6, 5.0±0.3, and 3.2±0.8 mm in length, width, and height, respectively. **Discussion:** SGN and cochlear hair cells are critical target cells affected by SNHL. Bony labyrinth structures are essential parameters for inner ear pharmacokinetic research. This study identified many key anatomical similarities in the cochlea between sheep and human reference data and shows that sheep is a potential translational model for SNHL research.

Primary Supervisor: Dr. Suzuki-Kerr, H.

9:30 : Saptorshi Gupta

Global spatial-temporal trends in scabies prevalence (1990-2021): results from the Global Burden of Disease study

Gupta S[1], Thornley S[1], Sundborn G[2]

[1]Section of Biostatistics and Epidemiology, School of Population Health, [2]Section of Pacific Health, School of Population Health

Background: Scabies is a microscopic mite that resides in human skin and has recently received attention, since, if left untreated, it can lead to serious diseases like glomerulonephritis and rheumatic heart disease. Scabies is also frequently misdiagnosed. **Objectives:** We estimate global scabies prevalence by time and consider factors that may explain variation between countries. **Methods:** Temporal trends in prevalence and age-standardized rates (ASR) were ascertained in 204 countries and regions from 1990 to 2021 and summarised into an estimate-annual percentage change (EAPC). We used a locally-weighted regression model to estimate the association between socio-demographic index (SDI) and ASR. We analysed regional clusters of scabies burden and its association with socioeconomic factors using a spatial error model. **Results:** ASR of scabies prevalence overall decreased by 2.6% (EAPC = -0.02) over three decades, although the trends were not homogenous. In high-income North America, for example, scabies increased (EAPC: 1.2). The relationship between ASR and SDI is complex, with scabies increasing between low to middle SDI values, followed by a steep negative association thereafter. Spatial cluster of high scabies prevalence was present in tropical Latin America, South-East Asia and Pacific Island nations. The spatial regression model revealed a significant association of scabies with urbanization and per capita gross domestic product. **Discussion:** A small decline in the global prevalence of scabies has occurred in the last three decades. Further focused effort to improve community awareness, accurate diagnosis, and effective treatment of scabies is likely to accelerate progress to reduce scabies and its sequelae.

Primary Supervisor: Dr. Thornley, S

9:45 : Estelle Miller

Psychedelic Microdosing in Aotearoa

Miller E[1], Muthukumaraswamy S[1], Menkes D[2], Noller G[3], Ponton R[1]

[1]School of Pharmacy, [2]Department of Psychological Medicine, [3]Bioethics Centre, Dunedin School of Medicine, University of Otago

Background: The practice of "microdosing" has recently become a fashionable form of drug use. Microdosing involves taking minute amounts of psychedelic compounds on a schedule for well-being benefits. It is a relatively new and understudied concept, therefore, guidelines and harm reduction information do not exist for microdosing; this information largely exists online as anecdotal reports. Studies have investigated microdosing practices globally, but this is the first study of its kind to investigate microdosing in Aotearoa. **Objectives:** To investigate microdosing practices in Aotearoa to inform harm reduction guidelines. **Methods:** People who microdose in Aotearoa were recruited via social media. Participants completed an anonymous online survey detailing their microdosing practices. In-person interviews were conducted with a small cohort of Auckland-based survey participants. **Results:** From both survey and interview results, 105 people indicated they were microdosing. From these results, psilocybin mushroom use was reported by 71% (N = 73) of participants, and lysergic acid diethylamide (LSD) use was reported by 22% (N = 23). Reported dose ranges and preparation methods, namely cutting blotter paper and volumetric dosing (LSD) and grinding dried mushroom material (psilocybin), matched global findings. **Discussion:** Aotearoa microdosing practices are consistent with global findings, except that psilocybin use was higher, and LSD use was lower. This may be due to the ease of access to mushrooms that grow in Aotearoa. This has important harm reduction implications, in particular, a need for mushroom identification education and easily accessible testing methodology, especially to identify dangerous mushrooms that are "lookalikes" to psychedelic species.

Primary Supervisor: Dr. Ponton, R

10:45 : Catriona Miller

Autism prediction using sex-dependent common variation

Miller C[1], Portlock T[1], Nyaga D[1], Jacobsen J[2,3], O'Sullivan J[1]

[1]Liggins Institute, [2]School of Biological Sciences, [3]Centre for Brain Research

Background: Genetic factors significantly contribute to autism, with approximately 50% of the genetic risk attributed to common variation. Autism diagnosis is more prevalent in males than females (4:1 ratio). Prior research using common variation for autism prediction has been limited by small sample sizes, a narrow set of single nucleotide polymorphisms (SNPs) and neglecting the sex difference. **Objectives:** To identify the sex dependent genetic factors contributing to autism prediction. **Methods:** We used whole genome sequencing data of 1,732 individuals (42% autistic, 58% neurotypical) to train a machine learning model. The data was split (56:24:20). The training split (56%) was used to train models using 1) autism risk genes, 2) polygenic risk scores (PRS) and 3) significant SNPs (Fisher test; $p<5e-5$). These models were combined with sex and used for predictions on the test split (20%). A validation dataset of 10,000 individuals, characterised using a different genotype array, was reserved. **Results:** Our model had an accuracy of 0.68 (female: 0.65, male: 0.69), area under the curve (AUC) of 0.72, and F1 score of 0.69 in the test dataset. On the validation dataset, we observed an accuracy of 0.63, AUC of 0.66, and F1 score of 0.66. The SNPs had the strongest contribution; however, this contribution was greater in males. **Discussion:** These findings indicate that multiple factors contribute to the genetic risk for autism and support the hypothesis of sex dependent genetic factors. Future work should incorporate clinical data to cluster individuals based on genetic and phenotypical data and enhance diagnostic predictability.

Primary Supervisor: Prof. O'Sullivan, J

11:00 : Andrew Holmes

Machine/Deep Learning to Identify Novel Clinical Risk Factors for Glaucoma

Holmes A[1], Danesh-Meyer H[1,2], Schierding W[1,2]

[1]Department of Ophthalmology, [2]Vision Research Foundation, Auckland

Background: Primary open-angle glaucoma (POAG) is the leading cause of irreversible blindness worldwide. As POAG is typically asymptomatic until advanced, and treatment cannot reverse vision loss, prevention and early detection are vital. However, intraocular pressure (IOP) currently remains the only widely accepted modifiable risk factor for POAG. A range of emerging risk factors have been reported, but their importance is unclear. **Objectives:** Develop interpretable predictive models to identify clinical factors that can indicate which individuals are at a high risk of POAG. **Methods:** Machine learning models were trained using data from the UK Biobank, a large prospective study of 40-69 year-olds in the United Kingdom. We selected a cohort of 14,242 cases and 427,990 controls. 57 risk/predictive factors and biomarkers were extracted based on previous reports of their association with POAG. We trained four types of models: demographic, ophthalmic, systemic, and an ensemble model incorporating all factors. Models were evaluated using cross-validation and a held-out test set corresponding to 10% of the data. **Results:** The best individual model was ophthalmic, but the ensemble model achieved a promising accuracy, with an area under the receiver operating characteristic curve (AUROC) of 0.88 (95% CI 0.85-0.91), sensitivity of 75% and specificity of 87%. **Discussion:** Preliminary results indicate that machine learning is a promising approach for identifying risk factors, which might further identify individuals with the highest risk of developing glaucoma. Subsequent analyses will include an interpretation of the importance of emerging risk factors, while future models will aim to identify novel predictors.

Primary Supervisor: Dr. Schierding, W

11:15 : Chaiquan Li

Using natural language processing and machine learning to categorise text-based cardiovascular death

Li C [1], Poppe K[2], Jackson R[1], Wells S[3], Liang J[1]

[1]Department of Epidemiology and Biostatistics, [2]Department of Medicine, [3]Department of General Practice and Primary Healthcare.

Background: Our research group holds copies of text-based cause of death (CoD) information from all NZ death certificates written between 1988-2023. However, only records before 2019 have been classified using the International Classification of Disease (ICD-10), which prevents us from identifying cardiovascular (CV) deaths after 2019. **Objectives:** To apply and test an auto-classify algorithm using natural language processing combined with machine learning for the classification of CoD from death certificate text within 2020-2023 as either CV or non-CV. **Methods:** In this study, adult deaths with valid ICD-10 codes from 2000-2016 were used to train the algorithm (n = 430,471) and data from 2017-2018 used for validation (n = 59,186). After preprocessing, text was transcribed to series of numbers and fed into a decision tree-based model (EXtreme Gradient Boosting) with three covariates (age, sex, country of birth), and model performance assessed. **Results:** CV and cancer-related words were the most frequently occurring in the validation dataset, with 21,306 (36%) classified as CV death. The area under the receiver operating characteristic curve (AUROC) was 0.972 (95% confidence interval: 0.971-0.973). The model correctly identified 92% of the CV deaths and 92% of the non-CV deaths. Eighty-four percent of CV deaths identified by our model were true CV deaths and 96% of non-CV deaths identified by our model were true non-CV deaths. **Discussion:** The algorithm identifies CV deaths with sufficient accuracy to be used to classify CV and non-CV deaths in the 2020-2023 national mortality datasets.

Primary Supervisor: Assoc Prof. Poppe, K

11:30 : Withdrawn

11:45 : Enzo Allevard

Tibia and fibula bones prediction from external shank skin shape in a paediatric population

Allevard E[1], Besier T[1], Choisne J[1]
[1]Auckland Bioengineering Institute

Background: Several devices or software solutions are now available for 3D body scanning using LiDAR (Light Detection and Ranging) sensors, laser scanners, images, and videos. Predicting bone surfaces from 3D body scans can enhance clinical and orthopaedic practices. Statistical shape models (SSMs) have demonstrated promising results in predicting bone structures in paediatric populations, leading to personalised child anatomy based on their shape. **Objectives:** To predict tibia and fibula bone surfaces using shank skin surface data as input for an SSM. **Methods:** Forty-eight post-mortem CT (computed tomography) scans of children (20F; 4-18years; 14-84kg; 97-185cm) were segmented to extract the shank skin and tibia/fibula bones meshes. Each mesh was non-rigidly registered and fitted to a template mesh, using radial basis functions to achieve nodal correspondence, then rigidly aligned after merging bones and skin meshes. A Principal Component Analysis was conducted to use the resulting weights for fitting the external shank mesh and predict the tibia/fibula bone structure associated with this child's shank surface. **Results:** A leave one out analysis resulted in an average root mean square distance error of 2.07±2.20 mm between the CT reconstructed and SSM predicted tibia/fibula and a dice score of 0.86±0.08. **Discussion:** This study demonstrated the potential to predict bone structures from external skin scans with reasonable accuracy. The accuracy of these predictions is mainly influenced by the participant's anthropometric data, with extreme height having the highest error. This research serves as a proof of concept, encouraging further studies, including femur and pelvis bones, and more participants.

Primary Supervisor: Dr. Choisne, J

Elevator Pitch EP

EP 1: Yevetta Xiang

Exploring how the liver circadian clock regulates the host response to infection

Xiang Y[1], Rolland L[1], Astin J[1], Hall C[1]
[1]Department of Molecular Medicine and Pathology

Background: Circadian rhythms in behaviour and physiology help organisms prepare for daily environmental challenges. At the cellular level, these rhythms are transcriptionally controlled by a circadian clock encoded by conserved clock genes. While the host response to bacterial infection is known to have circadian rhythmicity, how clock genes regulate antibacterial protection is poorly understood. **Objectives:** To expand upon previous findings in the Hall group that the clock gene *per2* regulates the host response to infection by controlling infection-responsive expression of *c3a.3*, an antibacterial gene expressed in the liver. Additionally, we will examine the liver's role in modulating the host response to infection, using the larval zebrafish as a model organism. **Methods:** Splice-blocking morpholinos will be used to suppress *c3a.3* expression and transgenic lines to rescue *per2* expression in the liver of *per2*$^{-/-}$ mutants, to knock out *c3a.3* specifically in the liver, and to genetically ablate the liver. *Salmonella enterica* will be injected into larval zebrafish and the above tools will be used to further investigate how *c3a.3*, *per2*, and the liver contribute to the host response to infection. **Results:** Results so far suggest that *c3a.3* plays an antibacterial role, with its depletion corresponding to a decreased survival of larval zebrafish when challenged with *S. enterica* ($p < 0.001$). **Discussion:** The project will expand our understanding of the innate immune system and its capacity to adapt in anticipation of infection, and will also yield novel insights into the molecular clock's regulation of the complement system.

Primary Supervisor: Dr. Hall, C

EP 2: Cristal Salatas

Investigating and mapping the factors associated with preterm birth in New Zealand: cross-sectional geospatial study

Cristal Salatas[1], Wall C[2], Alexander T[1,3], Hobbs M[4], Bloomfield FH[1]
[1]Liggins Institute, [2]Department of Nutrition, [3]Neonatal Unit, Kidz First, Middlemore Hospital, Te Whatu Ora, [4]University of Canterbury

Background: Preterm birth (PTB), defined as delivery before 37 weeks of gestation, is a significant public health concern worldwide. PTB currently affects 8% of New Zealand (NZ) babies. The causes and risk factors vary, although some potential influencers, such as diet and supplementation, may be modifiable. **Objectives:** We aim to identify and map the factors (i.e. sociodemographic, environmental, and nutritional factors) associated with PTBs in NZ from 2003-2021. **Methods:** We employ Geographic Information Systems (GIS) to analyse the geospatial patterns of PTB rates from the Growing Up in New Zealand Study and the Integrated Data Infrastructure for nationwide data. Birth data were linked with sociodemographic information, nutritional data (dietary patterns, supplementation, adherence to dietary guidelines, etc.), and environmental data (natural disasters, water quality, food environment, etc.). Multiple logistic regression and deep learning models were used to identify the key factors associated with PTB risk. **Results:** Preliminary results show that poorer dietary patterns and supplementation practices before and during pregnancy were associated with the risk of PTB [Odds Ratio (OR)=1.18, 95% CI (1.03,1.33), p=0.011, OR=1.67, 95% CI (1.05,2.71), p=0.03, respectively]. The initial spatial analyses revealed that the food environment (access to food outlets) can explain some variation in PTB rates. **Discussion:** This study enhances our understanding of the multifaceted aetiology of PTB risk. We anticipate identifying high-risk areas and populations in NZ. Additionally, GIS analyses will reveal any geographic clusters of high PTB rates guiding resource allocation and further risk factor investigation to reduce preventable PTBs in NZ.

Primary Supervisor: Prof. Bloomfield, F

EP 3: Megan Kemp

Determining the optimal approach to initiating lithium in people with mania: A clinical pharmacokinetic approach

Kemp M[1], Harrison J[1], Hannam J[2], Chan A[1]

[1]Department of Pharmacy, [2] Department of Pharmacology and Clinical Pharmacology

Background: Mania, a period of abnormally and persistently elevated or irritable mood. Lithium is the initial choice for the immediate treatment of acute mania. Standard practice, relying on empirical dosing, does not consider patient-specific characteristics. Population pharmacokinetic (popPK) models have become widely applied in the field of pharmacology, to optimise and individualise dose regimens. There is currently limited evidence directly comparing a popPK approach to standard practice for lithium therapy in acute mania. **Objectives:** To investigate whether a model-based approach can significantly improve clinical outcomes, compared to standard practice. **Methods:** Two popPK two-compartment models, using nonlinear mixed effect modelling, were identified from the literature and successfully reproduced in NONMEM v.7.5.1. Both models, conducted in inpatient children and adolescents, utilised lithium immediate-release formulations. Data from a three-year New Zealand retrospective audit, in patients presenting with acute mania, was used to validate the predictive performance. Visual predictive check (VPC) graphs and performance metrics; mean prediction error (MPE), mean absolute prediction error (MAPE) for bias and root mean square error (RMSE) for precision, were computed. **Results:** Weight and renal function were reported as significant covariates. Landersdorfer's model outperformed in statistical accuracy for population predictions; MPE (p=0), MAPE (p=0) and RMSE (p=6.451414×10−51), with a superior visual fit on the VPC graphs. **Discussion:** The selected popPK model will be used to support the design of a randomised controlled trial in NZ patients with acute mania to determine whether a model-based approach can significantly improve clinical outcomes.

Primary Supervisor: Prof. Harrison, J

EP 4: Duy Nguyen

Mutational analysis of the gene *DDX41* in myelodysplastic syndromes and acute myeloid leukaemia

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Background: About 100 genes have been reported to be somatically mutated in Myelodysplastic syndromes (MDS) and acute myeloid leukaemia (AML). Co-occurrence of a somatic and a germline mutation in the DEAD-box RNA helicase-1 (*DDX41)* are associated with familial MDS and AML, and are found in about 5% of patients. In 12 out of 19 *DDX41* mutation positive samples analysed in the LBCRU, using targeted gene panel, both germline and somatic variants were detected. However, in 7 samples only germline *DDX41* mutations were detected and no somatic second-hit mutations. **Objective:** To identify the second hit *DDX41* mutations in those 7 samples and determine the spectrum of *DDX41* mutations and co-operating mutations in other genes in the *DDX41* mutation(s) positive MDS/AML patients. **Method**: Long-range polymerase chain reaction (LR-PCR) to amplify the *DDX41* locus from genomic DNA (gDNA), followed the by preparation of next-generation sequencing (NGS) libraries, sequencing and analysis and restriction enzyme digestion to detect bigger genetic changes like deletions, inversions or translocation. Using existing gene panel data to determine the mutation spectrum in the LBCRU *DDX41* positive MDS/AML cohort. **Result:** The *DDX41* LR-PCR and library preparation protocols were successfully established and optimized to enable *DDX41* focused NGS analysis. Our *DDX41* focused NGS method yields even coverage across the exons and introns of the DDX41 gene. **Discussion:** The *DDX41*-focused NGS method can be used to identify bigger rearrangements and potentially pathogenic variants in *DDX41*. Our method will provide clinicians with crucial information to guide the management of patients.

Primary Supervisors: Prof. Bohlander, SK; Dr. Kakadiya, PM

EP 5: Jonathan Zong

Investigating EEG-Derived Biomarkers of Major Depressive Disorder: Lempel-Ziv Complexity, Spectral Power and Peak Alpha Frequency

Zong JZ[1], Moloney BD[1], Forsyth A[1], Sumner RL[1], Lin JC[1]
[1]School of Pharmacy

Background: Major Depressive Disorder (MDD) is a prevalent and debilitating mental health disorder, yet its diagnosis often relies on subjective assessments. Current treatments are ineffective for about one third of patients, highlighting the need for improved diagnostic tools and more tailored treatment plans. Identifying objective biomarkers with electroencephalography (EEG) could enhance diagnostic accuracy and provide insights into underlying biological mechanisms and treatment options. **Objectives:** To identify potential EEG biomarkers that could facilitate diagnosis and improve understanding of the neurobiological underpinnings of depression. **Methods:** Resting-state EEG was recorded from a preliminary cohort of 16 patients with MDD and 16 healthy controls. Preprocessed data were analysed to compare spectral power changes, peak alpha frequency, and Lempel-Ziv Complexity (LZc) between the two groups. **Results:** LZc across centro-parietal regions was higher in the depressed group than in the non-depressed group with a maximal effect at electrode CP4 ($t(30) = 2.4431$, $p = 0.0142$). No significant changes were seen in spectral power or peak alpha frequency between the groups. **Discussion:** Our findings of increased LZc in the depressed cohort are consistent with previous research, suggesting this heightened complexity may reflect impaired neural communication and processing efficiency. This could serve as a potential biomarker for MDD, offering insights into its neurobiological underpinnings. Having established this biomarker in this cohort, future research will assess LZc before and after administering low-dose naltrexone, an emerging adjunct treatment for MDD. This will help determine if LZc can be modulated by treatment and if changes correlate with antidepressant effects.

Primary Supervisor: Dr. Forsyth, A

EP 6: Meiliana Meiliana

Minimum reporting set for measures of nutrition and growth in preterm studies: A Delphi study

Meiliana M[1], Bloomfield FH[1], Harding JE[1], Luling L[1]
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Background: Optimum nutrition is important for growth of preterm babies. However, there is no consensus on what optimum nutrition is, and current nutritional guidelines for preterm infants are inconsistent in their recommendations. Limited progress in determining the optimum nutrient intakes is partly due to incomplete or inconsistent outcome reporting in preterm nutrition intervention trials, complicating comparisons between studies. **Objectives:** To develop a minimum reporting set for measures of nutritional intake and growth in preterm nutrition studies. **Methods:** This study will comprise three phases: (1) a scoping review to generate a list of measures of nutritional intake and growth outcomes; (2) a real-time Delphi survey to prioritise measures of nutritional intake and growth outcomes; (3) a consensus meeting to agree on the minimum reporting set. **Results:** The scoping review identified 6 365 records, included 250 studies, and found wide variation and incomplete reporting of nutritional intakes and growth outcomes. Measures from recent studies were collected for a real-time Delphi survey for prioritisation. **Discussion:** Significant gaps and variations in reporting measures persist in recent preterm nutrition studies. Developing and applying a standard reporting set would help synthesise data from multiple studies to identify effective nutrition interventions for preterm infants. We will recruit participants from professional and consumer stakeholder groups with expertise in preterm infants, nutrition, and growth to rate the importance of each measure on a 9-point Likert scale. After data analysis, candidate measures will be prioritised in a consensus consultation meeting to be included in the final minimum reporting set.

Primary Supervisor: Dist. Prof. Harding, J

EP 7: Suci Hermita

Kawakawa and Its Antidiabetic Effects: A Mechanistic Approach

Hermita S[1], Lee K[2], Ramzan F [1],
[1]Liggin's Institute, [2]Molecular Medicine and Pathology

Background: Insulin resistance (IR) has a critical role in chronic diseases, including type 2 diabetes mellitus and cardiovascular diseases. These diseases become a significant cause of mortality and morbidity worldwide, including in New Zealand, with greater prevalence in Māori. Therefore, understanding and developing new therapies targeting IR is crucial. Given that, diet is one of the modifiable risk factors for treating IR. A recent clinical study has shown that kawakawa *(Piper excelsum)* tea consumption, a medicinal plant of Rongoa Māori, improves postprandial insulin. However, the mechanism by which kawakawa affects insulin remains unknown. **Objectives:** investigate the mechanistic action of kawakawa extract on insulin signaling pathways in different cell models from metabolically active organs. **Methods:** Cell lines representing liver (HepG2), skeletal muscle (L6 GLUT2), pancreas (INS-1E), and adipose (3T3-L1) will be cultured and treated with kawakawa extract. Then, glucose uptake will be measured using the 2-NBDG uptake assays. The key genes and proteins, including GLUT2, IRS-1, PPAR-γ, and PI3K/Akt, will be analysed using western blot and quantitative polymerase chain reaction (qPCR) analysis. **Results:** This research is ongoing. However, we hypothesise that kawakawa will differentially regulate key genes involved in insulin signaling pathways, including GLUT2, IRS-1, PPAR-γ, and PI3K/Akt, across various tissues. **Discussion:** the findings of this study have the potential to identify key targets of kawakawa regulation in multiple metabolically active organs. This will potentially lay the foundation for future research investigating the potential of kawakawa as a functional food to manage chronic metabolic diseases.

Primary Supervisor: Dr. Ramzan, F

EP 8: Mariam Alhilali

Optimising MRD-Seq: an improved method for measurable residual disease detection in acute myeloid leukaemia

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Background: Acute myeloid leukaemia (AML) is a genetically complex disease with a very poor prognosis. With over 200 genes found to be mutated in AML, most patients present with unique mutation combinations. It is very important for the physician to know how well a patient's treatment is working. Therefore, being able to assess the number of remaining cancer cells (minimal residual disease, MRD) with high sensitivity is crucial to guide treatment decisions. Using qPCR-based MRD assays is challenging as they require individual assay development and calibration for each mutation. Thus, at present, sensitive MRD assays are not available to most AML patients. **Objectives:** To establish a new method of measuring MRD in AML using Next Generation sequencing (NGS): MRD-Seq. **Methods:** MRD-Seq involves preparation of error-correcting PCR amplicons targeting a region of the genome that harbours a somatic mutation, followed by NGS. Amplicons were prepared from cell lines carrying *nucleophosmin 1* (*NPM1*)-TypeA and *isocitrate dehydrogenase 1* (*IDH1*)^{R132H} mutations. The sequencing reads were de-duplicated using UMItools, followed by counting the number of reads with and without specific mutation using an R- code developed in our lab. **Results:** Both *NPM1*-TypeA and *IDH1*^{R132H}-specific MRD-Seq assays demonstrated a sensitivity of 1 x 10^{-3}. **Discussion:** We aim to achieve a sensitivity between 1x10^{-4} and 1x10^{-5} by MRD-Seq, comparable to MRD-qPCR. Unlike, MRD-qPCR, MRD-Seq can be easily adapted for any mutation by designing a mutation-spanning PCR, allowing MRD monitoring in most patients. MRD-Seq approach has a potential to improve measurement accuracy and precision in monitoring AML.

Primary Supervisors: Prof. Bohlander, S and Dr. Kakadiya, P

EP 9: Holly Wilson

"If they had actually listened to me" – Identifying patients at risk of preventable hospital readmissions

Wilson H[1], Harrison J[1], Donkin L[2], Brackley K[3], Lim G[4], Chan A H Y[1]

[1]School of Pharmacy, [2]Department of Psychology and Neuroscience, Auckland University of Technology, [3]Department of Pharmacy, Te Whatu Ora, [4]School of Nursing

Background: In New Zealand one out of every eight people will return to hospital after discharge, experiencing a hospital readmissions. Up to a third of these readmissions are preventable. Effectively being able to identify patients at high risk and understanding why they are at a high risk of readmission, could help reduce preventable hospital readmissions. Modifable risk factors are the key to identifying these patients, yet they are poorly understood. **Objectives:** To identify modifable risk factors associated with preventable readmissions from the perspectives of patients and healthcare professionals (HCP). **Methods:** Patients who had been readmitted to Auckland Hospital between June 2021 and April 2022 participated in semi-structed interviews. HCPs working in public hospitals participated in focus groups and interviews between February and November 2023. Data were analysed using inductive thematic analysis to identify factors associated with readmissions. **Results:** Overall, 30 patients (53% female; 17% Māori; 20% Pacific; mean (SD) age 50(17) years) participated. Several themes related to modifable risk factors for hospital readmissions were identified from patients' perspective, including communication, beliefs, information, health literacy, medicines management and systemic factors. 38 HCP participated (45% Pharmacists; 34% Nurses; 18% Physicians; 3% Allied health) with several themes related to modifable risk factors were identified from HCP perspective, including communication, social support, medicines management, patient beliefs and systemic factors. **Discussion:** Patients and HCP identified several modifable risk factors of readmission. These risk factors could help identify who and why patients are at risk of readmissions and provide practical insights to reduce readmission risk.

Primary Supervisor: Associate Prof. Chan, A

EP 10: Muna Dhakal

Reducing the construction load: Nurr1 variants as switch for viral vector therapy for Parkinson's disease

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[1]Department of Pharmacology & Clinical Pharmacology

Background: Adeno-associated viruses have become the leading delivery platform for gene therapy in treating Parkinson's Disease (PD). However, their relatively small gene-carrying capacity poses a significant limitation, restricting the insertable gene construct size to about 4.7 kilobases (kb). Developing gene constructs with smaller activators or "keys", which will provide greater flexibility for swapping different promoters and transgenes, is a potential way to overcome this limitation. We have developed a novel gene regulation system that harnesses an endogenous ligand-dependent transcription factor called nuclear-related factor 1 (Nurr1) for its dual action – as a "key" as well as therapy for PD. **Objectives:** To develop different lengths of Nurr1 variants and characterise their ability to drive exogenous transgene expression. **Methods:** Nurr1 variant plasmids were cloned using standard molecular techniques. Six Nurr1 variants were cloned, with sizes of 1.8 kb (wildtype), 1.7 kb, 1.3 kb, 1.2 kb, 0.52 kb and 0.43 kb. Nurr1 variant expression and functionality was determined in transfected HEK293 cells using immunocytochemistry and western blotting. **Results:** The construction of Nurr1 variant plasmids was confirmed by restriction digestion. All variants effectively activated exogenous green fluorescent protein (GFP) transgene expression. Shorter variants were as effective as 1.8 kb full-length variant in GFP expression. **Discussion:** This preliminary data enhances our understanding of the structure of Nurr1 and the correlation between Nurr1 expression levels and its functionality. Subsequently, we will transfect these variants in *in vitro* and *in vivo* PD models to assess their therapeutic impact on endogenous dopaminergic targets.

Primary Supervisor: Associate Prof. Young, D

EP 11: Mary Spring

The impact of fetal sex on placental vascular development and function in fetal growth restriction.

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[1]Department of Obstetrics, Gynaecology and Reproductive Sciences, [2]Auckland Bioengineering Institute

Background: There is a greater risk for adversity in pregnancy if the fetus is male. Statistically, male neonates have higher rates of placental abnormalities, FGR, stillbirth, and neonatal death than females. *In-utero*, male and female fetuses have different growth characteristics– whereby female fetuses prioritise placental reserve capacity, whilst male fetuses prioritise fetal growth. Consequently, male fetuses have reduced feto-placental adaptability rendering them more vulnerable to adverse conditions *in-utero*. However, sex-specific differences in placental vascular structure and function, or how they contribute to FGR, are poorly understood. **Objectives:** My PhD aims to quantify sex-specific differences in placental anatomy and vascular reactivity in FGR and relate these to placental function. **Methods:** Current *in-silico* models of the human placenta are being parameterised with sex-specific morphometric data from normal and FGR placentae obtained both from literature, and from stereology of IHC-stained placental tissue sections. Initial models will guide parameters for pressure myography studies of placental stem vessel arteries, enabling the incorporation of sex and pathology-specific vascular compliance into refined models. **Results:** Understanding how changes in vascular anatomy impact placental haemodynamics (vascular resistance and flow distribution) will enable us to identify which sex-specific differences have the greatest functional impact. Incorporating data-driven vascular compliance elements into models will improve their accuracy in predicting Doppler ultrasound metrics. **Discussion:** Together, this work will enable us to determine if sex-specific differences impact umbilical artery Doppler ultrasound waveforms measured clinically, enabling us to determine if ultrasound metrics should be interpreted in a sex-specific manner to improve FGR detection.

Primary Supervisor: A/Prof James, J.

EP 12: Michael Ng

The role of Hap1 and Rhes in mediating selective striatal cell loss in Huntington's Disease.

Ng M[1], Grimsey N[1], McCaughey-Chapman A [1], Connor B[1]

[1]Department of Pharmacology & Clinical Pharmacology, Centre for Brain Research

Background: Huntington's disease (HD) is a neurodegenerative disorder characterised by the selective loss of medium spiny neurons in the striatum of the brain due to expression of mutant huntingtin (mHtt) protein. Huntingtin expression is found throughout the brain, implying the influence of other proteins such as Huntingtin-associated protein 1 (Hap1) and Ras homolog enriched in the striatum (Rhes) contribute to the selective degeneration of medium spiny neurons in the striatum. Both Hap1 and Rhes are involved in the post-translation modification SUMOylation pathway which mediates the formation of toxic soluble mHtt over neuroprotective aggregated mHTT. **Objective:** Investigate the role of Hap1 and Rhes in HD using adeno-associated virus (AAV) viral transduction and 3D striatal organoids generated using direct cell reprogramming. **Methods:** HD patient-derived human fibroblasts were directly reprogrammed into striatal neural precursors, then differentiated into mature striatal neurons. Organoids were formed using low-attachment plates in combination with a plate shaker and AAV viral transduction was carried out during differentiation. **Results:** Tissue clearing and immunocytochemistry confirmed striatal organoids express TUJ1 / DARRP32 positive striatal neurons. We confirmed HD patient-derived organoids exhibit aggregated and soluble mHTT. Expression of eGFP was used to determine the optimal transduction of AAV in striatal organoids. **Discussion:** This study demonstrates our ability to generate for the first time HD patient-derived striatal organoids and transduce with an AAV vector for gene modification studies. This forms the foundation for subsequent investigations utilising AAV gene delivery to determine the role of Hap1 and Rhes in selective striatal cell loss in HD.

Primary supervisor: Prof. Connor, B

Poster Presentations

Poster 01: Xin Yi Lim

Consumers' views on pharmacovigilance for natural health products: preliminary findings from a qualitative interview study.

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[1]School of Pharmacy

Background: Pharmacovigilance (safety monitoring) for natural health products (NHPs) is essential for public health protection. Currently, there is little information on consumers' views regarding the New Zealand NHPs industry's contributions to pharmacovigilance. **Objectives:** To explore consumers' views, experiences, and awareness of the NHPs industry's contributions to pharmacovigilance in New Zealand. **Methods:** One-on-one online interviews were conducted with NHPs consumers (n=19) using a semi-structured interview schedule focusing on: (1) experiences with adverse drug reaction (ADR) reporting through the NHP industry; (2) awareness of and views on regulatory changes regarding NHPs; (3) feasibility of active surveillance for NHPs. Interviews were recorded, transcribed verbatim, and analysed inductively. **Results:** Most participants had neither experienced nor reported ADRs associated with NHPs use. Few participants were aware of NHPs regulations but nearly all were supportive of regulations that protect consumer safety and rights. Preliminary themes emerging from the data include consumers' (mis)understanding of safety monitoring/pharmacovigilance as meaning that products meet pre-marketing standards, concerns about potential industry bias in handling consumer reports about side effects, and consumers' autonomy in self-selection of safe NHPs and ADR reporting. Clear and/or personally relevant pharmacovigilance study objectives, societal benefits, convenience/ease of participation, and incentives, are some factors that would encourage consumer participation in active surveillance studies. **Discussion:** These preliminary findings offer insights into New Zealand consumers' experiences and expectations of the NHPs industry's role in pharmacovigilance and feasibility of active surveillance methods. To further inform understanding, gathering perspectives from other stakeholders, such as the NHPs industry and medicines regulators, is required.

Primary Supervisor: Prof. Barnes, J

Poster 02: Amelie Back

Using Directly Reprogrammed Patient-Derived Oligodendrocytes to Model Huntington's Disease

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Background: Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder, traditionally characterised by medium spiny neuron loss in the basal ganglia, leading to widespread neurodegeneration. White matter damage and oligodendrocyte (OL) dysfunction precede this neurodegeneration, being one of the first pathological manifestations of HD. However, investigations into human white matter and oligodendrocyte dysfunction have been limited to imaging and postmortem studies due to a lack of human-based OL models. We propose the use of a direct reprogramming approach to generate a novel *in vitro* OL model from HD patient-derived human dermal fibroblasts (HDFs). **Objectives:** To characterise the transcriptional and morphological changes of HD directly reprogrammed human-induced oligodendrocytes (hiOLs). **Methods:** HD and healthy human-derived HDFs were directly reprogrammed to human-induced oligodendrocyte precursor cells (hiOPCs) and further differentiated to hiOLs within 35 days. At various time points, expression of OL maturation markers and the presence of mutant huntingtin were assessed by immunocytochemistry. Quantitative polymerase chain reaction and enzyme-linked immunosorbent assays were used to quantify transcriptional markers of OL maturation and myelin protein expression, respectively. **Results:** HD patient-derived HDFs can be directly reprogrammed into hiOPCs and further differentiated into hiOLs displaying disease characteristics. **Discussion**: This study generates, for the first time, a human and disease-specific, age-appropriate OL model of HD. Retention of disease-specific pathology in fully differentiated hiOLs provides an accurate and timely platform for the investigation of OL dysfunction in HD.

Primary Supervisor: Dr McCaughey-Chapman, A

Poster 03: Jess Kelly

Novel Three-Dimensional Brain Organoids for Modelling Huntington's Disease.

Kelly, J.[1], McCaughey-Chapman, A. [1], Grimsey, N. [1], Connor, B.

[1]Department of Pharmacology and Clinical Pharmacology, Centre for Brain Research

Background: Three-dimensional (3D) neural organoids are valuable tools for disease modelling. However, current protocols are lengthy and have limited applicability to diseases of aging due to the cells undergoing DNA rejuvenation. Direct-to-induced neural precursor (iNP) cell reprogramming converts human fibroblasts into region-specific neural precursor cells and allows the maintenance of aging factors. **Objectives:** To demonstrate the ability of striatal organoids created using direct reprogramming to recapitulate Huntington's Disease (HD) phenotypes. **Methods:** Induced neural precursors were directly reprogrammed from HD donor derived human fibroblasts by transient expression of *SOX2* and *PAX6*. Organoids were generated by suspending iNPs in ultra-low attachment plates with gentle rotation and timed growth factor exposure. Differentiation was evaluated using immunocytochemistry (ICC) and quantitative polymerase chain reaction (qPCR) for striatal markers. Huntington's Disease phenotype markers were assessed using ELISA, ICC, and Western Blot. **Results:** Striatal organoids were positive for the striatal lineage markers *CTIP2*, TUJ1 and DARPP32 at Days 7 and 14 of differentiation. HD-iNP-derived striatal organoids co-expressed DARPP32 with TUJ1. By Day 7 of differentiation, the HD organoids expressed mutant huntingtin protein. **Discussion:** This study demonstrates for the first time the ability to generate organoids from directly reprogrammed iNPs from healthy and HD donors, with region specific neuronal differentiation and disease phenotypes by D14 of differentiation. The reduced time required to generate organoids from iNPs, and the ability for direct-to-iNP reprogramming to maintain epigenetic and aging signatures advances current organoid methods and will facilitate future modelling of neurological diseases of aging.

Primary Supervisor: Prof. Connor, B

Poster 04: Harpinder Brar

Polymeric micelles for nose-to-brain delivery of Crizotinib-IR786 conjugate in the treatment of Glioblastoma

Brar H[1], Jose J[2], Wu Z[1], Park T[3], Lee C[3], Dragunow M[3], Sharma M[1]

[1]School of Pharmacy, [2]Auckland Cancer Society Research Centre, [3]Centre for Brain Research

Background: Glioblastoma (GBM) is one of the most challenging tumours to treat with limited treatment options. Tyrosine kinase inhibitors (TKIs) can target multiple pathways aberrantly activated in GBM; however, their clinical application is largely limited by their poor brain distribution and lack of tumour selectivity. Heptamethine cyanine dyes (HMCDs) have emerged as promising tumour-targeting agents and a conjugate of crizotinib (a TKI) with a HMCD IR-786 has been reported to have improved cytotoxic activity in GBM cells. **Objectives:** Formulate and characterise polymeric micelles to encapsulate crizotinib-IR786 conjugate for nose-to-brain delivery. **Methods:** Methoxy poly(ethylene glycol)-*block*-poly(lactic acid) micelles were prepared by thin film hydration method. Micelle size and zeta potential were determined by dynamic light scattering. Morphological properties were determined by transmission electron microscopy (TEM). Encapsulation efficiency of micelles was determined using centrifugal filters. Cell viability of glioblastoma cells (U87 and KNS42) was measured by the percentage of Hoechst-positive cells. Lactate dehydrogenase cytotoxicity assay was used to determine cellular toxicity. **Results:** Crizotinib-IR786 micelles were 99.6 ± 9.1 nm in diameter with a zeta potential of 12.8 ± 2.2. TEM revealed their spherical morphology with uniform size distribution. Average encapsulation efficiency of micelles was 99.6% and average drug loading was 2.9%. Micelles were stable over a period of one month. Cytotoxicity studies revealed that crizotinb-IR786 micelles have comparable cytotoxicity to that of free crizotinib-IR786. **Discussion:** Size and zeta potential of micelles is suitable for nose-to-brain delivery and the developed micelles have the potential to be used as suitable delivery vehicle for crizotinib-IR786.

Primary Supervisor: Dr Sharma, M

Poster 05: Mikayla Chetty

The effects of an impaired blood-brain barrier on microglial phenotype in Alzheimer's Disease.

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[1]Department of Pharmacology and Clinical Pharmacology, [2]Centre for Brain Research, [3]Department of Molecular Medicine and Pathology

Background: Microglia are central to the brain's inflammatory response in Alzheimer's disease (AD). Blood-brain barrier (BBB) breakdown in AD can allow blood-derived molecules, such as fibrinogen which is a plasma glycoprotein, to enter the brain and promote microglial activation. Fibrinogen infiltration is also reported to increase oxidative stress and neuronal injury. Microglial activation is a complex and only partially understood, process. Glycoprotein NMB (GPNMB) and secreted phosphoprotein-1 (SPP1) are novel proteins transcriptomically upregulated in AD. Changes at the protein level are yet to be understood. **Objectives**: To investigate fibrinogen deposition in the AD cortex and human microglial responses of GPNMB and SPP1 expression to fibrinogen treatment. **Methods:** Fibrinogen deposition and GPNMB and SPP1 protein expression in the AD cortex was investigated using immunohistochemistry. Primary human and induced pluripotent stem cell-derived microglia were treated with fibrinogen and GPNMB and SPP1 expression assessed by immunocytochemistry. Enzyme-linked immunosorbent assays were undertaken to investigate changes in secreted GPNMB and SPP1. **Results:** Fibrinogen deposition was significantly elevated in the AD cortex, and GPNMB and SPP1 were expressed in activated microglia near leaky vessels. GPNMB and SPP1 increased in response to fibrinogen both intracellularly and extracellularly and promoted morphological changes towards an activated state. **Discussion:** These findings suggest that GPNMB and SPP1 are elevated in microglia in response to fibrinogen deposition in the AD brain, warranting further investigation into their functional implications. Understanding microglial phenotypes associated with AD could reveal therapeutic strategies to mitigate chronic inflammation in neurodegenerative diseases.

Primary Supervisor: Dr. Smith, A

Poster 06: Nathaniel Singleton

The Influence of Oxidative-Stress Induced Neuroinflammation on Bach2 Gene Expression in Rodent Glial Cells

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[1]Department of Anatomy and Medical Imaging, [2]Department of Physiology

Background: Neurological diseases like spinal cord injury (SCI) often encompass neuroinflammatory pathways. The central nervous system (CNS) regulates the inflammatory response via glial cells (astrocytes, microglia and oligodendrocytes) and activation of transcription factors. Previous work in our lab using an RNA array indicated that Bach2, a transcription factor, may be a key regulator of inflammation and is known to be expressed on glial cells. Thus, investigating Bach2's expression and function may provide insights into neuroinflammation. **Objectives:** Investigating individual glial cell type expression and the response of Bach2 under conditions of oxidative-stress inducing neuroinflammation. **Methods:** Primary glial cell cultures were established from newborn rat cortices, and microglia were isolated. Following culture for seven days, microglia underwent treatment with energy failure and oxidative-stress inducing drugs. Cells were treated with 50-200 uM diethylmaleate or 1-10 uM iodoacetate or a combined treatment of diethylmaleate with 5 uM iodoacetate. Cell viability was measured via Alamar blue assay fluorescence at 1-, 3-, and 6-hours post-treatment. **Results:** Microglia alamar blue assay trials with oxidative-stress drugs show decreases in metabolic activity. Combined treatments had a 30% decrease in cell viability by 6 hrs. **Discussion:** Drug treatments impacted microglia cell viability. The optimal drug treatment is currently being determined. The sequential isolation of microglia, oligodendrocyte and astrocyte populations from primary cultures is underway. Experiments will study expression of Bach2 via western blots and PCR. The generation of a Bach2 knockdown model analysing the effect of Bach2 gene reduction on cell viability following oxidative stress will also be undertaken.

Primary Supervisor: Dr. O'Carroll, S

Poster 07: Kaya Girdlestone

Targeting hypoxia-ischemia damage in astrocytes via kinase inhibition in a model of spinal cord injury.

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[1]Department of Anatomy and Medical Imaging [2]Department of Pharmacology and Clinical Pharmacology

Background: Hypoxia-ischemia, characterized by reduced oxygen and blood supply, plays a critical role in spinal cord injury (SCI). Ischemic conditions trigger apoptotic pathways, excitotoxicity, and inflammatory responses in astrocytes, highlighting their dual role in neuroprotection and neuroinflammation. Kinase inhibitors show promise in mitigating astrocyte damage, prompting research into their therapeutic potential. **Objectives:** This study aims to establish a viable model of hypoxia-ischemia in both rodent and human astrocytes to evaluate the efficacy of kinase inhibitors Dasatinib, Imatinib, and A-770041 to mitigate hypoxic-ischemic damage. **Methods:** Astrocytes were exposed to iodoacetate and diethylmalonate to induce oxidative stress, assessing viability via Alamar Blue fluorescence. Kinase inhibitor efficacy will be evaluated by comparing changes in fluorescence with and without treatment post-oxidative stress exposure. Ischemia-associated signalling pathways will be characterized using western blotting and Human Phospho-Kinase Antibody Arrays. **Results:** Rodent cell-line data revealed a concentration-dependent decrease in metabolism after treatment with 5-100 uM iodoacetate, accompanied by observable morphological changes under light microscopy. The next steps involve applying kinase inhibitors to rodent astrocytes to assess their potential to protect cell viability and metabolism. Insights gained will inform the adaptation of this model to human iPSC-derived astrocytes. **Discussion:** This research addresses the role of hypoxia-ischemia in SCI, focusing on astrocytes' responses and potential neuroprotective strategies. Initial findings in rodent cell lines demonstrated concentration-dependent metabolic decline and morphological changes under oxidative stress. The efficacy of kinase inhibitors in preserving astrocyte viability and metabolism warrants further investigation across human models bridging species-specific gaps in neuroprotection research.

Primary Supervisor: Dr. O'Carroll, S

Poster 08: Angeline van Kuilenburg

Assessment of the developing white matter in the neonatal rat using advanced magnetic resonance imaging

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Background: Brain injury in preterm infants is associated with microstructural changes. Neurite orientation dispersion and density imaging (NODDI) is an advanced magnetic resonance imaging (MRI) modality proposed to more precisely describe changes in cellular microstructure compared with diffusion tensor imaging (DTI). However, changes in NODDI parameters in the developing white matter have not been validated with histological correlates. **Objectives:** To validate the developmental changes in DTI and NODDI parameters in the white matter with histology. **Methods:** Brain tissues were collected from Sprague-Dawley rat pups on postnatal days (P)1, 3, 7, 14, 21, and 35 (n=5/timepoint) for immunofluorescence or e*x-vivo* MRI-NODDI (9.4T) analyses. The process density of microglia, astrocytes, and oligodendrocytes was assessed in the corpus callosum (CC) and external capsule (EC) using the Spaceball probe (Stereoinvestigator). Changes in fractional anisotropy (FA) and neurite density index (NDI) were calculated in the same regions. **Results:** FA increased from P35 and P14 in the CC and EC, respectively, whereas NDI in both regions peaked at P7—P14, progressively decreasing thereafter. Histology showed that microglial process density progressively increased in both regions, peaking at P21 and decreasing at P35. Astrocytic process density was comparatively greater at all time points but showed minimal developmental changes in either region. Oligodendrocyte data is still being collected. **Discussion:** Astrocytes contribute more to the restriction of water diffusion than microglia during brain development. However, neither showed a strong relationship with changes in MRI diffusion parameters, suggesting that other cell types, such as oligodendrocytes or axons, may have greater contributions.

Primary Supervisor: A/Prof. Justin Dean

Poster 09: Catriona Miller

Linking causal ADHD genes to co-occurring conditions

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Background: Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental condition with substantial variation in long-term outcomes (including the likelihood of co-occurring conditions) between individuals. Whilst epidemiological and clinical studies have identified many co-occurring conditions, the genetic links have not been fully explored. **Objectives:** To identify traits that co-occur with ADHD and the biological mechanisms behind the co-occurrence. **Methods:** We undertook a two-sample Mendelian Randomisation analysis in fetal and adult cortical tissue to identify causal ADHD genes (*ST3GAL3* and *TIE1* in adult; *ST3GAL3, PIDD1,* and *PTPRF* in fetal). Data from genome wide association studies (GWAS), gene expression, spatial organisation (Hi-chromatin), and protein-protein interaction databases were integrated in a network analysis to identify the genetic relationships between ADHD and co-occurring traits. We used the causal ADHD genes to create a causal gene network and genetic variants from GWAS to create an associated gene network. **Results:** From our causal gene network, we identified biological pathways linking ADHD genes with eye conditions and rheumatoid arthritis, both associated with ADHD in previous epidemiological studies. We identified different causal pathways linking ADHD with potential biomarkers, including lymphocyte count and lipoprotein a levels. In the associated analysis, we identified genetic variants associated with neurological traits, cognition, and metabolic traits. **Discussion:** This study has identified both neurological and non-neurological traits that are genetically associated with ADHD. The results link novel causal ADHD genes with known co-occurring conditions and provide genetic evidence for potential biomarkers. Future work should assess the usability of these results for diagnosis in an ADHD population.

Primary Supervisor: Prof. O'Sullivan, J

Poster 10: Hailey Yoon

The Role of Cannabinoid Receptor 2 in Interferon-γ Stimulated Human Macrophage Function

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[1]Department of Pharmacology and Clinical Pharmacology, [2]Department of Molecular Medicine and Pathology

Background: The excessive activity of pro-inflammatory macrophages can produce immune-mediated disease. Cannabinoid receptor 2 (CB2), a G protein-coupled receptor, is a promising target for treating immune disorders due to its anti-inflammatory effects. However, much existing research on CB2 function in immune cells may have limited translatability as it has been conducted under conditions that do not necessarily reflect human physiology. **Objectives:** Investigate the effects of CB2-selective ligands on human primary macrophage function. **Methods:** Human primary monocytes were differentiated into pro-inflammatory macrophages using granulocyte-macrophage colony-stimulating factor (GM-CSF) and interferon-γ (IFN-γ), with or without CB2 ligand co-incubation. Cytokine secretion, cell surface CD marker expression, and phagocytosis were assessed by cytometry bead array, immunocytochemistry, and fluorescent bead uptake, respectively. **Results:** Cytokine and CD marker profiling confirmed differentiation of monocytes to pro-inflammatory macrophages. GM-CSF differentiated macrophages exhibited robust phagocytosis, which was suppressed by IFN-γ treatment. Phagocytosis was further reduced by CB2 inverse agonist, SR144528. Conversely, SR144528 had an opposing effect on IFN-γ-stimulated TNF-α production, but did not alter other pro-inflammatory cytokines. **Discussion:** The mixed effects of SR144528 on IFN-γ-polarised macrophage function may indicate a complex modulatory role for CB2. Although CB2 has potential to act as an anti-inflammatory drug target, these findings emphasise the necessity for further research to better characterise and validate CB2 function in physiologically relevant models.

Primary Supervisor: Dr. Grimsey, NL

Poster 11: Malak Alshakhouri

Investigating the Neurosteroid Withdrawal Hypothesis of Catamenial Epilepsy in Humans using Visually Induced Gamma Oscillations

Alshakhouri M[1], Kothiwala F[1], Muthukumaraswamy S[1], Hamandi K[2], Hofman P[3], Bergin P[4], Sharpe C[5], Sumner RL[1]

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Background: The menstrual cycle worsens seizures for 40% of females with epilepsy (FE). The main pattern, perimenstrual catamenial epilepsy, is linked to the premenstrual withdrawal of allopregnanolone (ALLO). ALLO, a progesterone metabolite, enhances the brain's major inhibitory system via Gamma-aminobutyric acid type-A receptors (GABAAR), similar to most seizure abortive medications. **Objectives:** To investigate changes in excitation and inhibition balance across the menstrual cycle by measuring changes in visually induced gamma oscillations. **Methods** Visually induced gamma was recorded using encephalography (EEG) in 10 FE and 25 female controls (FC) during the perimenstrual, mid-follicular, and mid-luteal phases. The visual gamma task involves 4 blocks of 84 trials, where a black and white annular grating is presented on a screen at 90% contrast, subtending 16° visual angle. Blood samples were collected and analysed for progesterone, oestradiol and ALLO concentrations. **Results:** In FC, visually induced gamma frequency in the follicular phase was 4.8 Hz lower than the luteal phase ($t(16)= -3.24$, $p= 0.005$) and 3.8 Hz lower than the perimenstrual phase ($t(16)= -2.24$, $p= 0.039$). In FE, there were no significant changes in gamma frequency over the menstrual cycle. Interestingly, there was no correlation between hormone concentrations and gamma frequency. **Discussion:** Our findings suggest that changes in gamma frequency are not mediated by absolute hormone concentrations but may be correlated with GABAARs density, which increases post-ovulation during the luteal phase and increases further in the perimenstrual phase upon ALLO withdrawal. The lack of change in gamma frequency in FE may indicate GABAARs dysregulation.

Primary Supervisor: Dr. Sumner, R

Poster 12: Liam Zhang

Comparison of Human Atrial Tissue Composition between Diabetic and Non-Diabetic Patients

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[1]Department of Physiology

Background: Type 2 diabetes has been implicated in the development of diabetic cardiomyopathy, that includes pathological changes in heart structure, and function. Diabetes has been shown to cause heart tissue (myocardium) remodelling in animals, which may impair heart muscle function. However, little is known about the diabetes-induced changes in the human myocardium. **Objective:** To quantify human atrial tissue composition and compare between diabetic and non-diabetic patients. **Methods:** Small blocks of human right atrial appendage (RAA) tissue were collected from consenting patients during coronary bypass graft surgery. Samples were micro-dissected from the endocardial surface of the RAA tissue, paraformaldehyde-fixed, and cryo-sectioned. Tissue section labelling was carried out for heart muscle cells (cardiomyocytes), extracellular proteins (types I & III collagen), and collagen-producing fibroblasts using immunohistochemistry. Immunolabelled sections were imaged with confocal microscopy. **Results:** Images from longitudinal and transverse tissue sections showed cardiomyocytes occupy the majority of human RAA tissue, with type III collagen dominating the extracellular space by volume. However, fibroblasts were the major cell population by number. **Discussion:** Fibroblasts have a major role in regulating extracellular proteins in human tissues, and were the most prevalent cell type in the human RAA tissue samples examined. Comparison of myocardial fibroblast and collagen composition between diabetic and non-diabetic patients, may provide insight into the mechanisms of myocardial remodelling observed in diabetic cardiomyopathy. Additionally, combining tissue composition and functional data from the same patient samples will elucidate the impact of myocardial remodelling has on human atrial function.

Primary Supervisor: Dr. Ward, M

Poster 13: Dilsha Gimhani

The Abundance and Morphology of the Cardiac Lymphatic Vasculature in Sheep with HFpEF

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[1]Manaki Manawa – The Centre for Heart Research, Department of Physiology

Background: Half of all patients with heart failure have heart failure with preserved ejection fraction (HFpEF) which is a condition where the heart has impaired ability to relax. Despite the rising prevalence (~+1% per year), there is a large gap in our knowledge about how HFpEF progresses and a critical need for novel treatments. One major symptom in HFpEF is myocardial oedema which is a build-up of interstitial fluid in the tissue. Interstitial fluid is generally drained by the lymphatic system but how the cardiac lymphatic system is altered in HFpEF is not known. **Objectives:** To investigate and characterise changes in the cardiac lymphatic vasculature in control sheep and sheep with HFpEF. **Methods:** Immunohistochemistry methods were utilised on cryosections (10-12µm) of paraformaldehyde fixed left ventricular tissue from control sheep and sheep with HFpEF. These sections were incubated with primary antibodies selectively present in lymphatic vessels; LYVE-1 (lymphatic vessel endothelial hyaluronic acid receptor-1), VEGFR3 (Vascular Endothelial Growth Factor-3 Receptor) and Podoplanin, followed by incubation with a fluorescent secondary antibody. Sections were then imaged using confocal microscopy. **Results:** As lymphatic antibodies have not previously been optimised for sheep tissue, we are currently in the process of doing so. We hypothesise that there will be a smaller network of lymphatics in cardiac tissue from sheep with HFpEF compared to controls. **Discussion:** My project will specifically determine if there are structural changes in the cardiac lymphatic vasculature in HFpEF which may be responsible for the increased levels of myocardial oedema and subsequent cardiac dysfunction.

Primary Supervisor: Associate Prof. Ramchandra, R

Poster 14: Simone Watkins

Factors Associated with Critical Congenital Heart Disease Mortality: A National Cohort Study

Watkins S,[1] Sadler L,[2] Cloete E,[3] Wang Z,[1] Ward K,[4] Brown R,[5] Crengle S,[6] de Laat MWM,[2] Percival T,[7] Gorinski R,[8] Bloomfield FH,[1] Gentles TL[2]

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Background: Critical congenital heart disease (CCHD) significantly contributes to infant mortality. Ethnicity is associated with CCHD mortality, but factors contributing to the association of ethnicity and CCHD infant mortality in New Zealand (NZ) are unclear. **Objective:** To identify factors associated with CCHD mortality to one year and examine how ethnicity influences this outcome in NZ. **Methods:** A retrospective population-based cohort study of CCHD cases in NZ through dataset linkage from 2006–2019. Terminations were excluded. The primary outcome was all-cause mortality, including stillbirth to the end of the first postnatal year. Survival and Cox regression analysis was undertaken. **Results:** There were 1,278 CCHD cases, 1,039 met the inclusion criteria. All-cause mortality occurred in 23.2% (64 stillborn and 177 postnatal deaths). Mortality risks for Māori, Pacific, and Asian CCHD cases were higher than for European, with univariable hazard ratios (HR) of 1.5 [95% CI 1.0-1.8], 1.6 [95% CI 1.1-2.4], and 1.8 [95% CI 1.2-2.7], respectively. Multivariable Cox regression models identified CCHD mortality risk to be independently associated with surgical management pathway [HR 0.11, 95% CI 0.08-0.20], higher deprivation level [HR 1.08, 95% CI 1.02-1.15], increasing birthweight Z-score [HR 0.82, 95% CI 0.72-0.95] and cardiac diagnosis, all of which were also associated with ethnicity. **Discussion:** Ethnicity was unrelated to CCHD mortality when accounting for other variables. Equitable survival for at-risk ethnic groups could be advanced through reducing the impact of modifiable, independent mortality drivers in future policy and healthcare practice. Research into management decision-making would further elucidate underlying mechanisms in CCHD disparity.

Primary Supervisor: Professor Bloomfield, F

Poster 15: Ben Buttle

Generating T-cells for Cancer Immunotherapy Using Advanced Gene Editing Tools

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[1]School of Biological Sciences

Background: Exogenous T-cell receptors (TCRs) can be introduced to autologous T-cells to redirect them to kill cancer cells through adoptive cell therapy. Historically, these cells have been generated through non-targeted retroviral insertion, which carries risks, including insertional mutagenesis. Recent advances in CRISPR/Cas9 gene editing have allowed for targeted insertion of TCRs into T-cells, reducing these risks. However, targeted insertion efficiency is low, and no well-established platform exists for this method. **Objectives:** To develop a platform for large-insert gene editing that can be used to insert TCRs into T-cells using CRISPR/Cas9 for use in immunotherapy. **Methods:** We will use 5' RACE-seq (Rapid amplification of cDNA ends) to sequence TCRs from high-affinity-TCR T-cell clones that target melanoma. These sequences will be used to create various homology-directed repair templates that will insert TCRs into the TCRα locus constant region (*TRAC*) to create genetically modified "TCR-T-cells". We will evaluate the potential of these TCR-T-cells to recognise target antigens on cancer cells and compare their stability, efficiency, and function to TCR-T-cells created through lentiviral transduction. **Results:** We have successfully sequenced a TCR from a well-characterised melanoma-specific clone using 5' RACE-seq, thus validating our methods. Further results will be obtained following amplification of T-cell clones with unknown sequences. **Discussion:** This research could significantly advance T-cell-mediated immunotherapy and facilitate the development of a platform that will allow for the generation of pools of T-cells that can recognise viral and tumour-specific antigens. Beyond TCR insertion, methods developed from this research may be applicable to all large-insert gene editing.

Primary Supervisor: Dr. Sheppard, H

Poster 16: Janneke Grundemann

Friend or Foe: Deconstructing cancer-immune interactions using patient-derived tumour models

Grundemann J,[1] Henare K,[1] Nolan E[1]

[1]Auckland Cancer Society Research Centre

Background: Breast cancer is the leading cause of death in women under 65 in New Zealand (NZ). Breast tumours exist as a heterogenous collection of cancerous cells and non-malignant cells, collectively termed the tumour microenvironment (TME). Improving our understanding of breast cancer biology, therapeutic responses and the influence of the TME through clinically-relevant tumour models, could contribute to improved health outcomes and open up avenues for precision medicine. **Objectives:** This project aims to optimise and validate two NZ-specific patient-derived breast cancer models; patient-derived explants (PDEs), and 3D primary tumour organoids, and evaluate their potential to explore tumour-immune cell interactions. **Methods:** PDEs were cultured for up to 10 days and treated with anti-tumour therapies, followed by analysing the tumour architecture, viability, proliferative capacity and TME. Optimisation of organoid-macrophage co-cultures was performed using mouse macrophages and organoids treated with chemotherapy, and tumour-immune interactions were analysed using confocal microscopy. **Results:** Explants remained viable for up to 10 days, while maintaining the same histopathological features of the original tumour. Fluorescent staining indicated PDEs were sensitive to anti-tumour therapies, and immune cell infiltrate and biomarker expression could be visualised. Development of a primary mouse organoid-macrophage co-culture model demonstrated striking heterogeneity in macrophage-cancer cell interactions, with 3D microscopy and flow cytometry analyses suggesting macrophages may provide protection from chemotherapy-induced cytotoxicity. **Discussion:** These models offer new insights into tumour heterogeneity and the pro-tumorigenic role of the breast tumour microenvironment, setting up a platform of 3D breast cancer models which provide a strong foundation for future studies.

Primary Supervisor: Dr Nolan, E

Poster 17: Sophia O'Brien-Gortner

Evaluation of new DNA-dependent protein kinase inhibitors as radiosensitisers of head and neck cancer cells

O'Brien-Gortner S[1], Wong W[1], Liew L[1], Dickson B[2], Airey R[1], Jaiswal J[1], Hong C[1], Hay M[1]
[1]Auckland Cancer Society Research Centre, [2]Chemistry and Applied Physics, The University of Waikato

Background: Despite advances in radiotherapy technologies and treatment scheduling, radioresistance occurs in subsets of cancer patients, including those with human papillomavirus negative (HPV-ve) head and neck squamous cell carcinoma (HNSCC). The dominant role of DNA-dependent protein kinase (DNA-PK) in repairing radiation-induced DNA double-strand breaks (DSBs) through the non-homologous end-joining pathway makes DNA-PK an appealing target for the development of radiosensitisers. **Objectives:** To characterise two new DNA-PK inhibitors (SN40318 and SN40905) as radiosensitisers in HNSCC cells. **Methods:** SN40318 and SN40905 were mechanistically evaluated. Their potency and selectivity for DNA-PK compared to related kinases were measured with biochemical assays and their ability to inhibit cellular radiation-induced DNA-PK activity was assessed with Western immunoblotting. Radiosensitisation by SN40318 and SN40905 was evaluated in HAP1 wild type and DNA-PK knock out (*PRKDC*$^{-/-}$) isogenic cells with growth inhibition assays to ensure DNA-PK-dependence. Radiosensitisation was further evaluated in human (FaDu) and murine (MOC1 and MOC2) HNSCC cells using growth inhibition and clonogenic survival endpoints. **Results:** Both SN40318 and SN40905 were potent and selective DNA-PK inhibitors in biochemical assays, inhibited cellular DNA-PK autophosphorylation, and effectively radiosensitised HNSCC cells with no observable single-agent cytotoxicities. In clonogenic survival assays, 0.3 µM of SN40318 and SN40905 provided robust radiosensitisation of FaDu cells with sensitisation enhancement ratios at 10% survival of 3.1 and 4.5, respectively. **Discussion:** This research provides compelling evidence for the application of SN40318 and SN40905 as radiosensitisers for the treatment of HNSCC. Further evaluation of the compounds *in vivo* is recommended.

Primary Supervisor: Associate Prof. Hay, M

Poster 18: queenie yong

Tackling Resistance to HER2-Targeted Antibody-Drug Conjugates in Breast Cancer

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Background: Human epidermal growth factor 2 (HER2)-positive breast cancer accounts for 15-20% of breast cancer cases and is associated with rapid disease progression and worse clinical outcomes. HER2-targeting antibody drug conjugates (ADC) have shown antitumour activity in HER2-positive and HER2-low metastatic breast cancer. Second-generation HER2-targeting ADCs, including trastuzumab deruxtecan (T-DXd) and trastuzumab duocarmazine (SYD985) have demonstrated effectiveness in addressing resistance that arises with the first-generation HER2-targeting ADC trastuzumab emtansine (T-DM1). Unfortunately, most patients who initially respond to HER2-targeting agents eventually cease to respond, as intrinsic and acquired resistance remains a major clinical challenge. **Objective:** Efforts to understand the mechanisms of resistance will identify potential strategies to overcome them. **Methods:** We employed two methods to elucidate the mechanisms underpinning HER2-targeting ADC resistance: 1. Whole-genome CRISPR/Cas9 screens in HER2+ breast cancer cell lines were transduced with the MinLibCas9 library. Transduced cells were exposed to ADCs and their respective cytotoxic payloads for 30-45 days. Genomic DNA was extracted and subjected to next-generation sequencing. Sequencing identified gene knockouts enriched or depleted in response to ADC or payload treatment in each cell line. 2. ADC-resistant cell lines were generated through prolonged exposure to the ADC. RNA was extracted and subjected to RNA sequencing to comprehensively profile transcriptomic alterations associated with resistance. **Results:** Analysis of the whole-genome screen and RNAseq data is underway. **Discussion:** Both approaches provide insights into the molecular basis of ADC resistance and suggest potential targets for overcoming resistance, ultimately enhancing the therapeutic efficacy of ADCs in cancer treatment.

Primary Supervisor: Associate Prof. Jamieson, S

Poster 19: Ashton Machado

Assessing dihydropyrimidine dehydrogenase dimer formation as a technique to understanding missing factors within 5-fluorouracil-related toxicity.

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Background: 5-Fluorouracil (5-FU) is a commonly administered chemotherapy in gastrointestinal and breast cancers. 5-FU toxicities may arise due to variants within the highly polymorphic *DPYD* gene, which encodes the enzyme dihydropyrimidine dehydrogenase (DPD). A previous study observed aberrant DPD dimerization in HEK293T/c17 cells transfected with 43 known *DPYD* variants. However, the impact of *DPYD* polymorphisms on DPD dimerization in primary human tissue is unknown. **Objectives:** To investigate interindividual variability in DPD dimerisation within primary human liver cytosol (HLC), buccal cell (BC), and peripheral blood mononuclear cell (PBMC) samples of known *DPYD* genotype. **Methods:** Blue native-polyacrylamide gel electrophoresis (BN-PAGE) before immunoblotting will be conducted to observe dimerization, as it is a non-denaturing method that migrates proteins through the gel bound by Coomassie Blue-G250 and visually observed using antibody detection. Migrated native proteins will be transferred onto a polyvinylidene fluoride membrane through a semidry transfer method. Standard immunoblotting techniques will be used with DPD bands visualised using enhanced chemiluminescence reagent and imaged on a BIORAD Chemidoc chemiluminescence machine. **Results:** Initial assay optimisation using pooled human liver cytosol resolved a DPD homodimer at approximately 220 kDa alongside a weaker DPD monomer at 110 kDa. Primary HLC, BC, and PBMC samples from individual donors will be assayed to examine inter-individual differences in DPD dimerization. **Discussion:** This work seeks to elucidate the relationship between *DPYD* genotype and DPD dimerization in primary human samples, in order to better understand their role in 5-FU toxicity.

Primary Supervisor: Prof. Helsby, N

Poster 20: Ben Watkin

Novel Generation of iPSC-Derived Lymphatic Endothelial Cells for Functional Assays

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Background: The lymphatic system, primarily comprised of lymphatic endothelial cells (LECs), plays a crucial role in fluid homeostasis, immune responses, and lipid metabolism. Research into lymphatics is typically performed *in vivo* as current lymphatic *in vitro* models are limited. However, induced pluripotent stem cells (iPSCs) offer a promising alternative. **Objectives:** To develop a reproducible and efficient protocol for the generation of functional LECs from iPSCs. **Methods:** We used established methods for mesodermal differentiation and iteratively added factors and molecules involved in LEC development *in vivo* to induce an LEC fate across 3 iPSC lines. Lymphatic identity was confirmed via immunocytochemistry, flow cytometry, and RNA sequencing. To assess functional similarity to *in vivo* LECs, we evaluated secretion patterns of induced LECs (iLECs) to inflammatory stimuli using a chemokine profiler array. Lymphangiogenic response was verified by vascular endothelial growth factor (VEGF) receptor 3 internalization using flow cytometry and EdU assays. We examined iLECs' ability to self-assemble into tubes using microfluidics and collagen sandwich approaches. **Results:** iLECs expressed all canonical markers and upregulated genes related to endothelial development, differentiation and lymphangiogenesis. In response to inflammatory cytokines, iLECs secreted chemokines and upregulated adhesion molecules. VEGFC treatment led to concentration-dependent VEGFR3 internalisation and EdU incorporation. iLECs formed 3D lumenised lymphatic networks in both collagen sandwiches and microfluidics. **Discussion:** This study generated a reliable method for studying lymphatic biology, disease and personalised therapeutic strategies with potential for improving patient outcomes afflicted by lymphatic disorders.

Primary Supervisor: Dr. Rustenhoven, J

Poster 21: Xini Puah

A Novel Synthetic Hydrogel for Studying Megakaryocytic Differentiation and Bone Marrow Fibrosis

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Background: Normal megakaryocytes mature in the bone marrow to produce platelets. In primary myelofibrosis (a chronic blood cancer), atypical megakaryocytes embedded in a fibrotic bone marrow are the main disease drivers. However, the impact of bone marrow fibrosis on megakaryocytic differentiation is poorly understood, partly due to the lack of suitable 3D culture models. **Objectives:** To investigate whether a novel synthetic and thermo-responsive oligo poly-isocyanate peptide (PIC) hydrogel conjugated with integrin ligands can support megakaryocytic differentiation in 3D culture, and if increasing the gel's stiffness can model bone marrow fibrosis. **Methods:** Human megakaryoblastic cell line Meg-01 and peripheral blood-derived haematopoietic progenitors were cultured in a PIC hydrogel. Proplatelet formation and cytoskeletal rearrangements were visualised using confocal microscopy. Expression of megakaryocyte-associated antigens (CD41a, CD61, CD42b) was monitored using flow cytometry. qPCR was employed to analyse the expression of genes involved in megakaryocytic differentiation and the cell stress response. **Results:** Unstimulated Meg-01 cells seeded in the PIC hydrogel ceased proliferating and underwent atypical differentiation (with increased ploidy but reduced antigen expression), followed by cell death. In contrast, after induction of differentiation with valproic acid, Meg-01 cells survived and differentiated well in the hydrogel. Excitingly, human progenitors exhibited robust megakaryocytic differentiation in softer hydrogels, while increased gel stiffness was associated with abnormal differentiation and a cell stress response. **Discussion:** The PIC hydrogel provides a novel model to culture megakaryocytic cells in 3D. Higher hydrogel stiffness impairs megakaryocytic differentiation, presenting an opportunity to uncover novel mechanisms involved in primary myelofibrosis.

Primary Supervisors: Dr Choi, A and Dr Kalev-Zylinska, M

Poster 22: Leilei Xu

Phenotypic difference of osteoblasts isolated from macroscopically normal or osteoarthritic zones in hip versus knee.

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Background: Osteoarthritis (OA) is a leading cause of disability in adults worldwide. Osteoblasts from bone within the joint are involved in driving OA pathogenesis, but little is known about the mechanisms involved. Emerging evidence also indicates OA pathogenesis differs in different joints. **Objectives:** To compare osteoblast phenotype in macroscopically normal (MN) and OA areas of hip versus knee joints. **Methods:** Osteoblasts were isolated from 30 patients and phenotype marker gene and protein expression assessed by real-time quantitative polymerase chain reaction, western blot and ELISA. Osteoblast differentiation and mineralization were quantified by Alkaline phosphatase (ALP) assay and Alizarin red staining, respectively. **Results:** Knee osteoblasts expressed higher *ALPL*, *GLUT1*, *OPG* and *IL1R1* (all $P<0.01$) mRNA levels than hip, regardless of MN or OA groups. Similarly, knee osteoblasts had higher ALP activity than hip ($p=0.0371$). However, there was no difference in GLUT1 protein levels or mineralisation between hip and knee osteoblasts. At the protein level, IL1R1 (IL-1 receptor) showed higher levels in OA compared to MN in hip ($P<0.0001$) but lower levels in OA vs MN in knee ($P=0.026$). **Discussion:** These data demonstrate that osteoblast phenotype differs between hip and knee suggesting osteoblast involvement in OA pathogenesis may differ between the two joints. IL-1 is strongly implicated in OA development. That IL1R1 levels differ between knee and hip osteoblasts in OA suggests the sensitivity of osteoblasts to IL-1 and the involvement of IL-1 in OA development may differ in hip vs knee.

Primary Supervisor: Dr. Poulsen, R.

Poster 23: Greer Pugh

Understanding standing… Exploring vascular properties in Postural Orthostatic Tachycardia Syndrome (POTS)

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Background: Postural Orthostatic Tachycardia Syndrome (POTS) is the most common form of orthostatic intolerance. Patients with POTS experience significant increases in heart rate (>30 beats per minute; bpm) and excessive venous pooling upon standing. However, mechanisms underlying the orthostasis and vascular properties remains unclear. **Objective:** The aim of the study was to determine whether patients with POTS exhibit reduced central arterial stiffness and increased venous capacity. **Methods:** In seven patients with POTS and seven healthy controls (all female; age [mean±SD]: 22 ± 3, p=0.214), we assessed arterial stiffness using pulse wave analysis (PWA; SphygmoCor) and central pulse wave velocity (PWV; carotid-femoral) whilst supine. Calf venous volume was measured with air plethysmography during standing until the veins reached maximal capacity. **Results**: POTS patients tended to exhibit a higher PWA (Augmented Index at 75 bpm; 15 ± 12 vs. 0 ± 15%; p=0.062) and increased central PWV compared to controls (5.7 ± 0.7 vs. 4.9 ± 0.6 ms^{-1}; p=0.016) indicative of raised central arterial stiffness. Calf venous volume was greater in POTS during standing (89 ± 31 vs. 60 ± 14 mL; p=0.021), despite the comparable filling time (254 ± 121 vs. 216 ± 102 s; p=0.434). **Discussion**: These preliminary findings indicate that patients with POTS exhibit increased central arterial stiffness and increased venous capacity. The greater venous capacity in POTS patients likely contributes to the excessive venous pooling and orthostasis that characterize this condition. Further research is required to understand the underlying mechanisms and to devise effective treatment targeting venous regulation.

Primary Supervisor: Dr. Fisher, JP

Poster 24: Antalya Stevens

Embodiment in Health Communication: Harnessing Patient Posture to Optimise Recall of Health Information

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[1]Department of Psychological Medicine, [2]Department of Medicine

Background: Research in embodied cognition demonstrates that upright body postures are associated with greater memory performance, approach motivation, and alertness, compared to slumped postures. These findings may have clinical applications by improving recall of health information and other cognitive processes related to adherence. **Objectives:** To investigate the effect of posture during a medical consultation on the recall of personally relevant health information, approach motivation, and alertness. **Methods:** A randomised trial was conducted with a general population sample of 108 healthy adults. Participants were randomly allocated to either an upright seated or reclined posture condition during a skin check consultation with a consultant dermatologist. Posture was manipulated discreetly by asking participants to sit upright in a chair or lay reclined in a bed during a brief skin check and education about sun protection. Questionnaires were completed before the consultation, immediately after and four weeks later. The primary outcome was recall of sun protection information. Secondary outcomes were motivation to perform sun protection behaviours, adherence to sun protection recommendations and alertness. **Results:** Immediately after the consultation, the upright group recalled significantly more health information than the reclined group (p = .039), but motivation to perform sun protection behaviours and alertness did not differ between groups. At follow up there were no significant differences between groups in recall or sun protection behaviour. **Discussion:** This preliminary research demonstrates some support for the application of embodiment theory in health. An upright posture during medical consultations may be beneficial for supporting short term recall of health information.

Primary Supervisor: Prof. Broadbent, E

Poster 25: Genevieve Boom

Developing a SERS surface for analysis of small extracellular vesicles

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Background: Extracellular vesicles (EVs) are lipid bound particles released by cells throughout the body and have been demonstrated to play a role in both physiological and pathological processes. Surface-enhanced Raman spectroscopy (SERS) is a useful analysis technique for EV samples, particularly those of low sample volume and concentration. A unique fingerprint of small EVs (<200nm) can be generated with SERS, occurring when EVs fall into hot-spots on the SERS-active surface. **Objectives:** To develop a SERS surface capable of producing a unique, enhanced spectra of small EVs from a choriocarcinoma cell line (Jeg-3). **Methods:** Laser induced periodic surface structures (LIPSS) were used as a SERS substrate. These structures were lasered onto stainless steel wafers and coated in a thin gold layer to create a SERS-active surface. EV concentration, gold thickness (20-100nm), and laser parameters, including power (0.35-11mW), speed (500µm/sec or 1000µm/sec), and polarisation (linear or circular) were tested. **Results:** Laser settings of 1000µm/sec speed, 11mW power, linear polarisation, and a gold thickness of 80nm produced the optimal Raman signal enhancement of small EVs from the Jeg-3 cell line. **Discussion:** The successful development of this SERS surface producing enhanced spectra of Jeg-3 small EVs is a useful proof-of-principle that the surface is a functional SERS-active surface and demonstrates the suitability of SERS for analysing low EV concentrations and volumes. This allows for ongoing work using this SERS surface to progress, with the ability to study minute differences between biological EV samples, and potentially establish small EVs as biomarkers according to these differences.

Primary Supervisor: Dr. Cree, L

Poster 26: Janice Yeoman

Optometrists' and ophthalmologists' views on the utility of scleral shell prostheses for disfigured eyes

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Background: Scleral shells can be fitted over blind disfigured eyes to restore appearance. Findings from a parallel study by this research group suggest they are under-utilised in New Zealand. **Objectives:** This study investigated the views of optometrists and ophthalmologists on the utility of scleral shells. **Methods:** Clinicians responded to survey questions about their: (i) judgments about the suitability of scleral shells for ten specific clinical presentations, (ii) concerns about scleral shell wear, and (iii) advice on scleral shell cleaning and wear schedules. **Results:** Responses from 140 optometrists and 50 ophthalmologists were collected. Responses on scleral shell suitability for the ten different presentations were wide ranging, although half of ophthalmologist agreed shells were “probably suitable” for phthisical eyes and microphthalmic eyes, and half of optometrists agreed shells were “probably suitable” for blind disfigured eyes with a full-sized globe. Bacterial keratitis with shell wear was the top concern for most optometrists (56.1%) and ophthalmologists (42.1%), while patient discomfort was the second most common concern for optometrists (21.4%) and ophthalmologists (36.0%). Optometrists most frequently advise that shells should be cleaned daily using contact lens products and not worn overnight, while ophthalmologists’ advice was mixed. **Discussion:** Views on scleral shell indications, maintenance, and wear were varied amongst clinicians. Bacterial keratitis and patient discomfort were key concerns. Clinicians need evidence-based guidelines to identify suitable scleral shell candidates and support ongoing scleral shell wear.

Primary Supervisor: Associate Prof. Misra, S

Poster 27: Aleisha Carter

The Characterisation of the effect of Proton Pump Inhibitors on the Cellular Uptake of Pyrimidine Nucleosides.

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Background: Colorectal cancer patients are often prescribed capecitabine, the oral prodrug of 5-fluorouracil. Several recent studies have reported that co-administration of capecitabine with proton pump inhibitors (PPI) results in poorer patient outcomes. However, a definitive association and proposed mechanisms of this potential adverse drug-drug interaction (DDI) have yet to be established. **Objectives:** To investigate how PPI alters the cellular transport of capecitabine's active metabolite 5-Deoxy-5-fluorouridine (5'DFUR) into human colorectal cancer cells (HCT116). **Methods:** Cellular uptake of 5'DFUR into HCT116 cells will be measured using radiolabelled uridine (^{3}H uridine), as radiolabelled 5'DFUR is not commercially available. Initial optimisation experiments will determine Michaelis-Menten uptake kinetics for first-order time and substrate concentration, and the concentration of pre-incubated and co-incubated PPI needed to inhibit ^{3}H uridine uptake into cells at pH 7.4, pH 5, 37°C and 4°C. Intracellular ^{3}H uridine concentrations will be quantified using liquid scintillation counting. PPI effect under these conditions will be compared with an appropriate positive control, *p*-chloromercuribenzene sulfonate. Additionally, the ability of dithiothreitol to reverse any observed inhibition will be assessed. All experiments will be replicated. **Results:** Under acidic conditions (pH 5), PPI are hypothesised to inhibit the uptake of ^{3}H uridine into HCT116 cells at 37°C. Descriptive statistics will be used, and any statistically significant differences ($p<0.05$) will be determined using appropriate tests (e.g., *t*-tests). **Discussion:** This study seeks to identify whether PPI can alter the cellular transport of 5'DFUR into cancer cells *in vitro,* contributing valuable insights into potential DDIs affecting capecitabine efficacy and patient outcomes.

Primary Supervisor: Prof. Helsby, N

Poster 28: Emily Caldelari-Hume

Investigating the consequences of experimental evolution of the mouse enteropathogen *Citrobacter rodentium* using deletion mutants

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Background: *Citrobacter rodentium*, a gut bacterium, infects laboratory mice similarly to the human pathogenic bacteria Enteropathogenic and Enterohaemorrhagic *Escherichia coli*. The Bioluminescent Superbugs Lab have investigated the evolution of *C. rodentium* during infection and transmission, with an array of phenotypic changes arising. Whole genome sequencing identified mutations in several genes, *espF*, a known virulence factor, *narX*, involved in nitrogen reduction and *nuoG*, involved in the electron transport chain. The relationship between genetic and phenotypic changes can be investigated by deleting these genes. Edwards and colleagues developed a suicide vector with chloramphenicol and *SacB* negative selection for creating deletion mutants by homologous recombination. **Objectives:** This project creates strains of *C. rodentium* lacking either *espF*, *narX*, or *nuoG*. **Methods:** A 2-kilobase insert, comprising the upstream and downstream regions of each gene was created using overlap PCR, and ligated into plasmid pRE112. This plasmid was transformed into *C. rodentium*, and underwent two recombinations, the first into the genome, selected for by sucrose susceptibility, the second removing from the genome and generating the deletion mutant, selected for by chloramphenicol susceptibility. **Results:** PCR and gel electrophoresis indicate I have successfully constructed a derivative of pRE112, enabling me to make a deletion mutant of *nuoG* in *C. rodentium*. **Discussion:** The construction of deletion mutants and suitable complementation vectors will allow me to perform phenotypic assays to investigate the role of EspF, NarX, and NuoG in the transmission and hyper-infectivity of *C. rodentium*. Elucidating the dynamics of pathogen evolution is important for aiding responses to outbreaks.

Primary Supervisor: Associate Prof. Wiles, S

Poster 29: Kate Pennycuick

RNase HI as a drug target in *Neisseria gonorrhoeae*

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Background: *Neisseria gonorrhoeae (N. gonorrhoeae)* is a significant global pathogen, estimated to cause over 80 million new infections annually, with high rates of antibiotic resistance and the emergence of strains resistant to all available treatments. With this developing resistance, finding new targets for the development of antibiotic compounds is essential in retaining the ability to treat infection. RNase HI is an enzyme that removes R-loops (RNA:DNA hybrids that can form during transcription) and is essential in *N. gonorrhoeae*, making it an attractive target for new antibiotics. **Objectives:** This study aimed to identify compounds that inhibit both recombinant *N. gonorrhoeae* RNase HI enzyme activity and the growth of *N. gonorrhoeae* bacteria. **Methods:** The *N. gonorrhoeae* RNase HI protein was expressed in *E. coli* and purified using affinity chromatography. An enzyme assay was used to identify compounds that inhibit the RNase HI activity. A live-dead assay was used to determine bacterial viability in the presence of the identified inhibitors. **Results:** The *N. gonorrhoeae* RNase HI enzyme was successfully expressed and purified. Several hits have been identified from a curated library of compounds that inhibit both enzyme activity and bacterial growth. **Discussion:** These results provide evidence supporting the validity of RNase HI as a target for new antibiotics against *N. gonorrhoeae*. Future work will include determination of the *N. gonorrhoeae* RNase HI structure to map the interactions of the inhibitory compounds with their target, enabling the structure-guided design of improved inhibitors.

Primary Supervisor: Assoc. Prof. Lott, JS

Poster 30: Ishana Ratti

Investigating the role of the CobC domain in promoting RNase HI function in *Mycobacterium tuberculosis*

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Background: RNase HI, the enzyme responsible for degrading RNA-DNA hybrids, is vital for maintaining genome stability in all organisms and is a validated drug target in *M. tuberculosis,* the causative agent of TB. In *M. tuberculosis,* RNase HI is a two-domain fusion protein with RNase HI and Cobalamin phosphatase (CobC) domains. Previous research showed that the CobC domain enhances RNase HI activity by an unknown mechanism. **Objectives:** To investigate how the CobC domain promotes RNase HI activity by studying how the domains interact with each other and with nucleic acid substrates. **Methods:** Small-angle X-ray scattering of the wildtype and catalytically dead mutant enzymes, with and without substrate, will provide structural insights regarding domain-domain interactions and domain arrangement on the substrate. Surface plasmon resonance will measure the binding affinity and specificity of the wildtype and mutants for the substrate. **Results:** Preliminary models suggest that a pocket located on the CobC domain allows for domain-domain interaction. Therefore, we expect mutations at the domain interface to disrupt their interaction. Furthermore, the models suggest that both domains interact with RNA-DNA substrate. Thus, we expect mutations at the substrate binding site for either domain to impair substrate binding affinity and specificity. The protocol for protein purification is currently being optimised. **Discussion:** Structural and activity experiments will reveal how and where the CobC domain interacts with substrate to enhance RNase HI activity. This will provide the opportunity to specifically target the activities of both the CobC and RNase HI domains in *M. tuberculosis*.

Primary Supervisors: Dr. Dawes, S and Dr. Lott, JS

Poster 31: Saptorshi Gupta

Prevalence and determinants of scabies: a global systematic review and meta-analysis

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Background: Scabies is a neglected skin disease that disproportionately affects people from resource poor and overcrowded countries. **Objectives:** Global data on prevalence and risk factors are limited. This study attempts to estimate scabies prevalence at a global level. **Methods:** Databases (PubMed, Scopus and Cochrane Reviews) were accessed to identify observational studies published between 2000 and 2024. Results were pooled to estimate prevalence and identify factors which explained between-study heterogeneity. Odds ratios, risk of bias, subgroup analyses and meta-regression were used to describe variation in effect size and heterogeneity based on country-level demographic and economic variables. **Results:** Seventy studies yielded a pooled prevalence of 11.9% (95% confidence interval [CI] 9.60%-14.7%) with substantial heterogeneity ($I^2 = 100\%$; $\tau^2 = 1.04$). Prevalence was highest in Oceania (17.9%; 95% CI 13.9-22.8) compared to other regions. Significant associations for behavioral factors was found including contact with someone with itch (odds ratio [OR] 11.3; 95% CI 4.82-26.51; $I^2 = 96\%$), non-use of soap (OR 3.41; 95% CI 2.56-4.54; $I^2 = 44\%$), bed sharing (OR 2.64; 95% CI 1.50-4.63; $I^2 = 76\%$), cloth sharing (OR 2.52; 95% CI 1.58-4.03; $I^2 = 85\%$), infrequent bathing (OR 2.13; 95% CI 1.41-3.22; $I^2 = 77\%$), presence of pets (OR 1.76; 95% CI 1.08-2.87; $I^2 = 84\%$) and gender (OR = 1.19; 95% CI 1.04-1.37; $I^2 = 83\%$). Socio-economic factors were not convincingly associated with scabies' prevalence. **Discussion:** Prevalence of scabies is associated with geographic location and behavioural factors, but not socioeconomic status. This study identifies risk factors for which targeted behavioural interventions addressing interpersonal interaction, personal hygiene practices and specific treatments create the potential to reduce scabies.

Primary Supervisor: Dr. Thornley, S

Poster 32: Angelina Soh

Effects of targeting hyaluronidase enzymes following hypoxic-ischemic brain injury in the preterm fetal sheep

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[1]Department of Physiology

Background: Perinatal hypoxia-ischemia remain an important contributor to neonatal brain injury and is associated with adverse neurodevelopmental outcomes, such as cerebral palsy. Established evidence supports a role for hyaluronidase family of extracellular matrix (ECM) remodelling enzymes in the pathogenesis of evolving brain injury, including seizures and damage to the white and grey matter. **Objectives:** This study examined the therapeutic potential of Sulfuretin, a selective hyaluronidase inhibitor, after acute hypoxia-ischemia in chronically instrumented preterm fetal sheep. **Methods:** Fetal sheep at 0.7 gestation (day 103; term ~145 days) received sham asphyxia (n=3) or asphyxia induced by umbilical cord occlusion for 25 minutes. Immediately after occlusion, fetuses received either a continuous intracerebroventricular infusion of vehicle (n=3) or Sulfuretin (3.3mg; n=3). Fetuses were continuously monitored until 7 days recovery. **Results:** Electrographically, Sulfuretin was associated with a significant reduction in both the number and burden of seizures between 12-24 hour following asphyxia, with a reduction in the total number of seizures over the 72 h recovery period (*vs.* asphyxia-vehicle; *P*=0.049, *P*=0.046 respectively). Histologically, Sulfuretin was associated with a significant increase in the number of total and mature oligodendrocytes within the periventricular white matter (*vs.* asphyxia-vehicle; P=0.049, P=0.028 respectively). However, Sulfuretin did not significantly change the number of neurons in the cortex, striatum and hippocampus (*vs.* sham asphyxia & asphyxia-vehicle). **Discussion:** These data suggest that targeting hyaluronidase inhibitors, via Sulfuretin, offers therapeutic benefit by modulating seizures and preserving myelination in a physiological manner. Further studies of its effect on ECM integrity and evolving injury are required.

Primary Supervisor: A/Prof Justin Dean

Poster 33: Claire O'Shea

Have services for diabetes, eye, hearing, foot health been integrated for adults? A scoping review.

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Background: The global population is ageing and by 2050 there will be almost 2.1 billion people aged over 60 years. This means conditions associated with ageing such as diabetes, vision impairment, hearing impairment and foot problems are increasing. These conditions often co-occur; therefore, could the integration of Audiology, Diabetes, Optometry and Podiatry services reduce the burden of care seeking and improve health outcomes for affected older adults. **Objectives:** This scoping review aimed to summarise the literature describing integration of services for adults of two or more of diabetes, eye, hearing, or foot services. **Methods:** We searched Medline and Embase without language restrictions, for studies published from 1 January 2000 describing the integration of services for two or more of diabetes, eye, hearing, and foot health for adults aged ≥40 years. Screening and data extraction were completed in duplicate in Covidence systematic review software. **Results:** Of 925 publications identified in the search, 40 met the inclusion criteria; these were undertaken in 13 countries. Studies described integration of services for diabetes and eyes (n=17, 43%), diabetes, eyes and feet (n=14, 35%), diabetes and feet (n=6, 15%) and eyes and hearing (n=3, 7%). Co-location of clinical services was a common integration approach. While many studies discussed the benefits of integration, few assessed effectiveness of the implemented approaches. **Discussion:** Given the interest in the potential of integrated care to improve clinical care, there is very little evidence on whether integrating services for any of diabetes, eye, hearing or foot services is effective.

Primary Supervisor: Associate Prof. Ramke, J

Poster 34: Audrey Zhu

Bandpass filtering changes the correlations between age and Blood Oxygen Level-Dependent (BOLD) variability

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Background: Understanding the neural correlates of healthy aging and age-related cognitive decline is crucial due to our aging population. Intraindividual variability of the fMRI BOLD signal (BOLD-var) is considered a powerful predictor of age and cognitive performance. However, the direction of this relationship is inconsistent in the literature, likely due to small sample sizes and varied analytical pipelines. **Objectives:** To investigate the differences in correlations between age and BOLD-var with and without high-frequency bandpass filtering with a large sample. **Methods:** Task-based fMRI images of 725 healthy participants (aged 36-100+ years) were provided by the Human Connectome Project-Aging (HCP-A). Two BOLD-var measures, standard deviation (SD) and percentage amplitude fluctuation (PerAF), were calculated in each brain region across task runs. The age effect on BOLD-var was assessed using a partial least square analysis. This procedure was repeated after applying a bandpass filter (0.008-0.09Hz) to the original data. **Results:** Preliminary results show that the age effect is positive on SD (R=.3292, p<.001) and PerAF (R=.4188, p<.001) before bandpass filtering, and negative on SD (R=-.4505, p<.001) and PerAF (R=-.5688, p<.001) after bandpass filtering. The age effect patterns before and after the filter are spatially orthogonal. **Discussion:** BOLD-var is a strong predictor of age. The removal of high-frequency components significantly alters the directionality and spatial pattern of this relationship, suggesting that neural (low-frequency) and non-neural (high-frequency) components have an opposing relationship with age. Further studies are required to clarify the relationship between BOLD-var and cognitive decline and its relationship to neurodegenerative diseases (e.g., Alzheimer's Disease).

Primary Supervisor: Dr Roberts, R

Poster 35: Zara Collins

Characterisation of the placental glycocalyx throughout gestation and in fetal growth restriction

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[1]Department of Obstetrics and Gynaecology

Background: Fetal growth restriction (FGR) is a pregnancy condition from insufficiencies in the placenta that prevents proper exchange between the mother and the fetus. The glycocalyx is a carbohydrate layer covering endothelial cells in the lumen of blood vessels has a role in regulating exchange. During numerous pathologies there is an increase of glycocalyx shedding into the blood creating a potential biomarker. The term placenta has a glycocalyx covering the syncytiotrophoblast, the barrier cell between placental tissue and maternal blood, but little is known about any changes across gestation or in pathologies. **Objectives:** My honours work aims to quantify the thickness and composition of the syncytiotrophoblast glycocalyx in term, first trimester and FGR placentae. **Methods:** To quantify glycocalyx thickness transmission electron microscopy (TEM) is employed in combination with Alcian Blue staining. To quantify glycocalyx composition, stimulated emission depletion microscopy (STED) is used to detect glycocalyx components syndecan-1, glypican-1, biglycan, versican and perlecan. **Results:** Initial TEM has enabled visualisation of the first trimester syncytiotrophoblast glycocalyx. Optimisation is currently underway for both imaging methods. Thickness results from TEM allow us to see if the syncytiotrophoblast placenta grows across gestation and if it is degraded in FGR. STED will allow us to see any changes in syncytiotrophoblast composition that may affect normal function. **Discussion: C**haracterisation of the placental glycocalyx throughout pregnancy and in FGR may allow for identification of a placental signature of glycocalyx dysfunction to aid in predicting or detecting FGR by understanding how serum glycocalyx levels relate to placental glycocalyx damage.

Primary Supervisor: Associate Prof. James, J

Poster 36: Grace Donaldson

Development of a Non-Invasive Embryo Quality Evaluation Tool for Equine Embryos

Donaldson G[1], Morris L[2], Fitzgerald S[3], Bianca Nijmeijer[1,3], Cree L[1]

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Background: 20% of Intra Cytoplasmic Sperm Injection-derived horse embryos result in pregnancy loss before 60 days gestation, primarily attributed to chromosomal aneuploidy in well-managed breeding mares. Morphological assessments of embryo quality cannot detect chromosomal abnormalities, necessitating invasive embryo biopsy. **Objectives:** We aim to investigate (i) whether the characteristics of extracellular vesicles (EVs) secreted by the horse embryos into culture media are associated with embryo quality. And (ii) whether DNA secreted into culture media can be used as a non-invasive marker for quality by performing proof of principle studies, including non-invasive sex selection. **Methods:** Equus Callabus 3.0 genome was downloaded from NCBI. Multicopy X and Y primers and single-copy mitochondrial primers were designed and optimised with Standard nested PCR and genomic DNA. ddPCR assays will be developed to determine sex from embryo culture media. EV quantity and size will be analysed using the ZetaVeiwer. **Results:** ddPCR assays targeting both the nuclear and mitochondrial genomes have been designed and preliminary results demonstrate the ability to amplify from low template copy number. **Discussion:** This research will develop a non-invasive method to assess embryo quality. By characterising the nature of EVs and analysing their role in establishing and maintaining pregnancy, it is possible to investigate factors contributing to poor embryonic development to better mitigate pregnancy loss in the mare. Furthermore, analysis of this DNA may provide an opportunity to diagnose genetic disorders in the equine embryo that lead to embryonic loss and facilitate genetic selection. Further research is needed to complete the objectives.

Primary Supervisor: Dr. Cree, L

Poster 37: Tram Bui

The impact of short-chain fatty acids on Tregs and T cell proliferation in neonates

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[1]Liggins Institute

Background: T cells and regulatory T cells (Tregs) play a vital role in establishing immunological tolerance in neonates. Impairment can lead to allergies and autoimmunity. Recent studies indicate that the presence of short chain fatty acid (SCFAs) in plasma correlates with an increase in T cells and Tregs. Nevertheless, the mechanisms behind the upregulation of these cells via SCFAs in neonates remain unclear. **Objectives:** The goal is to determine the impact of plasma SCFAs on the prevalence of Tregs and T cell proliferation in neonates. **Methods**: We assessed the suppressive function on immunity of neonatal T cells and Tregs and how these were altered by exposure to SCFAs using T cell proliferation assays. Neonatal T cells were isolated from blood mononuclear cell samples. Irradiated white cells were used as stimulator cells. These cells were then cultured in the presence or absence of SCFAs (acetate, propionate, and butyrate) and subsequently stained with antibodies. Proliferation was measured by flow cytometry. Adult cells were used as comparation. **Results:** In acetate, T cells and Tregs significantly increased their proliferation at 20mM, while butyrate and propionate showed efficiency at 1mM in both neonates and adult samples (p=0.056). Neonatal cells were more sensitive to SCFA levels compared to adults. **Discussion:** Understanding how SCFAs alter the suppressive capacity of Tregs in neonates is crucial for gaining a better understanding of the development of the adaptive immune system. SCFAs could potentially serve as a promising future therapeutic approach for reducing inflammation in newborns.

Primary Supervisor: Dr. Toldi, G

Poster 38: Ayamita Paul

Optimisation of T cell isolation from human milk

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Background: A more excellent knowledge of the immune cell composition of human milk and its relationship to the development of the newborn immune system during lactation is of growing interest. Currently, no streamlined, optimised method for separating T cells from human breast milk exists. **Objectives:** To isolate T cells optimally by comparing available cell isolation techniques, including centrifugation and immunomagnetic separation from human milk. **Methods:** The preliminary studies involved refining centrifugation settings based on existing literature to remove fat without compromising cell retrieval manually. We also explored the feasibility of immunomagnetic separation, a method commonly used for isolating T cells from the blood. We collected human milk samples from eight healthy donors and employed three distinct methods— centrifugation alone, a combination of centrifugation and immunomagnetic separation, and a 1:1 diluted sample subjected to immunomagnetic separation. **Results:** The findings revealed that immunomagnetic separation is a viable method for isolating CD3+ T lymphocytes from human milk, mirroring its success in blood. Centrifugation yielded the highest absolute number of lymphocytes, but magnetic isolation excelled in enhancing CD3+ cell enrichment and viability, particularly beneficial for characterising rare cell types. Notably, magnetic beads avoided excess cell activation (CD25 positivity). **Discussion:** The final decision about the cell isolation technique is made in light of the criteria for each experiment and the cells' intended usage

Primary Supervisor: Dr. Toldi, G

Poster 39: Elisa Weiss

The Impact of Western-Style Parental Diet on Offspring Metabolic Health: Initial Parental Phenotype

Weiss E[1], Toor K [2], Abbasi M[2], Muralidharan S [3], Davenport M[3], Ponnampalam A[3], Vickers M[2], Albert B[2], Hedges C[1], Musson D[1]
[1]Department of Nutrition and Dietetics, [2]Liggins Institute, [3]Department of Physiology

Background: In Aotearoa NZ, 34.3% of adults and 12.7% of children are obese, with Māori and Pacific populations disproportionately affected. Evidence is emerging that parental diet can predetermine the metabolic health of their offspring. However, most data focuses on maternal effects, and little is known about paternal or combined effects of both parents' diets. Understanding the relative impact of both parents' diets could lead to better guidelines for prospective parents. **Objectives:** To characterise the phenotype of parent rats consuming high-fat, high-sugar (HFHS) diets and their offspring's birth characteristics from a larger study. **Methods:** Forty male and eighty female Sprague-Dawley rats were randomised to consume a standard diet (SD) or HFHS diet. After four weeks, they were mated in factorial combinations to create the following parental groupings: SDmum-SDdad, SDmum-HFHSdad, HFHSmum-SDdad, and HFHSmum-HFHSdad. A subgroup of parents' (n=40) body composition (DEXA) and metabolic profiles (Prometheon metabolic cages) were assessed, and offspring birth weights and lengths recorded**. Results:** HFHS diet successfully induced obesity. HFHS-fed group had higher body weight (p=0.0472), fat percentage (p=0.0014) and lower Respiratory Exchange Ratio (RER) (p=0.0018) compared to those on SD. Offspring from both parents who consumed a HFHS diet had significantly lower birth weight and length (<0.0001). In male offspring, paternal HFHS diet had an additive effect in reducing birthweight (<0.0431). **Discussion:** HFHS diet effectively induced obesity in parents in this study, affecting offspring birth weight and length. This initial study highlights the significant impact of parental diet on offspring and the need to develop effective interventions.

Primary Supervisor: Dr. Musson, D

Poster 40: Flora Lam

Neuroprotective effects of progesterone given before hypoxia ischemia in near-term fetal sheep

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[1]Department of Physiology

Background: Ischemia at birth is the leading cause of neonatal mortality and morbidity. Progesterone has shown neuroprotective effects in neonatal rodent models of ischemia but has not been investigated in a large animal translational model. **Objective:** To investigate the neuroprotective effects of progesterone on ischemic brain injury in near-term fetal sheep. **Methods:** Pregnant ewes were randomised into four groups, vehicle-sham (n=9), progesterone-sham (n=7), vehicle-ischemia (n=7), and progesterone-ischemia (n=6). Ewes received either 150 mg medroxyprogesterone acetate intramuscularly or vehicle and four days later 30 minutes bilateral carotid occlusion (ischemia) or sham ischemia. Physiological data was continuously recorded. Brain tissue was collected at 7 days for immunohistochemistry. **Results:** Both ischemia groups had reduced electroencephalogram intensity and reduced neuronal counts compared with sham groups (p=0.008). Total cortical length was significantly reduced in the ischemia groups compared with sham groups (p=0.006). Ischemia groups had significantly smaller cortical neuronal cell size in the parasagittal gyrus (base) compared with sham groups (p=0.001). However, neuronal cell size in the parasagittal gyrus (top) in the progesterone-ischemia group was partially preserved, compared with both sham groups and vehicle-ischemia. Whole cortical area and average thickness were reduced in ischemia groups compared with sham groups, but both measures were higher in progesterone-ischemia, compared with vehicle-ischemia (p=0.006). Cortical lesions were present in vehicle-ischemia (6/7) and progesterone-ischemia (2/6). **Discussion:** Progesterone administration was associated with a partial neuroprotective effect. Further studies optimising the dosing and timing of progesterone are required and may lead to better treatment of brain damage for babies after ischemia.

Primary Supervisor: A/Prof. Davidson, J

Poster 41: Anja Bronnert

Vitamins for preterm infants

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Background: Vitamins are essential nutrients that have important biochemical functions. Adequate supply is necessary to maintain health. Vitamin deficiency, and also vitamin surplus, can have detrimental effects on health. Little is known about the vitamin requirements of preterm infants, how vitamin status affects clinical outcomes, nor the actual vitamin status of preterm infants shortly after birth. **Objectives:** To determine: 1) the effects of vitamin supplementation and serum vitamin concentrations on in-hospital outcomes, and 2) vitamin status of preterm infants soon after birth. **Methods:** 1) Systematic review and meta-analysis on the effects of vitamin supplementation on in-hospital outcomes in very preterm infants (born <33 weeks' gestation). 2) Prospective cohort study analysing serum vitamin concentrations in the first week after birth and associations with clinical course in extremely low birthweight (< 1000 g) infants. **Results:** 1) Forty-three studies were identified in the systematic search. Supplementation of vitamins A, D, E, and C has a small beneficial effect on the risk of developing lung disease, sepsis, brain bleeding, and retinopathy of prematurity. Few studies on water-soluble vitamins were identified. 2) Concentrations of water-soluble vitamins increase over the five days following birth but do not correlate with reference ranges, with some below and others above current references. Increased vitamin content of intravenous nutrition leads to increased serum vitamin concentrations. **Discussion:** Data on effects of supplementation and requirements of preterm infants are lacking for some vitamins and inconsistent for others. More research is required to establish vitamin requirements and reference ranges for preterm infants.

Primary Supervisor: Prof. Bloomfield, F

Poster 42: Anmol Sandhu

Evaluating Barrier Function in Differentiated Human Umbilical Vein Endothelial Cells for Corneal Endothelial Cell Therapy

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Background: Fuchs endothelial corneal dystrophy (FECD) is a progressive eye disease characterised by corneal endothelial cell (CEC) dysfunction, leading to impaired corneal transparency and vision loss. Currently, the primary treatment option is corneal transplantation; however, a global shortage of donor corneal tissue restricts accessibility, with only 1 in 70 patients able to receive a transplant, creating an urgent need for alternative therapies. Human umbilical vein endothelial cells (HUVECs) sourced from the umbilical cord may have potential as a CEC replacement therapy. **Objectives:** To determine the functional properties of HUVECs differentiated into CEC-like cells. **Methods:** HUVECs (n = 8) were differentiated into CEC-like cells using a CEC-conditioned medium. Differentiation was evaluated through morphology, polymerase chain reaction (PCR), immunocytochemistry (ICC), and flow cytometry. Functional properties of differentiated CECs were assessed using electric cell-substrate impedance sensing (ECIS) and the dye-leak assay. Additionally, the scratch assay was employed to evaluate migratory and proliferative abilities. **Results:** Differentiated HUVECs exhibited a polygonal morphology typical of CECs and expressed key CEC markers, notably ZO1 and ATP1A1. They demonstrated higher electrical resistance compared to immortalised CECs and effectively prevented fluorescein isothiocyanate-dextran flow across the cell membrane, indicating robust barrier function. Moreover, the cells displayed regenerative potential, evidenced by their migratory and proliferative responses following injury. **Discussion:** These findings demonstrate successful differentiation of HUVECs into functional CEC-like cells, offering a promising therapeutic approach for treating FECD. Future studies will evaluate these cells in a rabbit model of FECD, to further investigate clinical application.

Primary Supervisor: Prof. Sherwin, T

Poster 43: Lilia Delgado Paramo

Does exposure to the smell and taste of milk accelerate feeding in preterm infants?

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Background: Preterm infants often struggle to coordinate sucking, swallowing and breathing when oral feeding, requiring initiation of gastric tube feeding. This bypasses smell and taste, stimuli which aid digestion and absorption, hence potentially hindering infants' feeding progression. **Objectives**: to assess whether providing smell and taste of milk with tube feedings accelerates the transition to full sucking feeds in preterm infants. **Methods**: We undertook a systematic review of trials comparing smell or taste exposure, or both, with tube feeding with no provision. Two authors independently extracted data and assessed eligibility, risk-of-bias and certainty of evidence; random-effects meta-analyses were performed using risk ratios and mean differences (MDs) with 95% confidence intervals (CIs). **Results**: Eight trials (1277 preterm infants) were included. Smell and taste exposure had little to no effect on the time to reach full sucking feeds (MD -1.07 days, CI -2.63 to 0.50; 3 studies, 662 infants; very low-certainty evidence). It may reduce the time to discharge home (MD -4.40 days, CI -5.65 to -3.15; five studies, 786 infants), but the evidence is very uncertain and mean postmenstrual age at discharge remained unchanged. Other outcomes (adverse effects, parenteral nutrition duration, necrotising enterocolitis) had no data or showed little to no effect. **Discussion**: Smell and taste exposure during tube feedings does not accelerate feeding in preterm infants. There is very low-certainty evidence to assess its effect on other outcomes. Without high-quality evidence on the effectiveness and safety of the intervention, its use should only be considered in the context of further research.

Primary Supervisor: Prof. Bloomfield, FH

Poster 44: Dansoa Tabi-Amponsah

Evaluating gout remission definitions in a randomized controlled trial: Nurse-led versus usual-care.

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Background: Gout is a disease of monosodium urate (MSU) crystal deposition resulting from elevated serum urate and characterised by intermittent episodes of acute inflammatory arthritis. Urate-lowering therapies lead to reduction in urate levels, MSU crystal deposition, and clinical features of gout, thus remission is a potential goal of treatment. **Objectives:** To compare the performance of the 2016 preliminary gout remission definition and a subsequent simplified gout remission definition. **Methods:** Data from a 2-year randomised controlled trial of 517 people with gout were analyzed. Participants were assigned 1:1 to receive nurse-led care or usual care by general practitioners. Logistic regression was used to compare intervention groups, and general linear models were used to compare Gout Impact Scale (GIS) scores between those in remission and those not, using either definition. **Results:** Participants in the nurse-led group were more likely to achieve remission using either definition; at Year 2 the odds ratio was 7.92 [95% CI 4.86-12.92] using the 2016 preliminary definition and 11.88 [95% CI 7.49-18.84] using the simplified definition. For all participants, the preliminary definition was fulfilled by 9.9% at Year 1 and 28.4% at Year 2, $p<0.001$ and the simplified definition was fulfilled by 17.6% at Year 1 and 42.7% at Year 2, $p<0.001$. People in remission using either definition had better gout outcomes assessed using the GIS, including greater control over their gout. **Discussion:** Both definitions discriminated between the intervention groups and showed high construct validity. The simplified definition is a feasible and valid option for defining gout remission.

Primary Supervisor: Prof. Dalbeth, N


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