HealtheX 2023

Celebrating Student Research

CONFERENCE PROGRAMME BOOKLET
FRIDAY, 8TH SEPTEMBER

THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau
NEW ZEALAND

MEDICAL AND HEALTH SCIENCES | LIGGINS INSTITUTE | AUCKLAND BIOENGINEERING INSTITUTE

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Message from the Dean

Dear Colleagues,

"Research is to see what everybody else has seen, and to think what nobody else has thought."
Albert Szent-Gyorgyi (1893-1986), a Hungarian-born biochemist and the first person to isolate vitamin C

On behalf of the Faculty of Medical and Health Sciences, it is my pleasure to welcome participants and visitors to HealtheX 2023, the seventeenth of our Faculty's celebrations of student health research and an opportunity for our students to showcase a lot of what nobody else has thought.

HealtheX is an opportunity to present, in one day, many of the research initiatives and themes that have helped our Faculty to be rated among the top one percent of biomedical and health faculties around the world. The event highlights the depth of talnt and dedication of our students, and reiterates the importance of a strong, well supported research culture in improving health outcomes for New Zealanders in the short, medium, and long terms.

HealtheX has been hugely successful in meeting the goals we as a Faculty set for it from the outset - to encourage and develop professionalism in the distillation and communication of our health research. The research projects on display at HealtheX 2023 span a wide range of topics and activities, from the better understanding of the fundamentals of disease processes at the cellular level, through to the application of population-based interventions.

I would like to acknowledge and thank the students and staff who collectively have ensured that HealtheX once again takes pride of place in the Faculty. Their efforts have ensured the event will again be a success and will again reflect well the tremendous quality of medical and health research being carried out across the Faculty of Medical and Health Sciences, and beyond.

It is very appropriate to also recognise the long-time support for HealtheX that is generously provided by the Auckland Medical Research Foundation, and the Maurice and Phyllis Paykel Trust, as well as that from newly established partnerships with external biomedical research-focused organisations. Without this support and encouragement, HealtheX would not have the impact and appeal it enjoys.

In closing, I hope each and every participant will enjoy the celebration of health research excellence by our students that is HealtheX 2023.

Professor John Fraser
Dean, Faculty of Medical and Health Sciences
The University of Auckland

On Behalf of the 2023 HealtheX Organising Committee

Dear Colleagues,

On behalf of the 2023 HealtheX organising committee, we are honoured to welcome you to the 17th anniversary of the HealtheX conference, the student-organised and led conference and health exposition designed to promote health-related research at the University of Auckland.

Our long-term goal has been to evolve HealtheX into a modern and reputable conference, comparable to many international conferences. Building on the progress and strengths of HealtheX 2022, we maintained a fully online and digitally secure submission system. This year we had a complete restructure of the abstract submission, reviewing, judging, and administration portals through the dedicated work and extensive expertise of our beloved faculty staff member, and FMHS Staff Special Achievement award winner, Ian Sayer. His help is indispensable in elevating HealtheX to the level of modern international conferences, providing an exciting platform for scientific networking, communication, and collaboration.

With HealtheX, we hope to provide students with ample opportunity for networking with each other and staff across and within faculties, creating an environment for research to be freely discussed, new ideas to flourish, and lasting collaborations to be forged. HealtheX therefore promotes and inspires research excellence, and has now become an annual celebration that is keenly anticipated and deeply embedded within the traditions of the Faculty and the University as a whole.

HealtheX 2020-2022 embraced the Zoom video conferencing platform to allow presenters, judges, and attendees to attend and compete despite the ongoing COVID-19 pandemic. This year, we are thrilled to be able to bring HealtheX 2023 back to an in-person event, to encourage networking and collaboration between participants and the wider scientific community. This year, we are also extremely proud to continue the success of previous HealtheX conferences, with an incredible number of presenters from both doctoral and non-doctoral research positions in biomedical, clinical, and public health fields. We are particularly pleased with the increasing numbers of Population Health participants, given the move of the school to Grafton campus, and the growing relationship with the Auckland Bioengineering Institute. Through avenues of oral, poster, and 3-Minute Elevator Pitch communication categories, HealtheX imparts an appreciation for the varied approaches taken by scientists to work towards the common goal of improving global health.

HealtheX is a conference organised by students, for students. The success of HealtheX 2023 is thanks, in no small part, to the commitment and hard work of the students and staff whose contribution continues to take HealtheX to greater heights. We thank our dedicated organising committee whose rigorous devotion over the past year has made this enjoyable and informative day possible. We are thankful for the supportive faculty academic and administrative staff for their invaluable mentorship and guidance. In particularly, we would like to thank Bronwyn Staples for her continued assistance with marketing the conference. Last, but certainly not the least, the entire team of HealtheX 2023 is grateful for the trusted, continuous and generous support of the Auckland Medical Research Foundation, the Maurice and Phyllis Paykel Trust, FMHS Postgraduate Student Association, Liggins Institute, and Abacus dx. HealtheX is also grateful to the new collaborations with, and sponsorships by the Auckland Bioengineering Institute, and the Pacific Clinical Research Network.

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

HealtheX Site Map

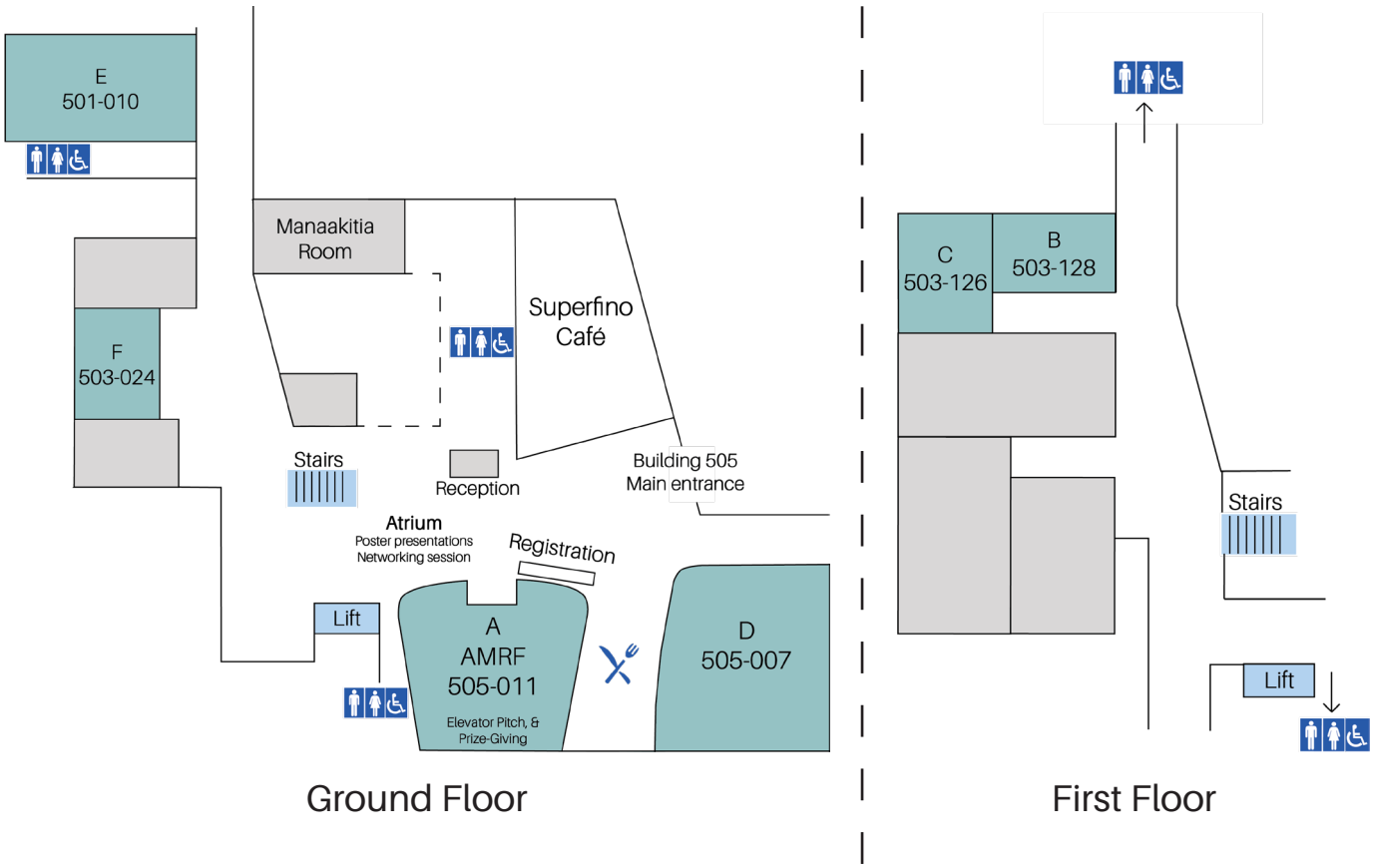
Registration - 8:30 am- 10:30 am
All judges, presenters, and invited guests are asked to register at the Registration Desk which can be found in the Grafton Atrium. This includes picking up ones' own name tag, other HealtheX items pertinent to ones' role (e.g., judging packs), and relevant HealtheX merchandise.

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.

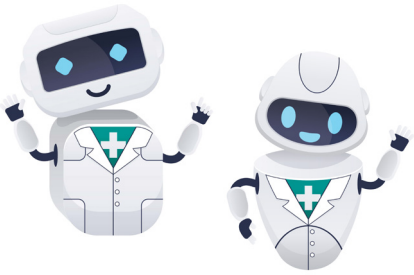
The day culminates in a catered Networking session for the entire Faculty research community to celebrate student research.



Conference Schedule

Date: Friday, 8th 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 503-128 B1 - B5	Room C 503-126 C1 - C5	Room D 505-007 D1 - D5	Room E 501-010 E1 - E5	Room F 503-024 F1 - F5
Break						
10:40 am - 12:00 pm	Oral Presentation Session 2					
	Room A 505-011 A6 - A10	Room B 503-128 B6 - B9	Room C 503-126 C6 - C10	Room D 505-007 D6 - D10	Room E 501-010 E6 - E9	Room F 503-024 F6 - F10
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 - A14	Room B 503-128 B10 - B12	Room C 503-126 C11 - C13	Room D 505-007 D11 - D15	Room E 501-010 E10 - E12	Room F 503-024 F11 - F15
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 - Minah Kim — Supervisor: Assoc Professor. Perry, J Antagonising the Growth Hormone Receptor to Combat Melanoma
9:15 am	A2 - Andrea Gu — Supervisor: Assoc Prof. Jamieson, S Whole-genome CRISPR-Cas9 screens reveal genetic vulnerabilities in NRAS-mutant melanoma cell lines
9:30 am	A3 - Michael Pudjihartono — Supervisor: Dr Schierding, W Network Analysis Links Melanoma Germline Risk Loci to Somatic Driver Genes Through Novel Genetic Pathways
9:45 am	A4 - Chantal Buckley — Supervisor: Assoc Prof. Perry, J Characterisation of novel inhibitory antibodies targeting growth hormone signalling in breast cancer cell lines
10:00 am	A5 - Kim Mizziana Paras — Supervisor: Dr Singleton, D Validation of Glucose-6-phosphate dehydrogenase as a new therapeutic target for treating IDH1 mutant lower-grade glioma.
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	A6 - Judith Glasson — Supervisor: Dr Domigan, L Crystallising the Concepts of Corneal Constructs: A Tale of Two Systems
11:00 am	A7 - Yuting Xiao — Supervisor: Dr Zhang, J Support of limbal mesenchymal stem cells for transition zone cells: an emerging stem cell niche
11:15 am	A8 - Anmol Sandhu — Supervisor: Prof. Sherwin, T Investigating umbilical cord stem cells for the treatment of corneal endothelial disorders
11:30 am	A9 - Emily MacFarlane — Supervisor: Dr Grey, A Development of an animal model of age-related nuclear cataract
11:45 am	A10 - Dingchang Shi — Supervisor: Dr Guo, G Annotation and visualisation of spatially and temporally resolved isotope tracing MALDI imaging data of lenses
12:15 pm	Break and Poster Viewing Session
1:25 pm	Introduction by Chairperson
1:30 pm	A11 - Yongxin Wang — Supervisor: Dr Tomek, P Does arylformamidase drive production of immunosuppressive kynurenine in cancer?
1:45 pm	A12 - Win Thu — Supervisor: Dr Tin Tin, S Associations between transport modes and site-specific cancers: A systematic review and meta-analysis
2:00 pm	A13 - Sophia Bebelman — Supervisor: Dr Tomek, P Redefining the role of the arylformamidase enzyme in immunosuppressive tryptophan catabolism of cancer
2:15 pm	A14 - Thu Thu Win Myint — Supervisor: Prof. Douglas, R Oropharyngeal cancer trends in Aotearoa over 15 years: 2006 - 2020
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 - 503-128
8:55 am	Introduction by Chairperson
9:00 am	B1 - Harvey Walsh — Supervisor: Assoc Prof. Fisher, J Cerebrovascular carbon dioxide reactivity is impaired in atrial fibrillation patients with concurrent hypertension
9:15 am	B2 - Sryana Sukhdev — Supervisor: Dr Mcbryde, F Nebulised Sodium Nitrite to Preferentially Dilate Penumbral vessels, following Ischemic Stroke... a NO brainer
9:30 am	B3 - Olivia Gold — Supervisor: Professor. Paton, J Identifying the building blocks for learning and memory in the carotid body
9:45 am	B4 - Tania Warnakulasuriya — Supervisor: Assoc Prof. Ramchandra, R Directly recorded renal sympathetic nerve activity reduces with Impella ventricular pump support in cardiogenic shock
10:00 am	B5 - Tony Zhou — Supervisor: Dr Mcbryde, F Sympathetic innervation of the carotid body in blood pressure control
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	B6 - Joshua Chang — Supervisor: Assoc Prof. Ramchandra, R β-blockers further impair exercise capacity in heart failure with preserved ejection fraction
11:00 am	B7 - Hannah Caulton — Supervisor: Dr McBryde, F. Keeping the Rhythm: Improving Brain Blood Flow in States of Hypertension
11:15 am	B8 - Michael Plunkett — Supervisor: Assoc Prof. Fisher, J The skeletal muscle metaboreflex: a novel driver of exertional dyspnoea in pulmonary arterial hypertension
11:30 am	B9 - Suma Thampi — Supervisor: Dr McBryde, F Improving stroke endovascular thrombectomy outcomes: Blood pressure trends in hypertensive population under anaesthesia
12:15 pm	Break and Poster Viewing Session
1:25 pm	Introduction by Chairperson
1:30 pm	B10 - Aeson Chappell — Supervisor: Dr McBryde, F Characterizing metabolic, cardiac and cognitive impacts in a rat model of “glucotension”
1:45 pm	B11 - Caitlin Macrae — Supervisor: Assoc Prof. Merry, T. Inhibiting insulin signaling for weight loss in obese female mice
2:00 pm	B12 - Oluwatoyin Oladimeji — Supervisor: Distinguished Professor Harding, J Predictors and short-term outcomes of hypoglycaemia among neonates of mothers with gestational diabetes mellitus.
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 - 503-126
8:55 am	Introduction by Chairperson
9:00 am	C1 - Khushi Sehajpal — Supervisor: Dr Singh-Bains, M Characterisation of the substantia nigra in X-Linked Dystonia Parkinsonism
9:15 am	C2 - Laura McNamara — Supervisor: Prof Montgomery, J; Dr Cheyne, J Identifying the cellular mechanisms of Alzheimer's Disease (AD) in vivo.
9:30 am	C3 - Gia Tan — Supervisor: Dr Cheung, G Aged Residential Care Admission in Young Onset Dementia: A Cohort Study
9:45 am	C4 - Lieke Burgers — Supervisor: Prof. Connor, B Transplantation of directly reprogrammed striatal precursor cells into a rat model of Huntington's disease
10:00 am	C5 - Mariam Karhiy — Supervisor: Prof. Broadbent, E. A Randomized Trial: Can a Virtual Human Deliver Mindfulness to Reduce Stress?
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	C6 - Harrison Porritt — Supervisor: Assoc Prof. Malmström, J Stem cell derived models of diseased cardiac tissue, mediated by Mechanotransduction through specialised hydrogels.
11:00 am	C7 - Jess Kelly — Supervisor: Prof. Connor, B Novel Generation of Three-Dimensional Brain Spheroids Using Direct Cell Reprogramming.
11:15 am	C8 - Kevin Roy — Supervisor: Dr O'Carroll, S Testing the clinically-relevant kappa-opioid receptor agonist, nalfurafine, as a potential treatment for spinal cord injury
11:30 am	C9 - Brittany Hazelgrove — Supervisor: Assoc Prof. Svirskis, D Identifying propagating neural activity from the subdural surface of the rodent spinal cord
11:45 am	C10- WITHDRAWN
12:15 pm	Break and Poster Viewing Session
1:25 pm	Introduction by Chairperson
1:30 pm	C11 - Kyrah Thumbadoo — Supervisor: Dr Scotter, EL The X Factor: X-inactivation in the phenotype of the X-linked motor neuron disease gene UBQLN2
1:45 pm	C12 - Nicholas Pudjihartono — Supervisor: Prof. O'Sullivan, J Network analysis uncovers gene-regulatory intersections between juvenile arthritis and comorbid traits.
2:00 pm	C13 - Catriona Miller — Supervisor: Prof. O'Sullivan, J Uncovering the developmental intersection between autism and co-occurring traits
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 - 505-007
8:55 am	Introduction by Chairperson
9:00 am	D1 - Tim Hsu-Han Wang — Supervisor: Prof O'Grady, G Non-invasive Mapping Of Post-Pancreaticoduodenectomy Gastric Function Using Gastric Alimetry®
9:15 am	D2 - Farheen Kothiwala — Supervisor: Dr Sumner, R Using EEG to Asses Neural Effects of Estradiol:Progesterone Ratio in Females with and without Epilepsy
9:30 am	D3 - Alexandria Lim — Supervisor: Prof. O'Grady, G The Effect of the Menstrual Cycle on Normal Gastric Electrophysiology Using Gastric Alimetry
9:45 am	D4 - Hadassah Patchigalla — Supervisor: Assoc Prof. Blenkiron, C; Dr Cree, L. Exploring the Role of Extracellular Vesicles in Endometriosis Patients in Aotearoa
10.00 am	D5 - Nicki Macklin — Supervisor: Dr Wilkinson-Meyers, L Working with a global healthcare community to define, conceptualise and measure kindness in healthcare
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	D6 - Holly Wilson — Supervisor: Dr Chan, A "I didn't want to go home" – Modifiable risk factors associated with hospital readmissions
11:00 am	D7 - Nikki Singh — Supervisor: Assoc Prof Peiris-John, R Neither Pacific nor Asian: Investigating intersectionality of ethnicity and identity among Fiji-Indian youth in Aotearoa
11:15 am	D8 - Mohammad Shahbaz — Supervisor: Distinguished Professor. Harding, J Comparison of outcomes of a randomized trial assessed by study questionnaire and by data linkage
11:30 am	D9 - Nicolas Smith — Supervisor: Prof. Windsor, J EPIC PLEFF Study: Exploring the Prognostic ImpaCt of PLeural EFFusion in the Intensive Care Unit
11:45 am	D10 - Meiliana Meiliana — Supervisor: Distinguished Prof Harding, J A systematic review of nutritional guidelines for preterm infants
12:15 pm	Break and Poster Viewing Session
1:25 pm	Introduction by Chairperson
1:30 pm	D11 - Victoria King — Supervisor: Prof Bennet, L Fetal growth restriction and fetal sexes: brain versus brawn?
1:45 pm	D12 - Trent Meehan — Supervisor: Assoc Prof. Fraser, M; Dr Gamage, T Fetal plasma-derived extracellular vesicles as biomarkers of hypoxia-ischaemia-mediated preterm brain injury
2:00 pm	D13 - Michael Beacom — Supervisor: Prof. Bennet, L Assessing the Efficacy of Fetal Heart Rate Variability Measures as Biomarkers for mild Fetal Brain Injury
2:15 pm	D14 - Alice McDouall — Supervisor: Assoc Prof Davidson, J Erythropoietin improved recovery of brain activity after mild hypoxia-ischemia in the term-equivalent fetal sheep
2:30 pm	D15 - Jingyuan Liang — Supervisor: Prof. Jackson, R Five-year vs ten-year predicted cardiovascular disease risk in Aotearoa New Zealand
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 - 501-010
8:55 am	Introduction by Chairperson
9:00 am	E1 - Yufeng Wang — Supervisor: Assoc Prof. Shane, S Understanding risk factors for pharmacists' complaints through a nationwide database: a qualitative content analysis
9:15 am	E2 - Xin Yi Lim — Supervisor: Prof. Barnes, J Pharmacovigilance-related regulatory obligations for the natural health products (NHPs) industry: a scoping review
9:30 am	E3 - Pang Yuk Cheung — Supervisor: Dr Hollywood, J Can Cysteamine and Everolimus combination treatment prevent kidney dysfunction in cystinosis rats?
9:45 am	E4 - Rayna Sharma — Supervisor: Prof. Barnes, J The recreational use of natural health products/substances for psychoactive effects in New Zealand: a review
10:00 am	E5 - Ellen Kingston — Supervisor: Prof. Tingle, M Clozapine-Induced Cardiotoxicity: Investigating reactive species associated with metabolite cycling.
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	E6 - Michele Zuppi — Supervisor: Prof. O'Sullivan, J Faecal microbiota transplant-mediated alteration of the phageome composition in a clinical trial for obesity
11:00 am	E7 - Samantha Rickard — Supervisor: Assoc Prof. Flanagan, J Activated yet in-active; the paradoxical effect of dasatinib on Lymphocyte Specific Kinase
11:15 am	E8 - Estelle Miller — Supervisor: Dr Rhys Ponton Overcoming Barriers to Drug Checking Research in Illicit Drug Consumption
11:30 am	E9 - Te Xiao — Supervisor: Assoc Prof. Flanagan, J Structure guided poly-pharmacology targeting the bacterial GHKL proteins to overcome antibiotic resistance
12:15 pm	Break and Poster Viewing Session
1:25 pm	Introduction by Chairperson
1:30 pm	E10 - Selina Karmacharya — Supervisor: Dr Loh, J Group A Streptococcus vaccine development: Exploring M75 AP1 protein to expand pilus-based vaccine coverage.
1:45 pm	E11 - Risa Takahashi — Supervisor: Professor Dr Tsai, C Exploring the Immunostimulatory Properties of GAS Pili
2:00 pm	E12 - Marcus Ooi — Supervisor: Prof. Dunbar, R Spatial Analysis of Dendritic Cell Subsets in Human Lymph Nodes
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 - 503-024
8:55 am	Introduction by Chairperson
9:00 am	F1 - Sarah Primhak — Supervisor: Dr Best, E Treating Impetigo with Antiseptics, Replacing Antibiotics (TIARA): a randomised controlled trial comparing topical impetigo treatments
9:15 am	F2 - WITHDRAWN
9:30 am	F3 - Arne Koefoed — Supervisor: Dr Biswas, K Antibiofilm activity of a commercial antiseptic agent compared to antibiotics commonly prescribed for sinonasal disease
9:45 am	F4 - James Willoughby — Supervisor: Dr Biswas, K Antibiofilm activity of novel polymyxin B analogues
10:00 am	F5 - Krish Sethi — Supervisor: Dr Misra, S Ocular surface in health and diabetes: from young children to young adults
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	F6 - Simone Watkins — Supervisor: Prof. Bloomfield, F Parents' and professionals' experiences of diagnosis and decisions for critical congenital heart disease in Aotearoa
11:00 am	F7 - Melenaite Tohi — Supervisor: Prof. Vickers, M Adolescent understanding of the developmental origins of health and disease concepts: a Pacific perspective
11:15 am	F8- Kamel Ahmed — Supervisor: Prof. Wu, Z Poloxamer 188-modified pH-sensitive liposomes for enhanced anti-tumour drug delivery.
11:30 am	F9 - Lilia Delgado Paramo — Supervisor: Prof. Bloomfield, F What factors influence successful breastmilk feeding in very preterm infants in Aotearoa?
11:45 am	F10 - WITHDRAWN
12:15 pm	Break and Poster Viewing Session
1:25 pm	Introduction by Chairperson
1:30 pm	F11 - Reece Joseph — Supervisor: Prof. Cornish, J Paediatric osteomyelitis: Identification of bacterial genes and phenotype that predispose to adverse health outcomes
1:45 pm	F12 -Lauren Carlton — Supervisor: Assoc Prof. Moreland, N Discovery of novel autoantigen biomarkers for Acute Rheumatic Fever
2:00 pm	F13 - Janneke Grundemann — Supervisor: Dr Nolan, E Friend or Foe: Deconstructing cancer-immune interactions using patient derived tumour models.
2:15 pm	F14- Hannah Rapata — Supervisor: Assoc Prof. Cormack, D A Kaupapa Māori Critique of Māori Food and Nutrition Data in Aotearoa
2:30 pm	F15 - Madeline Shelling — Supervisor: Dr Anderson, A Rangatiratanga o te Kai - Reconceptualising Food Security in Aotearoa
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 - Xiaojuan Zhu	Supervisor: Assoc Prof. Acosta, M
Developing Equipment for Rat Ocular Biometry Measurement	
P2 - Tim Hsu-Han Wang	Supervisor: Professor O'Grady, G
Objective modalities of delayed gastric emptying following pancreaticoduodenectomy- a systematic review	
P3 - Thai Nguyen	Supervisor: Assoc Prof. Young, D
Functionality analysis of a novel molecular switch in YAC128 transgenic mouse model of Huntington's disease	
P4 - WITHDRAWN	
P5 - Stian Thomson	Supervisor: Dr Shanks, J
Beat-to-beat regulation of the coronary arteries by the cardiac vagus nerve.	
P6 - Sihan Wang	Supervisor: Dr Helsby, N
Towards the development of an assay for urinary uracil for prediction of severe 5-fluorouracil toxicity	
P7 - Shruti Sharma	Supervisor: Dr Ryan, B
Diagnosis of Young-Onset Dementia in New Zealand	
P8 - Sasithorn Bureechai	Supervisor: Dr Chen, Y
A Scoping Review of Healthy Nutrition Interventions among University Students: Exploring Socio-ecological Landscape	
P9 - Santosh Bhujbal	Supervisors: Assoc Prof. Rupenthal, I and Dr Agarwal, P
Development and validation of a stability indicating HPLC method for tonabersat assay	
P10 - Queenie Yong	Supervisor: Assoc Prof. Jamieson, S
Genetic determinants of sensitivity and resistance to HER2-targeting antibody drug conjugates	
P11 - Pang Ying Cheung	Supervisor: Dr Cheyne, J
In vivo imaging of developmental neural activity in postnatal mice	
P12 - Narjis Adnan	Supervisor: Assoc Prof. Wiles, J
The power of words and its effect on older people	
P13 - WITHDRAWN	
P14 - Mejo Chiratteparambil Korah	Supervisor: Prof. Proft, T
Development of Vaccines against Gonococcal Disease using the PilVax Platform	
P15 - Malak Alshakhouri	Supervisor: Dr Sumner, R.
Investigating the Neurosteroid Withdrawal Hypothesis of Pericatamenial Epilepsy using Visual Long Term Potentiation	
P16 - Gbohunmi Idowu	Supervisors: Assoc Prof. Acosta, M and Dr Freestone, F
Dopaminergic Retinal Neurons in a Dopamine Transporter Knockout (DAT-KO) Model	
P17 -Frankie Day	Supervisor: Dr Pook, C
Faecal microbiome transplants leave footprints in the plasma metabolome	
P18 - Even Chen	Supervisor: Dr Poulsen, R
How the primary cilium influences chondrocyte phenotype and energy metabolism	
P19 - Ederlyn Perolina	Supervisor: Dr Thakur, S
A cell-based platform for studying the effects of ultrasound on neurons following stretch injury	
P20 - Eamon Walsh	Supervisor: Dr Djurkov, A
Factors influencing the development of metabolic syndrome in patients prescribed a second-generation anti-psychotic: Systematic review/Meta-analysis	
P21 - Dansoa Tabi-Amponsah	Supervisor: Prof. Dalbeth, N
The Patient Experience of Gout Remission: A Qualitative Study	

Poster Session - Grafton Atrium	
P22 - Courtney Thorne	Supervisor: Assoc Prof. Lim, J
Strategies for delaying diabetic cataracts: Developing a bovine model to understand changes associated with hyperglycaemia	
P23 -Claire Dunham	Supervisor: Assoc Prof. McGlashan, S
Characterising the obese osteoarthritic phenotype: Developing a novel protocol for spatial lipidomics analysis of cartilage	
P24 - Christine Kim	Supervisor: Dr Choi, P
Development of hypoxia-activated prodrugs of second generation analogues of bedaquiline for treatment of latent Tuberculosis	
P25 - Carina Lee	Supervisor: Dr Park, T
Developing Novel Therapeutics for Glioblastoma	
P26 - Bruno Batinica	Supervisor: Prof. Jackson, R
Predicting cardiovascular risk across whole populations using administrative data, laboratory results and deep learning	
P27 - Maximus Yeatman-Biggs	Supervisor: Assoc Prof. McGlashan, S
Unlocking the Secrets of Shark Cartilage	
P28 - Benjamin Prince	Supervisor: Prof. Montgomery, J
Examining structural plasticity within human heart neurons and its role in Atrial Fibrillation	
P29 -Ben Moloney	Supervisor: Dr Lin, J
Exploring chronic low-grade inflammation-associated white matter alterations in major depressive disorder	
P30 -Anna Behling	Supervisor: Prof. O'Sullivan, J
Assessing the dynamics of horizontal gene transfer after faecal microbiota transplantation in obese adolescents	
P31 -Amanda Groenewald	Supervisor: Dr Ward, M
The Acute Effects of Clozapine and Valproate on the Heart	
P32 -Alexandria Lim	Supervisor: Prof. O'Grady, G
The Contraceptive Conundrum: The Influence of Systemic Hormonal Contraception on Functional Gastroduodenal Symptoms	
P33 -Aimee Mills	Supervisor: Dr Mugisho, L
Microglial and astrocytic responses in the human midcingulate cortex in Huntington's disease	

3-Minute Elevator Pitch Competition - AMRF Lecture Theatre (505-011)	
EP1 - Tim Hsu-Han Wang	Supervisor: Prof. O'Grady, G
Gastric electrical activity and histological effects of gastrointestinal anastomosis- a chronic animal study	
EP2 - Santosh Bhujbal	Supervisors: Assoc Prof. Rupenthal, I and Dr Agarwal, P
Dual Action Preservative Free Non-Aqueous Eye Drop: Revolutionizing Dry Eye Disease Treatment	
EP3 - Oyedele Olaoye	Supervisor: Prof. O'Sullivan J
Decoding the non-coding genome in Parkinson's disease	
EP4 - Nishantika Mitra	Supervisor: Prof. Mithen, R
Optimising a protocol for the isolation and characterization of plasma extracellular vesicles	
EP5 - Nicholas Pudjihartono	Supervisor: Prof. O'Sullivan, J
Decoding Autoimmune Disease: Playing Detective with DNA Mutations.	
EP6 - Jennifer Park	Supervisor: Dr Wilkinson-Meyers, L.
The effectiveness of an internet-delivered intervention for gaming disorder	
EP7 - Isabel Cowlishaw	Supervisor: Assoc Prof. Clarke, R
Optimisation of corneal tissue engineering to facilitate epithelial wound healing	
EP8 - Hossein Jahedi	Supervisors: Professor Print, C; Assoc Prof. Blenkiron, C
Hyaluronic Acid Biology and its Significance in Pancreatic Ductal Adenocarcinoma	
EP9 - Cristal Salatas	Supervisor: Prof. Bloomfield, F
Kiwi Preemies: What's the crunch?	
EP10 - Charisse Kuo	Supervisor: Dr Mugisho, O (Lola)
Inflammation in Diabetic Retinopathy	
EP11 - Brooke Hawker	Supervisor: Dr McCaughey-Chapman, A
Utilizing 3D hydrogels to promote survival and maturation of directly reprogrammed human-induced oligodendrocyte precursor cells	
EP12 - Ashok David Jose	Supervisor: Dr Thakur, S
Sensitisation of radiation resistant colon cancer: The oxygenated microbubble hydrogel approach	
EP13 - Anja Bronnert	Supervisor: Prof. Bloomfield, F
Analysing Vitamin status and early Intravenous Nutrition in the NICU (The AVIatioN Study)	
EP14 - Angelica Clarke	Supervisor: Prof. Crowther, C
Who develops gestational diabetes mellitus in New Zealand and what are the health risks?	
EP13 - Abbey Lissaman	Supervisor: Dr Ponnampalam, A
Androgens in the endometrium: A forgotten piece of the puzzle	
Followed by the Prize-Giving Ceremony - AMRF Lecture Theatre (505-011) Networking Session - Grafton Atrium	

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"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."

Dr Robyn May, 2021 HealtheX winner says:

"The clinical computational models I'm developing will help us understand how being born early affects the development of the cardiovascular system and why there is a greater risk of cardiovascular disease later in life for those born small or early. I am incredibly grateful for this travel award which will allow me to attend an international conference to share my research findings and build up my research networks. Being able to present and receive feedback on my project in the international research community will doubtless improve the quality and impact of my research. My sincerest thanks to the Auckland Medical Research Foundation and the donors who support it."

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HealtheX greatly appreciate the assistance of the Faculty of Medical and Health Sciences, Liggins Institute, Auckland Bioengineering Institute, FMHS Postgraduate Student Association and Abacus dx in the funding and staging of HealtheX 2023.

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FRIDAY, 8TH SEPTEMBER

ABSTRACTS

Oral Presentation Room A - 503-011

A1

Antagonising the Growth Hormone Receptor to Combat Melanoma

Kim M[1], Wang Y[1], Sousa K[2], Tran K[2], Shepherd P[2,3], Jamieson S[3,4], Langley R[2], Perry J[1]
[1]Liggins Institute, [2]Department of Molecular Medicine and Pathology, [3]Auckland Cancer Society Research Centre, [4]Department of Pharmacology and Clinical Pharmacology

Background: Despite recent advances, metastatic melanoma is largely refractory to clinically available therapies, suggesting the need for novel therapeutics. Recent studies have found that growth hormone receptor (*GHR*) mRNA expression was almost 50-fold higher in melanoma cell lines compared to other cancer cell lines. Growth hormone has been shown to contribute to cell proliferation, survival, and chemoresistance. Pegvisomant, the only clinically available GHR antagonist, is difficult to access for research so novel GHR antagonists are needed to investigate the role of GHR signalling in melanoma. **Objectives:** The aim of this study is to determine whether a GHR antagonist generated in the lab (GHA2) inhibits GHR signalling in melanoma cells and has potential therapeutic application. **Methods:** Recombinant GHA2 protein was expressed in *E. coli* and purified using a series of chromatographic methods. *In vitro* bioactivity was determined using cell-based assays that included cell viability and interrogation of GHR-mediated signal transduction by western blot (STAT5 phosphorylation). *In vivo* efficacy of GHA2 was determined in a mouse model of melanoma. **Results:** GHA2 inhibited GH-dependent cell viability and signal transduction in drug screening assays and in melanoma cell lines, and had higher potency against the mouse Ghr compared with pegvisomant. Vemurafenib-resistant cell lines had increased *GHR* mRNA expression and enhanced cell growth in response to GH treatment. A trend for decreased tumour volume was observed following *in vivo* GHA2 administration (daily subcutaneous injection). **Discussion:** GHR antagonism effectively reduced melanoma cell growth, highlighting its potential as a new therapeutic strategy for treating melanoma.
Primary Supervisor: Assoc Professor. Perry, J

A2

Whole-genome CRISPR-Cas9 screens reveal genetic vulnerabilities in *NRAS*-mutant melanoma cell lines

Gu A[1], Lee T[1,2], Khan A[1], Hunter F [1,2,3], Singleton D[1,2], Jamieson S[1,2,4]
[1]Auckland Cancer Society Research Centre, School of Medical Sciences, Faculty of Medical and Health Sciences, University of Auckland, NZ, [2]Maurice Wilkins Centre for Molecular Biodiscovery, University of Auckland, NZ, [3]Janssen Research & Development, PA, USA, [4]Department of Pharmacology and Clinical Pharmacology, School of Medical Sciences, Faculty of Medical and Health Sciences, University of Auckland, NZ.

Background: New Zealand has the highest incidence of malignant melanoma in the world. Melanomas with mutations in the *NRAS* gene are of particular clinical concern due to their association with a poor prognosis and a lack of treatment options. Therefore, there is a pressing need for novel approaches to address the treatment of *NRAS*-mutant melanoma. **Objectives:** This research aims to identify genetic dependencies in *NRAS*-mutant melanoma, which will potentially uncover novel drug targets to overcome the challenges of treating melanoma patients with *NRAS* mutations. **Methods:** To identify genetic dependencies in *NRAS*-mutant melanoma, whole-genome CRISPR/Cas9 dropout screens were conducted in six *NRAS*-mutant and seven *NRAS*-wild-type New Zealand Melanoma (NZM) cell lines that were established from NZ melanoma patients. The NZM cell lines were stably transduced with the full-genome Brunello lentiviral sgRNA library and screened for up to 35 days. **Results:** Bioinformatic analyses of the NZM whole-genome knockout screens revealed 45 prospective candidates that are deleterious to the fitness of each *NRAS*-mutant cell line. These genes are being further validated as essential genes for *NRAS*-mutant melanoma cells through custom sgRNA library knockout screens and *in vitro* individual gene knockout studies. In particular, we demonstrate that knockout of SHOC2, a scaffold protein essential for activation of the MAPK signaling pathway, prevents ERK phosphorylation and reduces growth in a subset of *NRAS*-mutant NZM cell lines. **Discussion:** The identification of genetic dependencies alongside *NRAS* mutations may provide new drug targets for the development of therapeutic strategies for the treatment of *NRAS*-mutant melanoma.
Primary Supervisor: Assoc Prof. Jamieson, S

A3

Network Analysis Links Melanoma Germline Risk Loci to Somatic Driver Genes Through Novel Genetic Pathways

Pudjihartono M[1,2], O'Sullivan J[1,2,3,4], Schierding W[1,2]

[1]Liggins Institute, The University of Auckland, Auckland, NZ, [2]The Maurice Wilkins Centre, The University of Auckland, Auckland, NZ, [3]Australian Parkinson's Mission, Garvan Institute of Medical Research, Sydney, New South Wales, Australia, [4]MRC Lifecourse Epidemiology Unit, University of Southampton, United Kingdom.

Background: Understanding the underlying biological mechanisms driving melanoma is crucial to develop targeted treatments. We have previously identified 151 target genes, across three distinct skin tissues, whose expression levels are altered by inherited single nucleotide polymorphisms (SNPs) in 42 melanoma risk loci. **Objective:** We hypothesize that these germline susceptibility target genes participate in larger co-regulatory mechanisms that involve gene regulatory networks (GRNs) and protein-protein interaction networks (PPINs). **Methods:** In this study, we constructed PPINs using the proteins encoded by the 151 target genes as the foundation, expanding the network to multiple levels. Furthermore, we integrated the 151 target genes into GRNs. **Results:** We observed a significant enrichment of interactions between the proteins encoded by melanoma target genes and the protein products of known melanoma high-penetrance germline and somatic driver genes. Notably, coregulatory connections to key somatic driver genes *TERT, BRAF, NRAS, CDKN2A, MAP2K1,* and *MITF* were captured within the first two levels of the constructed network. Through GRNs, we discovered that within skin cells these genes are involved in shared gene regulatory processes that link melanoma to many of its primary comorbid phenotypes, including skin pigmentation, immune response and other cancers. **Discussion:** Our results are consistent with melanoma as a systems-level network phenomenon, where germline susceptibility target genes impose risk, in part, from alterations to these larger regulatory networks. Our study presents a new way of scrutinising the biological implications of genetic variants associated with melanoma and provides a starting point for further experimental validation.

Primary Supervisor: Dr Schierding, W

A4

Characterisation of novel inhibitory antibodies targeting growth hormone signalling in breast cancer cell lines

Buckley C[1], Lu M[1,2], Wang Y[1], Langley R[3], Perry J[1]

[1]Liggins Institute, University of Auckland, [2]Auckland Cancer Society Research Centre, University of Auckland, [3]Department of Molecular Medicine and Pathology, University of Auckland.

Background: In breast cancer, tumour expression of both growth hormone (GH) and prolactin has been shown to be associated with poorer patient outcomes and are potential targets for treatment. GH can activate both the GH receptor (GHR) and the prolactin receptor (PRLR). One proposed method for complete inhibition of GH signalling is to use a monoclonal antibody (mAb) that targets the ligand. **Objectives:** The aim of this study was to characterise neutralising anti-GH mAbs and determine their utility as anticancer agents in breast cancer cell lines. **Methods:** Inhibitory activity was assessed using a Ba/F3-hGHR cell viability assay. Cross reactivity was determined by ELISA. Three breast cancer cell lines with high GHR and PRLR expression were chosen for *in vitro* assays. Inhibition of GH signalling was determined by measuring STAT5 phosphorylation by western blotting and cell viability assay. **Results:** Three mAbs with inhibitory activity against GH were characterised (8-2, 32-1 & 46-3). mAb 8-2 and 46-3 exhibited strong inhibitory activity against GH-induced cell growth with EC_{50} values of 1.00 ± 0.27 and 0.5 ± 0.06 µg/ml, respectively. All antibodies cross-reacted with placental lactogen and placental GH. mAbs 46-3, 8-2 and 32-1 inhibited GH-dependent signal transduction in T-47D, ZR-75-1 & MCF-7 cell lines, and reduced GH-dependent cell growth in the T-47D cell line. **Discussion:** Complete inhibition of GH signalling requires inhibition of both GHR and PRLR. Using monoclonal antibodies against GH may be more effective in breast cancer cells lines with high GHR and PRLR compared to GHR-specific antagonists.

Primary Supervisor: Assoc Prof. Perry, J.

A5

Validation of Glucose-6-phosphate dehydrogenase as a new therapeutic target for treating IDH1 mutant lower-grade glioma

Paras KM[1], Jamieson S[1], Lee TW[1], Singleton D[1]
[1] Auckland Cancer Society Research Centre, University of Auckland

Background: Isocitrate dehydrogenase 1 (IDH1) is the most frequently mutated gene in lower-grade gliomas. Mutant IDH1 reprogrammes cellular metabolism, initiating gliomagenesis, but also creating therapeutically exploitable metabolic vulnerabilities. Disrupted NADPH homeostasis, caused by the consumption of NADPH by mutant IDH1 to produce 2-hydroxyglutarate (2-HG), coupled with the loss of NADPH production by wildtype IDH1, presents a potential metabolic liability. We have found that mutant IDH1 glioma cells depend on the pentose phosphate pathway enzyme glucose-6-phosphate dehydrogenase (G6PD) and seek to validate this vulnerability. **Objectives:** To assess the sensitivity of *in vitro* mutant IDH1 glioma models to G6PD loss or inhibition and to characterise the underlying biological effects. **Methods:** Cell line models of mutant IDH1 glioma were generated by modifying U-118 and U-251 cells to stably express FLAG-tagged wildtype or mutant IDH1. Isolated clones were validated by immunoblotting and production of 2-HG. *G6PD* was knocked out (KO) in U-87 wildtype and mutant IDH1 cells using CRISPR-Cas9 editing. Isolated *G6PD* KO clones were screened for *G6PD* deletion via immunoblotting and DNA sequencing. **Results:** Immunoblots confirmed the protein expression of FLAG and wildtype or mutant IDH1 in 8 of 29 U-251 clones. In contrast, none of the 13 U-118 clones expressed the construct. The screening of isolated U-87 *G6PD* KO clones and functional validation of G6PD loss or inhibition are underway. **Discussion**: The models generated will allow us to evaluate the impact of targeting G6PD on cell survival, NADPH/$NADP^+$ ratio, and reactive oxygen species levels with G6PD inhibitor or *G6PD* KO.
Primary Supervisor: Dr Singleton, D

A6

Crystallising the Concepts of Corneal Constructs: A Tale of Two Systems

Glasson J[1,2,3], Domigan L[1,2], Sherwin T[3]
[1]Department of Chemical and Materials Engineering, [2]The MacDiarmid Institute for Advanced Materials and Nanotechnology, [3]Department of Ophthalmology

Background: The cornea is the outermost structure of the eye. 6-10 million people worldwide have blindness or a severe visual impairment attributed to corneal opacities. For most, surgical intervention is the only effective treatment. However, due to cadaveric donor corneal tissue shortages, only 1 in 70 people worldwide who require a corneal transplant will receive one. **Objectives:** To augment and characterise collagen-based corneal stromal equivalents with lens crystallin proteins to improve their mechanical properties and produce a biomimetic artificial cornea. **Methods:** A rabbit study was conducted to test the biocompatibility of lens crystallin proteins. Corneal health was scored according to a modified McDonald-Shadduck Scoring System, using indirect ophthalmoscopy and slit-lamp biomicroscopy. Immune cell infiltration has been accessed with histology. Lens crystallin proteins were combined with type I collagen bioinks for 3D tissue printing and layered, electro-compacted collagen stromal equivalents. Physiological-pressure inflation testing with ellipsoid modelling, nanoindentation and rheology will assess mechanical properties. Epithelial and stromal cell proliferation will be used to evaluate biocompatibility. **Results:** Animal study results show crystallin protein materials are well tolerated in biological systems and resistant to degradation on the ocular surface. No immune cell infiltration was seen in the histological analysis. Crystallin proteins integrate into both collagen systems. The inflation testing rig allows for accurate pressure monitoring and image capture. Corneal stromal cells have been isolated and cultured in vitro. **Discussion:** Current results show lens crystallin proteins to be a promising additive to collagen-based scaffolds to improve compatibility, longevity, mechanical strength, and overall fitness for purpose.
Primary Supervisor: Dr Domigan, L

A7

Support of limbal mesenchymal stem cells for transition zone cells: an emerging stem cell niche

Xiao Y[1], McGhee C[1], Zhang J[1]
[1]Department of Ophthalmology

Background: Stem cells for the corneal endothelium have been identified in the transition zone (TZ), but their functions and cellular interactions remain undefined. Posterior limbal mesenchymal stem cells (P-LMSCs) may support the stemness of TZ cells. **Objectives:** To investigate the effect of P-LMSCs on TZ cells. **Methods:** P-LMSCs were characterised by comparing with anterior limbal mesenchymal stem cells (A-LMSCs) via immunohistochemistry. Human P-LMSCs, A-LMSCs and TZ cells were isolated through explant culture. TZ cells were cocultured with P-LMSCs in a Transwell, with TZ cell + A-LMSC coculture and TZ cells only as control groups. The proliferation of TZ cells was evaluated by EdU assay and wound healing speed by scratch wound assay. Colony forming assay from single cells, droplet digital PCR and western blot were used to compare the stemness and gene and protein expression profile of TZ cells. **Results:** P-LMSCs were positive for mesenchymal marker Vimentin, stem cell markers TRA-1-60 and Oct3/4, and angiogenesis markers α-SMA and CD34. TZ cells cocultured with P-LMSCs had significantly more proliferating cells, stronger healing capacity after wounding, and formed more colonies than those cocultured with A-LMSCs and without coculture. TZ cells supported by P-LMSCs expressed higher levels of neural crest markers Nestin and Sox9, periocular mesenchyme marker Pitx2 and less corneal endothelial marker Slc4a11 than the control groups. **Discussion:** The proliferation and stemness of TZ cells were enhanced by P-LMSCs. This could be achieved through a stem cell niche in the posterior limbus. Our study provides an innovative strategy for corneal endothelial rejuvenation.

Primary Supervisor: Dr Zhang, J

A8

Investigating umbilical cord stem cells for the treatment of corneal endothelial disorders

Sandhu A[1], Parvathi A[1], McGhee J[1], Loh J[1], Ismail S[1], Zhang J[1], Sherwin T[1].
[1]Department of Ophthalmology

Background: Corneal endothelial disorders, such as Fuchs endothelial corneal dystrophy (FECD), are a leading cause for corneal transplantation. Due to a global shortage of donor corneal tissue, it is essential for alternative therapeutic strategies to be developed. The umbilical cord is a rich source of stem cells, including human umbilical vein endothelial cells (HUVECs). The optimisation of HUVECs for corneal endothelial cell (CEC) replacement will provide a therapeutic pathway for the treatment of corneal endothelial disorders. **Objectives:** To investigate the potential of HUVECs for corneal endothelial repair. **Methods:** HUVECs were isolated from five umbilical cords and characterised by polymerase chain reaction (PCR) and immunocytochemistry (ICC). HUVECs were differentiated into CECs by using different protein fractions of a CEC-conditioned medium. Differentiation was measured by changes in morphology, ICC, and PCR analysis. Mass spectrometry was used to identify proteins which are driving CEC differentiation. **Results:** Isolated HUVECs showed expression of HUVEC markers, CD31 and CD146. Following differentiation by conditioned medium, a clear change in cell morphology and the upregulation of CEC markers ATP1A1 and ZO1 was observed. Different levels of differentiation were achieved by protein fractions of the conditioned medium. Mass spectrometry analysis identified proteins in the conditioned medium which may be responsible for CEC differentiation. **Discussion:** These results show that HUVECs can be differentiated into CEC-like cells. Differentiated CECs show a hexagonal morphology and an upregulation of CEC markers. Proteins responsible for CEC differentiation can be identified, allowing for the development of targeted CEC replacement therapies.

Primary supervisor: Prof. Sherwin, T

A9

Development of an animal model of age-related nuclear cataract

MacFarlane E[1,2], Grey A[1], Lim J[1,2], Donaldson P[1,2]
[1]Department of Physiology, [2]Aotearoa NZ National Eye Centre

Background: Cataracts is the leading cause of blindness worldwide. One of the contributing factors to cataract formation is UV (sunlight) exposure, resulting in the depletion of the antioxidant glutathione (GSH) and elevated oxidative stress. Since donor tissue is difficult to obtain in sufficient quantities for research, animal models that mimic cataractogenesis in humans are required to be able to test potential anti-cataract therapies. **Objective**s: To develop a novel *ex vivo* lens cataract model using exposure of bovine lens to hyperbaric oxygen (HBO) and ultraviolet-A (UVA) emitting lights. **Methods**: Lenses were exposed to HBO for 15 hours, or UVA (one hour at 100% power or 24 hours at 70% power). Lens transparency was assessed through light and dark field microscopy. Lens viability was quantified using lactate dehydrogenase assays. GSH was quantified using a GSH/GSSG assay and visualized using mass spectrometry-based imaging. Lipid peroxidation, a marker of oxidative stress was measured through malondialdehyde formation. **Results**: Lenses treated with HBO or UVA remained clear and transparent. Pilot data suggests HBO or UVA does not affect lens viability but results in a decrease of GSH and increased signs of oxidative stress. **Discussion**: While lenses remained clear, biochemical changes were seen in bovine lenses treated with HBO or UVA which was consistent with that seen in aging human lenses. Further work will determine if a combination of HBO and UVA results in loss of lens transparency and biochemical changes and if so, will aid in the testing of therapies to delay cataract formation.
Primary supervisor: Dr Grey, A

A10

Annotation and visualisation of spatially and temporally resolved isotope tracing MALDI imaging data of lenses

Shi D[1], Guo G[1], Grey A[1]
[1]Department of Physiology, University of Auckland

Background: Dynamic biological processes can be studied using temporally resolved MALDI IMS, capturing snapshots of molecular distributions over time. Administering a stable isotopically labelled (SIL) compound to cultured tissue helps to trace active metabolic pathways due to the incorporation of rare isotopes from the tracer. However, comparing spatial information across time-series biological samples is challenging due to variations in tissue size. **Objective:** To create an automatic bioinformatics pipeline to interpret the spatiotemporal metabolic characteristics of cultured tissue using glucose behaviour in bovine lenses as an example. **Methods:** The MALDI data used in this study was acquired from a previous investigation on glucose uptake in bovine lenses. A universal rescale-hexagonal binning strategy was developed to spatially align all sampled lens sections. Dimensionality reduction methods (UMAP, t-SNE and PCA) with K-means machine learning were employed to visualise the spatial metabolic differences in lenses. Finally, the Mummichog algorithm was employed to annotate SIL metabolites and identify enriched metabolic pathways. **Results:** The bovine lenses were aligned within a unified coordinate system, enabling subsequent automated visualisation and comparison of spatial metabolic patterns of bovine lenses. The pipeline facilitated the annotation of SIL features and identified enriched glucose-related pathways such as “Starch and sucrose metabolism” and “Glycolysis and gluconeogenesis.” **Discussion:** We demonstrated an approach to handle the spatially and temporally resolved isotope tracing MALDI imaging data. While developed to map glucose metabolism in bovine lenses, this approach has potential for wider biomedical application where SIL IMS is used.
Primary supervisor: Dr Guo, G

A11

Does arylformamidase drive production of immunosuppressive kynurenine in cancer?

Wang Y[1], Bebelman S[1], Hogan O[1], Mowday A[1], Leung E[1], Tomek P[1]

[1] Auckland Cancer Society Research Centre

Background: A tryptophan metabolite called kynurenine undermines curative immunotherapies. Inhibitors targeting the haemoproteins IDO1 and TDO that initiate kynurenine production have not yet been successful due to toxicities caused by tendencies to inactivate other haem enzymes. To overcome these limitations, we propose to inactivate the final step of kynurenine production assumed to be catalysed by a haem-free hydrolase called arylformamidase (AFMID). But we first need to ascertain if AFMID is the only enzyme catalysing kynurenine production. These investigations are complicated by non-enzymatic kynurenine formation in cell culture media. **Objectives:** To establish a technique for measuring kynurenine production ex situ and apply it to investigate AFMID's essentiality for kynurenine production. **Methods:** We used our newly developed high-throughput 384-well microplate absorbance assay, liquid chromatography and immunoblotting to detect kynurenine production and AFMID expression, respectively, in lysates of 5 human and mouse liver cell lines and mouse liver. **Results:** Kynurenine production associated poorly with AFMID protein expression indicating the involvement of other enzymes. This is supported by 1.3 to 5-fold (233 ± 35 to 918 ± 29 μM) higher half-maximal kynurenine production (Michaelis-Menten constant) relative to pure recombinant AFMID and striking inter- and intra-species differential sensitivity of kynurenine production to two distinct pan-hydrolase inhibitors phenylmethylsulfonyl-fluoride [PMSF] and diazinon (IC_{50} 31.9 ± 12.0 vs 123.3 ± 20.2 μM). **Discussion:** Diverse cell type- or species-specific hydrolases appear to primarily drive kynurenine production, rather than solely relying on AFMID. This observation challenges the current assumption of 70-year old dogma of AFMID's importance in kynurenine production.
Primary Supervisor: Dr Tomek, P

A12

Associations between transport modes and site-specific cancers: A systematic review and meta-analysis

Thu W[1] , Tin Tin S [1,2], Cavadino A[1], 1 Woodward A[1]

[1]School of Population Health, University of Auckland, [2]Oxford Population Health, University of Oxford

Background: The choice of mode for transport is important for health and may influence cancer risks through its effects on levels of physical activity, sedentary time, and environmental pollution. **Objective**: This review synthesizes existing evidence on the associations of site-specific cancers with transport modes used (primary exposure) and walking and cycling in general (secondary exposure). **Methods:** Relevant literature was searched in PubMed, Embase and Scopus, and results were meta-analysed for cancer sites where two or more studies were identified. **Results:** Of the 11,829 publications identified up to 17th February 2023, 105 reporting 77 unique studies (72 cohort, 28 case-control and 5 case-cohort) were included. Eighteen site-specific cancers were assessed, of which breast, colorectal and endometrial cancers were most reported. Ten metabolic equivalent of task hours/week increment in walking (~ 30 minutes) or cycling (~ 17 minutes) for commute per day was associated with a 7% reduction in risk of colon cancer (95% CI: 0·88 – 0·99) and endometrial cancer (95% CI: 0·89 – 0·98), and marginally associated with a reduced risk of breast cancer (Relative Risk: 0.98; 95% CI: 0·97 – 1.00). Cycling, compared to motorized modes, was associated with a lower risk of overall cancer incidence and mortality. Walking in general was associated with a lower risk of breast, endometrial, lung (non-smokers only), colorectal, oesophageal and pancreatic cancers, and cancer mortality. **Discussion:** Active transport appears to reduce the risk of common cancers such as breast, colon, and endometrial cancers, but current evidence on other cancers is limited.
Primary supervisor: Dr Tin Tin, S

A13

Redefining the role of the arylformamidase enzyme in immunosuppressive tryptophan catabolism of cancer

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Background: The immunosuppressive tryptophan metabolite, kynurenine, is one of the key culprits that sabotages antitumour immunity. To stop kynurenine and sensitise patients to immunotherapy, enzymes IDO1 and TDO, catalysing the first step of kynurenine biosynthesis, are being targeted with inhibitors. These efforts have been unsuccessful due to difficulties blocking both. We hypothesise that arresting the second step of kynurenine biosynthesis, thought to be catalysed by only one enzyme called arylformamidase (AFMID), could surpass targeting IDO1/TDO. However, there is some evidence suggesting that cancers express mainly truncated AFMID isoforms that lack the active site. **Objectives:** To determine if cancers produce enzymatically active AFMID. **Methods:** We compared kynurenine production by absorbance microplate assay, and expression of AFMID RNA and protein by RT-PCR and Western blot, respectively, in 5 cancer and 1 non-cancer cell types of mouse and human liver origin, which should abound with AFMID. **Results:** AFMID RNA levels were fairly comparable, but protein expression varied highly, with high levels in mouse liver tissue and very low expression in most cancer cell lines. There was a poor association between kynurenine production and AFMID expression. Most strikingly, the mouse liver line Hepa1-6 produced AFMID RNA, but no protein, yet generated high kynurenine levels. Human cells, but not mouse cells, expressed additional truncated AFMID isoforms that seemed to have no bearing on protein expression or kynurenine production. **Discussion:** These data suggest that cancer cells likely express enzymatically competent full-length AFMID, but this AFMID unlikely drives kynurenine production, challenging the current dogma in the field.
Primary Supervisor: Dr Tomek, P

A14

Oropharyngeal cancer trends in Aotearoa over 15 years: 2006 - 2020

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Background: Oropharyngeal cancer (OPC) has increased in several countries with differences in demographic characteristics. The survival rate for OPC patients has improved steadily. Changes in incidences and survival are often as a result of an increase in human papillomavirus (HPV) infection. **Objectives:** The recent trends of OPC have not been studied in detail in the New Zealand (NZ) population. This study aims to report the incidence, trends and survival of OPC in NZ by demographic characteristics such as age at diagnosis, sex and ethnicity. **Methods:** The study included 2109 patients with a primary diagnosis of oropharyngeal squamous cell carcinoma from 2006 to 2020, identified from the National Cancer Registry. Age-standardised incidence rate (ASR), annual percent change (APC) and relative survival (RS) rate were calculated. **Results:** The average annual ASR of OPC was 2.2 per 100,000 population over the 15 year period, with a higher rate observed in males (3.7/100,000 population), 50-69 year olds (8.8/100,000) and Māori (2.8/100,000). The incidence increased steadily with 4.9% per year overall, 4.9% in males, 4.3% in females and 5.6% in Māori and 4.8% in Pākehā/European populations, but no increase was observed in Pacific or Asian populations. The 5-year overall RS rate was 75%, with an increase from 69% in 2006-13 to 78% in 2014–20. Survival rates were lower in older patients, females, and Māori patients. **Discussion:** This study reports a substantial increase in the incidence of OPC in Aotearoa NZ, over the last 15 years.
Primary Supervisor: Prof. Douglas, R

Oral Presentation Room B - 503-128

B1

Cerebrovascular carbon dioxide reactivity is impaired in atrial fibrillation patients with concurrent hypertension

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Background: Atrial fibrillation (AF) and hypertension (HT) are both independently associated with impaired cerebrovascular carbon dioxide reactivity (CVR_{CO2}), an indicator of cerebral vasodilatory reserve. It is unknown if these effects on CVR_{CO2} are synergistic when AF and HT are concurrently present (AF-HT). **Objectives:** To assess the hypothesis that CVR_{CO2} is reduced in AF-HT patients. **Methods:** Transcranial doppler ultrasound was used to measure middle cerebral artery blood velocity (MCA V_m) in AF (n=31) and AF-HT (n=57) during stepped increases and decreases in end-tidal carbon dioxide ($P_{ET}CO_2$). Cerebrovascular conductance index (CVCi) was calculated as the ratio of MCA V_m and mean arterial pressure (MAP). The linear slope of MCA V_m and MCA CVCi vs $P_{ET}CO_2$ was defined as CVR_{CO2}. **Results:** Baseline MAP was significantly higher in AF-HT (107 ± 9 mmHg) compared to AF (98 ± 9 mmHg; p<0.001). Baseline MCA V_m (AF, 51.69 [45.22-63.26] $cm.s^{-1}$; AF-HT, 49.61 [44.12-59.98] $cm.s^{-1}$; p=0.075) and MCA V_m CVR_{CO2} (AF, 1.74 [1.54-2.52]; AF-HT, 1.70 [1.47-2.19]; p=0.221) were not different between groups. Baseline MCA CVCi (AF, 0.54 [0.44-0.63] $cm.s^{-1}.mmHg^{-1}$; AF-HT, 0.46 [0.42-0.57] $cm.s^{-1}.mmHg^{-1}$; p<0.001) and MCA CVCi CVR_{CO2} (AF, 0.02 ± 0.01 $cm.s^{-1}.mmHg^{-1}$; AF-HT, 0.01 ± 0.00 $cm.s^{-1}.mmHg^{-1}$; p=0.047) were significantly lower in AF-HT compared to AF. Additionally, Patients' cardiac rhythm during data acquisition was indicated as a predictor of baseline MCA CVCi and MCA CVCi CVR_{CO2}. **Discussion:** MCA CVCi CVR_{CO2} is impaired in AF-HT patients, implicating HT as a driver of further cerebrovascular dysfunction important for the development of AF-related cerebrovascular events and cognitive decline.
Primary Supervisor: Assoc Prof. Fisher, J

B2

Nebulised Sodium Nitrite to Preferentially Dilate Penumbral vessels, following Ischemic Stroke… a NO brainer

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Background: Stroke is a major cause of death and disability in New Zealand, particularly among Māori and Pacific populations. Current hospital-based treatments have a narrow therapeutic window to improve patient outcome (~4.5-6h), which means that ~85% of all stroke patients are ineligible for reperfusion treatment in New Zealand. Nebulised nitrite is a cost-effective method of increasing nitric oxide (NO) bioavailability. **Objectives:** To assess if nebulised nitrite improves penumbral blood flow and reduces infarct volume following ischemic stroke. **Methods:** In aged-hypertensive rats, we compared the effects of nebulised nitrite (1 g/L) (n = 11) vs. saline (n = 11) following 90 min intraluminal thread occlusion of the middle cerebral artery. The primary outcome was infarct volume, functional recovery and indices of penumbra blood flow were also evaluated. **Results:** Nebulised nitrite treatment increased plasma levels >20-fold (0.3±0.1 to 8.5±1.2 µM; p=0.007). We observed an 80% reduction in infarct volume in nitrite-treated rats compared to saline-treated controls (31±20mm^3 vs 150±95mm^3; p=0.001). Accompanied with improved functional sensorimotor recovery after stroke in the nitrite-treated rats (Baseline: 4 ± 3s; Day 3: 17 ± 36s, p = 0.521) compared to the saline-treated controls (Baseline: 3 ± 1s; Day 3: 39 ± 36s, p = 0.042). **Discussion:** Insights gained from this research will lay the foundation for future clinical trials, and have the potential to make a major contribution to the field by identifying an inexpensive, effective treatment strategy for slowing the progression of stroke injury in the hyperacute phase.
Primary Supervisor: Dr Mcbryde, F

B3

Identifying the building blocks for learning and memory in the carotid body

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Background: An intricate connection exists between cardiovascular disease and the carotid body (CB), a chemoreceptor organ involved in respiratory and cardiovascular regulation. If CB is repeatedly activated (as seen in sleep apnoea) this leads to organ's increased sensitivity, sympathetic overactivity and cardiovascular complications. This suggests a 'learning' process to take place within the CB akin to neural plasticity in the brain, involving glutamate signalling through α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) and N-methyl-D-aspartate (NMDA) receptors. **Objectives:** To investigate the involvement of plasticity, and learning and memory that may be important for modulating chemoreflex responses in the CB. **Methods:** We mined high-throughput sequence data and used immunohistochemistry to map components underlying neuroplasticity in the CB in a rat model of experimental hypertension. Afferent CB discharge was measured as a functional readout. **Results:** We identified glutamate receptor and transporter expression in the rat CB. Targeted administration of glutamate activates the carotid sinus nerve, however, notably, glutamate modulates the CB response to chemical hypoxia. NMDA and AMPA antagonists potentiated these chemical hypoxia responses. Digital droplet polymerase chain reaction analysis confirmed altered levels of expression of NMDA and AMPA receptors in a model of experimental hypertension. **Discussion:** The CB contains the rudimentary components for synaptic plasticity, learning and memory including the presence of glutamate systems. It is conceivable that the CB's learning and memory process may initiate for the establishment of a reflex sensitivity set point. Given glutamate's role as a 'modulator' of CB discharge, it suggests a role in gain and/or loss function resembling neuroplasticity.

Primary Supervisor: Professor. Paton, J

B4

Directly recorded renal sympathetic nerve activity reduces with Impella ventricular pump support in cardiogenic shock

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Background: Cardiogenic shock (CS) following myocardial infarction carries a high mortality risk despite medical advancements. The use of mechanical support devices in CS has become an effective strategy to improve haemodynamics and prevents acute kidney injury. We hypothesised that mechanical support with the Impella pump would inhibit renal sympathetic nerve activity (RSNA), mediating renal protection in CS. **Methods:** Experiments were conducted in two groups of anaesthetised female sheep. CS was induced (n=8) using injections of polystyrene microspheres into the left coronary artery under fluoroscopic guidance in one group. After a 30-minute baseline period, the Impella pump was inserted into the left ventricle and run at different levels (P0 min-P6 max) randomly with two minutes at each pump level. The controls underwent the same protocol without embolisation of microspheres (n=6). **Results:** Circulatory support using Impella significantly increased mean arterial pressure (MAP) from 55 ± 4 mmHg to 68 ± 5 mmHg at pump level P6 (one-way ANOVA, $p<0.001$). Incremental pump support significantly decreased RSNA ($p<0.001$). At pump level P6, RSNA decreased by 25 ± 5 % compared to P0 and renal blood flow was improved by 21 ± 10% (n=7). In the control cohort with no cardiogenic shock, the changes in MAP and RSNA were qualitatively similar (MAP increased from 84 ± 9 to 94 ± 8 mmHg; RSNA decreased by 13 ± 5 % at P6; $p<0.001$). **Discussion:** Our data suggest that the improvements in kidney function following Impella use are mediated in part by renal sympathoinhibition.

Primary Supervisor: Assoc Prof. Ramchandra, R

B5

Sympathetic innervation of the carotid body in blood pressure control

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[1]Department of Physiology

Background: In New Zealand, uncontrolled high blood pressure continues to be a major public health concern, and has the second highest attributable cost to disease. A shift in research towards further understanding the underlying mechanisms that lead to hypertension is needed because known anti-hypertensive drugs have been exhausted. **Objectives:** Observe the systemic effects (i.e., blood pressure, cerebral blood flow, heart rate) of increased sympathetic drive to the carotid body (CB) to determine if this manipulation alone is sufficient to cause autonomic dysregulation. **Methods:** Isolation and electrical stimulation of the cervical sympathetic trunk in Wistar rats and use of potassium cyanide to evoke the peripheral chemoreflex response. To measure the systemic effects, a telemeter will be surgically implanted to measure blood pressure, a carotid artery flow probe will be surgically implanted to measure cerebral blood flow, and a plethysmography chamber will be used to analyse volume changes. **Results:** Experiments will start the week after this submission. **Discussion:** Hypothesise that overactivation of the sympathetic nervous system, as observed in hypertension, will cause vasoconstriction within the carotid body exacerbating the feedforward loop between carotid body output and further sympathetic activation, resulting in increased blood pressure; in other terms, we speculate increased gain/sensitivity of the peripheral chemoreflex.

Primary Supervisor: Dr McBryde, F

B6

β-blockers further impair exercise capacity in heart failure with preserved ejection fraction

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

Background: Heart failure with preserved ejection fraction (HFpEF) is a type of heart failure whereby cardiovascular function is relatively normal at rest but becomes markedly impaired during exertion, causing severe exercise intolerance. HFpEF is the predominant form of heart failure and despite its substantial burden and poor prognosis, has almost no clinically impactful therapies. While the sympathetic nervous system is a major mediator of cardiovascular physiology during exercise, its role in this context in HFpEF has remained relatively unexplored. **Objectives:** To determine the effect of pharmacological sympatholysis on exercise capacity in an animal model of HFpEF. **Methods:** HFpEF was induced via chronic two-kidney, one-clip hypertension in aged, female sheep while non-HFpEF sheep were age- and sex-matched without hypertension. Cardiovascular haemodynamic variables which determine exercise capacity were measured while sheep underwent graded treadmill exercise with and without the influence of a β-adrenoreceptor blocker (propranolol). **Results:** Compared to non-HFpEF sheep (n=6), HFpEF sheep (n=3) exhibited attenuated exercise cardiac output (peak Δ: +3.27±0.36 vs +5.57±0.37 L/min) and heart rate (peak Δ: +31.2±2.6 vs +37.2±2.7 beats/min) responses, and an elevated exercise pulmonary capillary wedge pressure/cardiac output (PCWP/CO) slope (0.99±1.28 vs 0.53±0.36 mmHg/L/min). Propranolol did not alter the exercise cardiac output response in HFpEF sheep (peak Δ: +3.31±0.83 vs +3.27±0.36 L/min) but augmented the exercise PCWP/CO slope (3.73±1.09 vs 0.99±1.28 mmHg/L/min). **Discussion:** These preliminary results suggest that in a clinically relevant large animal model of HFpEF, sympatholysis with β-blockers, which is taken by 50-80% of HFpEF patients, worsens the exercise intolerance that hallmarks this syndrome.

Primary Supervisor: Assoc Prof. Ramchandra, R

B7

Keeping the Rhythm: Improving Brain Blood Flow in States of Hypertension

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Background: The relationship between cerebral blood flow (CBF) and blood pressure (BP) is crucial for brain health. Recent findings suggest that the normal short- (cerebral autoregulation, CA) and long-term (circadian rhythm) BP-CBF relationships become disrupted in hypertension, correlated with poor prognosis. **Objective:** To assess the impact of hypertension on short- and long-term BP-CBF relationships. **Methods:** Rats with normal (Wistar, n=6) or high BP (SHR, n=6) were instrumented to chronically record BP, heart rate (HR), central venous pressure (CVP), and CBF. Circadian rhythm was evaluated using 60-minute averages taken over 48-hour weekend recordings. Short-segment autoregulatory index (SSARI) analysis was used on continuous 3-hour day and night recordings. This allowed evaluation of CA during short-term BP fluctuations on a range of time scales (0.5-20s). An SSARI near zero indicates good CA. **Results**: In Wistar rats, we observed a distinct nadir in HR during the inactive period (-30.7±9.5 bpm), with a corresponding reduction in BP (-1.1±1.3 mmHg) and CVP (-0.8±0.6 mmHg). In SHRs, while the fall in CVP was similar (-1.1±1.2 mmHg), the nadir in HR was dampened (-8.8±11.1 bpm) and an *increase* in BP was observed (1.2±3.6 mmHg). In Wistar rats, SSARI was better during active periods (0.41±0.33 for 0.5s and 0.14±0.24 for 10s) compared to inactive periods (0.48±0.37 for 0.5s and 0.72±0.55 for 10s). **Discussion:** Our preliminary results show that circadian rhythms are dampened under hypertensive conditions, and normotensive rats show better CA during active periods. Future studies will examine circadian patterns in CBF and compare SSARI between normotension and hypertension.

Primary Supervisor: Dr McBryde, F.

B8

The skeletal muscle metaboreflex: a novel driver of exertional dyspnoea in pulmonary arterial hypertension

Plunkett M[1], Sayegh A[1], McWilliams T[2], Sithamparanathan S[2], Paton J[1], Fisher J[1]
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Background: Exertional dyspnoea and exercise limitation affects most PAH patients, however the underpinning physiologic mechanisms remain incompletely understood. In PAH, skeletal muscle mitochondrial and microcirculatory abnormalities could lead to augmented activation of metabolically responsive skeletal muscle afferents (metaboreflex) during exercise, driving ventilation and dyspnoea. **Objectives:** We aimed to assess the effects of muscle metaboreflex activation (MMA) on ventilation, pulmonary artery pressure and the perception of dyspnoea in PAH compared to healthy subjects. **Methods:** 14 PAH patients and 14 age- and sex-matched healthy controls completed two trials of isometric handgrip exercise to 35% maximal voluntary contraction, followed by either 2 minutes of post-exercise circulatory occlusion (PECO) to active the muscle metaboreflex (MMA trial) or free-flow recovery (control trial), in a randomised order. Minute ventilation ($\dot{V}_E$; pneumotachometer), mean pulmonary artery pressure (mPAP; transthoracic echocardiography), and ratings of dyspnoea (Borg 0-10 dyspnoea scale) were measured. **Results:** PAH patients had an excess ventilatory response during MMA compared to healthy controls ($\Delta\dot{V}_E$ 2.23 $\pm$ 1.90 vs. 0.42 $\pm$ 1.36 L·min^{-1}, p=0.012), with no difference during the control trial (Group p=0.666). mPAP response was greater in PAH during MMA compared to healthy controls (ΔmPAP 10.34 $\pm$ 9.49 vs. 0.40 $\pm$ 5.02%, Group p=0.017). Ratings of dyspnoea were higher during MMA in PAH (ΔBorg 1.89 $\pm$ 1.21 vs. 0.81 $\pm$ 1.13 units, p<0.001). **Discussion:** Our findings indicate metaboreflex activation is augmented in PAH, stimulating excess ventilation, pulmonary artery pressure, and dyspnoea. Targeting of the metaboreflex should be further explored to improve exercise capacity in PAH.

Primary Supervisor: Assoc Prof. Fisher, J

B9

Improving stroke endovascular thrombectomy outcomes: Blood pressure trends in hypertensive population under anaesthesia

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Background: Although general anaesthesia (GA) during endovascular thrombectomy (EVT) improves procedural success, fluctuations in blood pressure (BP) can negatively affect stroke outcomes. Understanding hemodynamic fluctuations under anaesthesia is critical in improving EVT outcomes. **Objectives:** Determine whether patients, stratified on hypertension history and baseline BP, exhibited different BP trends during EVT under GA, and explore their association with functional recovery. **Methods:** Auckland City Hospital Stroke Registry yielded retrospective data. 1078 patients undergoing EVT since 2012, within 6 hours of symptoms or within 24 hours if wake-up stroke, were screened. Exclusion criteria were pre-hospital intubation, incomplete electronic data, or inadequate clot removal. Exposure BP variables were baseline, mean procedural (MnBP), nadir, change in MnBP from baseline (ΔBP). 90-day modified Rankin Score (mRS), a standard post-stroke disability rating scale, was primary outcome. **Results:** 427 patients were analysed (mean age 67.1±15.6 years, 51.8% males). 53% of normotensives and 69% of hypertensives had high baseline BP (>150 mmHg). ΔBP was greater in hypertensives vs normotensives (-8±22.5 vs -12.8±24.7 mmHg; p=0.024). Regardless of hypertension history, fall in blood pressure was significantly more in patients with high baseline BP (-22.0±20.2 vs 7.1±17.8 mmHg, p<0.001). mRS scores in both subsets did not show a significant difference. **Discussion:** Procedural BP falls during EVT are more common in hypertensives. However, baseline BP may be a better indication for larger relative falls in BP than hypertension history alone. Uniform approach to hemodynamic management maybe disadvantageous in such patients. Further research focused on guidelines for BP management in at-risk patients is warranted.

Primary Supervisor: Dr McBryde, F

B10

Characterizing metabolic, cardiac and cognitive impacts in a rat model of “glucotension”.

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Background: 75% of Type 2 Diabetes (T2D) patients have hypertension, and half of hypertensives exhibit glucose dysregulation. Comorbid hypertension and T2D (“glucotension”) exacerbates vascular complications and elevates cardiovascular risk compared to either disease independently. **Objective:** Develop models of glucotension, maximising relevance of therapeutic interventions. **Methods:** Normotensive (Wistar; n=10) and Spontaneously Hypertensive (SH; n=10) rats were given high fat (HFD) or control (CD) diets from age 6 weeks. Glucose tolerance (GTT), cognitive function (Barnes maze), and cardiac ultrasounds were performed at age 18 weeks. **Results:** Compared to Wistar+CD, Wistar+HFD showed increased body weight (692±34g vs 518±28g, P<0.0001) and GTT AUC (1984±352 vs 1094±105 mmol.h/L, P=0.0001). SH+HFD showed more rapid weight gain (0.87±0.47g/day vs 0.10±0.38g/day; P=0.0388), however, weight (398±38g vs 367±11g, P=0.1390) and GTT AUC (1299±63 vs 1047±193 mmol.h/L, P=0.2309) were slightly but not significantly higher than SH+CD. HFD groups had reduced cardiac diastolic function (higher E/A) compared to CD (Wistar+CD [E/A=1.41±0.25] vs Wistar+HFD [E/A=0.39±0.18] P=0.0029; SH+CD [E/A=2.88±0.65] vs SH+HFD [E/A=1.29±0.32] P<0.0001). Initial Barnes maze latency was significantly higher in SH+HFD (516±98s) compared to SH+CD (162±99s; P<0.0001), Wistar+CD (48±31s; P<0.0001), and Wistar+HFD (100±98s; P<0.0001). Along with a later plateau (SH+HFD=4 trials; Wistar+HFD & SH+CD=3 trials; Wistar+CD=2 trials), this indicates both hypertension and HFD impair spatial learning/memory. **Discussion:** Chronic HFD produced a T2D phenotype in Wistar, but not SH rats. However, HFD impaired cardiac and cognitive function in both strains. As SH+HFD showed more rapid weight gain at week 12, extending the HFD period may produce a diabetic phenotype in SH rats.

Primary Supervisor: Dr McBryde, F

B11

Inhibiting insulin signaling for weight loss in obese female mice

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Background: Obesity is often associated with hyperinsulinaemia and insulin resistance, and excess insulin signaling has been hypothesised to drive adipose overflow and ectopic lipid accumulation. PI3K, a downstream target of insulin, plays a critical role in lipid storage. We have previously found that a small-molecule PI3K inhibitor (PI3Ki) reduces body weight and fat mass in obese male mice. **Objective:** Since weight balance and insulin sensitivity are sexually dimorphic traits, here we investigated the effect of PI3Ki treatment in obese female mice. **Methods:** Female mice were fed a high-fat diet (HFD) for 8 weeks to induce obesity, after which they were randomised to receive either HFD + 0.4% DMSO (vehicle) or HFD + PI3Ki. Measures of body composition, energy metabolism, and metabolic health were assessed in these mice. **Results:** PI3Ki-treatment reduced body weight and fat mass in obese female mice, though this required a larger dose of PI3Ki than in obese males. PI3Ki-treatment increased energy expenditure and lipid oxidation, and reduced food intake. PI3Ki-treated mice also had decreased lipid storage in the liver and increase urine glucose. **Discussion:** Inhibition of PI3K has been able to reduce weight and fat mass in both male and female mice and further work is ongoing to understand the mechanisms underlying these effects. Female mice require greater amounts of inhibitor, and sex-dependent differences are apparent in the regulation of energy balance and glucose metabolism. This then also demonstrates the critical necessity of assessing both sexes when developing pre-clinical therapeutic treatments for obesity.
Primary Supervisor: Assoc Prof. Merry, T.

B12

Predictors and short-term outcomes of hypoglycaemia among neonates of mothers with gestational diabetes mellitus.

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Background: Hypoglycaemia is common among neonates born to mothers with gestational diabetes mellitus (GDM) and is associated with poor outcomes. However, little is known about the factors that predict its occurrence. **Objectives:** To determine factors that predict hypoglycaemia among neonates of women with GDM, and short-term outcomes associated with neonatal hypoglycaemia. **Methods:** A secondary cohort analysis of data from a multi-centre randomised trial (the TARGET trial), which took place in New Zealand between 2015 and 2017 was conducted. Data were analysed using univariate analysis and multivariable forward-stepwise logistic regression. **Results:** Among 1,085 included, those born to Asian mothers had reduced odds of hypoglycaemia [OR (95%CI): 0.54 (0.38, 0.75), p=0.001], as did those born at higher gestational ages [0.76 (0.68, 0.85), p <0.001]. Neonates born to Pacific mothers had increased odds of hypoglycaemia [1.57 (1.04, 2.39), p=0.034]. Neonates who experienced hypoglycaemia were more likely to experience neonatal intensive care unit admission (8.3% vs. 2.1%; p=<0.001), hyperbilirubinaemia (8.6% vs. 3.3%; p= <0.001), receive respiratory support (11.4% vs. 4.8%; p= <0.001), and less likely to be breastfed at discharge (92.4% vs. 96.2%; p=0.009). **Discussion:** Among neonates of women with GDM, maternal ethnicity and gestation at birth are independent predictors of hypoglycaemia, and hypoglycaemia is associated with short-term comorbidities. Additional surveillance may be appropriate for neonates in these high-risk groups.
Primary Supervisor: Distinguished Professor Harding, J

Oral Presentation Room C - 503-126

C1

Characterisation of the substantia nigra in X-Linked Dystonia Parkinsonism

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Background: X-linked Dystonia Parkinsonism (XDP) is a genetically inherited, neurodegenerative movement disorder first discovered in the Philippines. Although significant symptomatic heterogeneity is observed in XDP, the disorder is clinically characterised by the presence of dystonia and parkinsonism. The selective loss of the dopaminergic neurons in the substantia nigra (SN) is a characteristic feature of Parkinson's disease, a condition which shares partial symptomatology in XDP. The research reporting SN involvement in XDP, however, remains contradictory and limited. **Objectives:** We aim to identify and characterise the neuropathology profile of the SN in 24 XDP post-mortem cases and 14 neurologically normal cases. **Methods:** Immunohistochemical staining using single peroxidase labelling and fluorescence-based techniques was conducted on brain tissue using antibodies targeting a range of known nigral neuronal markers. **Results:** Preliminary findings suggest the loss of Calbindin and DARPP-32 positive fibres in the XDP SN. **Discussion:** Calbindin is a calcium-binding protein thought to be protective against neurodegeneration in dopaminergic neurons in Parkinson's disease, whereas DARPP-32 is a phosphoprotein highly involved in dopaminergic signalling. Thus, a loss of Calbindin and DARPP-32 in the XDP SN may point towards potential deficits in dopaminergic signalling in XDP, and may contribute towards the parkinsonism-like symptomology in XDP. Elucidating dysfunction in the XDP SN allows for an increased understanding of the overall pathogenesis of this disease, which may be used to guide the formation of future disease models and treatment strategies.
Primary Supervisor: Dr Singh-Bains, M

C2

Identifying the cellular mechanisms of Alzheimer's Disease (AD) *in vivo*.

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Background: Alzheimer's disease (AD) is the most common neurodegenerative disease, causing a gradual, fatal cognitive decline. Subtle neuronal changes occurring early in AD progression such as synapse loss and circuit changes are a precursor for eventual neuronal loss. Technological limitations have restricted our ability to collect data reflecting dynamic circuit changes. The recent development of head-mounted miniaturised fluorescence microscopes (miniscopes) allows the chronic recording of neuronal circuit activity while rodents engage in active behaviours. **Objectives:** To validate the use of miniscope technology in an aged, murine model of AD, then utilise this to correlate neuronal activity, behaviour, and plaque load. **Methods:** Aged male APP/PS1 mice were hippocampally injected with a GCaMP7s viral vector to report pyramidal cell calcium activity. They were subsequently implanted with a Graded-Index lens and affixed with a baseplate. Mice underwent two spatial memory behavioural testing sessions at 15 and 23 months of age, while the attached miniscope concurrently recorded CA1 calcium activity. Brain tissue was collected for fluorescence immunohistochemistry to assess inflammatory and synaptic changes. **Results:** Preliminary behavioural findings indicate ambulatory and anxiety differences between wild-type and APP/PS1 animals, while there is variability in spatial memory abilities across both genotypes, particularly at advanced ages. **Discussion:** An improved understanding of the pathophysiological mechanisms underlying AD development is required for the sake of identifying better treatment targets. Our methodology enables these findings to be tracked longitudinally, and we have indeed observed age- and genotype-dependent distinction in behavioural phenotypes. These will be corresponded to parallel changes in cellular activity.
Primary Supervisors: Prof Montgomery, J; Dr Cheyne, J

C3

Aged Residential Care Admission in Young Onset Dementia: A Cohort Study

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Background: Young onset dementia (YOD) is defined as dementia with onset before age 65. Research on the natural history of YOD is scarce, but it is essential to establish tailored care for people living with YOD. Most patients with YOD eventually require aged residential care (ARC), which is usually delivered in facilities designed for older adults and therefore may not be age appropriate. **Objectives:** To describe the natural history of YOD in a previously identified YOD cohort in the Waikato in terms of ARC admission. **Methods:** The cohort consists of 61 patients diagnosed with YOD in 2014-2016. Patients were retrospectively followed up for 5 years after diagnosis using routinely collected health data (interRAI). Survival analyses were performed to determine time to ARC admission and the influence of demographic factors (age at diagnosis, gender, ethnicity). **Results:** 34 out of 61 patients were admitted to ARC during the study period. Kaplan-Meier analysis showed the median time of ARC admission from date of diagnosis was 680 days (~22 months), while cox hazard proportional model showed 780 days (~26 months). Time to ARC admission was not affected by age at diagnosis, gender or ethnicity (European versus non-European). **Discussion:** This is the first New Zealand study (and second in the world) to describe the natural history of YOD in terms of ARC admission. The relatively short median time to ARC admission may be due to delayed diagnosis resulting in more advanced cognitive impairment at presentation.

Primary Supervisor: Dr Cheung, G

C4

Transplantation of directly reprogrammed striatal precursor cells into a rat model of Huntington's disease

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Background: Huntington's disease (HD) is a neurodegenerative disorder characterized by the loss of medium spiny neurons (MSNs). Currently there is no cure for HD. Cell replacement therapy is a potential option for the treatment of HD. Our lab developed a direct reprogramming protocol that generates human striatal precursors from dermal fibroblasts, providing a clinically viable cell source for transplantation therapy. **Objectives**: This study investigated the potential for striatal precursor cells generated by direct reprogramming to survive and generate functionally integrated MSNs following transplantation into a rat model of HD. **Methods:** Human striatal precursors were derived from dermal fibroblasts by direct reprogramming using *SOX2* and *PAX6*. Striatal precursors were transplanted into the rat striatum 3 weeks following quinolinc (QA) lesioning (n = 15). Control animals were injected with sterile saline (n = 15). Motor function was assessed up to 14 weeks post transplantation using the cylinder test. The rats were killed 14 weeks following transplantation and the survival and maturation of transplanted hiLGEPs determined by immunohistochemistry. **Results**: Striatal precursors expressed the human-specific marker STEM121 and co-expressed the neuronal marker MAP2 and the MSN specific marker DARPP32 14 weeks following transplantation. At 14 weeks post-transplant, transplanted rats demonstrated restoration of motor function with no difference in ipsilateral forelimb use compared to baseline ($p = 0.8$). In contrast, saline treated rats retained a significant increase in ipsilateral forepaw use compared to baseline ($p = 0.02$). **Discussion**: This study demonstrates the therapeutic potential of directly reprogrammed striatal precursor cells for transplantation therapy for HD.

Primary Supervisor: Prof. Connor, B

C5

A Randomized Trial: Can a Virtual Human Deliver Mindfulness to Reduce Stress?

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Background: Stress is a significant issue amongst university students, yet limited psychological services are available. Mindfulness is effective for stress reduction and can be delivered digitally to expand access to student populations. However, digital interventions often suffer from low engagement and poor adherence. A virtual human (VH) may improve engagement and adherence through humanlike appearance and behaviours. **Objective:** Examine whether a VH could reduce stress in university students compared to a chatbot, and teletherapist, using a mindfulness intervention. **Methods:** Stressed university students (N=108) were randomly allocated to the VH, chatbot, or teletherapist. Participants were asked to complete mindfulness homework sessions at least twice weekly for four weeks. Changes in measures of stress and mindfulness (physiological and self-report), homework completion, and perceptions of the agent were compared. Thematic analysis was conducted on responses. **Results:** There were significant reductions in stress and increased mindfulness across all groups. All groups had higher peripheral skin temperatures post-intervention, and only the teletherapy group had higher electrodermal activity compared to baseline. There were no significant changes in heartrate. VH delivery had the highest adherence, while chatbot delivery was associated with lower satisfaction and engagement. Suggestions for improvement targeted the robotic voice for the VH, audio preference for the chatbot, and feelings of judgement from the teletherapist. **Discussion:** Overall, results support use of VHs for delivering mindfulness. VHs may have the advantage over teletherapy and chatbots of increasing adherence in student populations, but more work is needed to increase perceived empathy and replicate results in other populations.

Primary Supervisor: Prof. Broadbent, E.

C6

Stem cell derived models of diseased cardiac tissue, mediated by Mechanotransduction through specialised hydrogels.

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Background: Heart failure arises from excessive formation of cardiac scar tissue due to the overactivation and transition of fibroblasts into myofibroblasts. Fibroblast transition is mediated through mechanotransduction pathways. Models which Control fibroblast phenotype paired with cardiomyocytes could replicate diseased tissue states, paving the way for patient specific rapid drug testing models. **Objectives:** This study aims to (1) asses the ability to spatially control hydrogel stiffness to elicit fibroblast transition and (2) determine the feasibility of accurate 3D modelling using cell co-culture to mimic the boundary region between healthy and fibrotic cardiac tissue. **Methods:** Human cardiomyocytes from iPSCs and cardiac fibroblasts are co-cultured within gelatin methacryol (GelMA) hydrogels, which are stiffness patterned using a projector system to control crosslinking density. **Results:** Light intensity variations during hydrogel crosslinking precisely patterns hydrogel stiffness between (1-50) KPa. Cardiomyocytes and fibroblasts both show high viability when encapsulated and fibroblasts exert greater myofibroblast phenotypes on stiffer substrates. **Discussion:** These results demonstrate the possibility to create models of cardiac scar tissue by altering the mechanical of hydrogels.

Primary Supervisor: Assoc Prof. Malmström, J

C7

Novel Generation of Three-Dimensional Brain Spheroids Using Direct Cell Reprogramming.

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Background: Three-dimensional (3D) brain spheroids are valuable tools for disease modelling. However current protocols are lengthy and have limited applicability to diseases of aging. Direct-to-induced neural precursor (iNP) cell reprogramming converts human fibroblasts into region-specific neural precursor cells allowing maintenance of epigenetic and aging factors. We propose the use of directly reprogrammed iNPs to generate brain spheroids provides an enhanced approach to modelling of neurodegenerative diseases. **Objectives:** To demonstrate the ability to generate brain spheroids from directly reprogrammed iNPs. **Methods:** Induced neural precursors were directly reprogrammed from human fibroblasts by transient expression of *SOX2* and *PAX6*. Spheroids were generated by suspending iNPs in ultra-low attachment plates with gentle rotation and timed growth factor exposure to drive differentiation to a striatal cell fate. Differentiation was evaluated using immunocytochemistry (ICC) and quantitative polymerase chain reaction (qPCR) for striatal markers. **Results:** Spheroids were positive for the striatal lineage markers CTIP2, TUJ1 and DARPP32 at days 7 and 14 of differentiation, as confirmed by qPCR and ICC. Spheroids increased in size evenly over time, reaching a maximum size of approximately 1mm. A plate shaker to distribute nutrients was critical to the success of the protocol. **Discussion:** This study demonstrates for the first time the ability to generate spheroids from directly reprogrammed iNPs, with striatal differentiation by day 7 of culture. The reduced time required to generate spheroids from iNPs and the ability for direct-to-iNP reprogramming to maintain epigenetic and aging signatures advances current spheroid methods, allowing for future modelling of neurological diseases of aging.

Primary Supervisor: Prof. Connor, B

C8

Testing the clinically-relevant kappa-opioid receptor agonist, nalfurafine, as a potential treatment for spinal cord injury

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Background: Spinal cord injury (SCI) is a life altering neurological condition. Currently, there are few treatment options for improving neurological outcomes following SCI. In other neurological diseases kappa-opioid receptor (KOR) agonists have been shown to modulate inflammation, the immune response and remyelination, all key components of an SCI. In this project we are exploring the use of the KOR agonist, nalfurafine, as a neuroprotective agent for SCI. **Objectives:** To examine if administering nalfurafine can reduce inflammation, promote remyelination and improve functional recovery in a rodent model of contusive spinal cord injury. **Methods:** Twenty-four Sprague Dawley rats were randomized into 3 groups and subjected to a moderate SCI contusion (175kdyne) using an Infinite Horizons Impactor. Animals were administered nalfurafine (0.1mg/kg or 0.03mg/kg) or vehicle daily for 4 weeks. The Basso Beattie and Bresnahan (BBB) locomotor scale and the Error Ladder were used to assess gross and fine motor function, respectively. Spinal cord tissue was sectioned for immunohistochemical analysis of changes in lesion size, astrocyte and microglia phenotypes and oligodendrocyte number/levels of myelination. **Results:** Tissue sectioning and immunohistochemistry is currently underway. Analysis of astrocyte and microglial number and phenotype along with oligodendrocyte number and myelination between the groups will be presented. BBB and Error Ladder analysis has been carried out and will be unblinded following the immunohistochemical analysis. **Discussion:** This project will determine if nalfurafine has potential as an effective therapy for SCI patients, by reducing inflammation and promoting the regeneration of oligodendrocytes and re-myelination of spinal neurons following injury.

Primary Supervisor: Dr O'Carroll, S

C9

Identifying propagating neural activity from the subdural surface of the rodent spinal cord

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Background: Recording directly from the surface of the spinal cord in freely behaving animals provides a promising means to understand spinal electrophysiology. Current literature typically examines spinal electrophysiology in stimulation experiments or during controlled behaviours. This research aims to identify quantifiable metrics of propagating spiking activity, recorded from the spinal cord during natural, freely moving activity. **Objectives:** To understand where electrical signals recorded from the surface of the spinal cord originate and whether these signals represent neural activity. **Methods:** Electrical activity was recorded from the surface of the dorsal spinal cord in freely moving rats. Signals were filtered using a 300-1200Hz bandpass filter, which uncovered spike-like activity. The separation of extracted spikes was investigated, before being validated as neural through investigation into the propagation of these waveforms. Micro-CT imaging was also used to validate the position of the implant atop the spinal cord and to hypothesis what spinal tracts we can expect to be recording from. **Results:** Extracted spikes can be represented by a single template. The propagation velocity of extracted spikes represents predominantly afferent activity, with a cluster between 20 and 100 ms^{-1}, further validated by micro-CT imaging revealing electrodes directly atop the dorsal columns. A smaller cluster of efferent velocities was also identified, likely recorded from the rubrospinal tract. **Discussion:** This analysis provides evidence that neural activity can be recorded from a subdural spinal implant. Future analysis will be carried out to understand how the electrical activity of the spinal cord changes following injury.
Primary Supervisor: Assoc Prof. Svirskis, D

C10

C11

The X Factor: X-inactivation in the phenotype of the X-linked motor neuron disease gene *UBQLN2*

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Background: X-inactivation balances X-linked gene dosage and expression between males (XY) and females (XX). Random silencing of one X-chromosome in each female cell creates diversity, with cells expressing either the maternal or paternal X-allele. This diversity may confer resilience to neurological disease. In familial cases of X-linked motor neuron disease (MND) and frontotemporal dementia (FTD), caused by *UBQLN2* gene mutations, striking phenotypic diversity is observed. *UBQLN2* is a known X-inactivation target, but its impact on MND onset, severity, and neuropathology remain unclear. **Objectives:** To examine clinical and neuropathological features of MND/FTD caused by *UBQLN2* mutations in literature and in human brain tissue, and identify sites within the *UBQLN2* promoter that are subject to sex-specific methylation, a marker of X-inactivation. **Methods:** A meta-analysis was conducted to examine MND/FTD clinical and neuropathological features in all published *UBQLN2* mutation carriers. Immunohistochemistry compared neuropathology across MND/FTD genotypes and sexes using human brain tissue. *UBQLN2* promoter cytosine methylation data from male and female brain tissue was extracted from publicly available datasets. **Results:** Age of MND/FTD onset in females with *UBQLN2* mutations, particularly within a unique proline-rich domain, was approximately 20 years later than in males. Three different pathogenic *UBQLN2* mutations showed a characteristic hippocampal ubiquilin 2 aggregation signature, with fewer aggregates in females. Further, females showed increased *UBQLN2* promoter methylation at specific cytosines consistent with X-inactivation. **Discussion**: The interplay between genetic sex, X-inactivation, and disease manifestation is complex and striking, emphasising the importance of considering sex-specific factors in understanding disease mechanisms and developing targeted therapies.

Primary Supervisor: Dr Scotter, EL

C12

Network analysis uncovers gene-regulatory intersections between juvenile arthritis and comorbid traits.

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Background: Juvenile idiopathic arthritis (JIA) is an inflammatory joint disease with complex genetic aetiology. As JIA progresses, patients commonly develop additional comorbid conditions, leading to challenges in clinical management. However, the gene-regulatory mechanism linking these conditions remains unknown. **Objectives:** To understand the gene-regulatory mechanism linking JIA to its comorbid conditions. **Methods:** We conducted a Mendelian-Randomization analysis to identify genes that have a causal role in JIA. By integrating data from expression quantitative trait loci (eQTL), 3D genome organization, and protein-protein interaction network, we identified sets of single-nucleotide polymorphisms (SNPs) that regulate the expression of these genes and their interaction partners. Querying these regulatory SNPs against a database of genome-wide association studies revealed 89 comorbid traits sharing gene aberrations within this network. **Results:** We highlighted a set genes on chromosome 6p22.1 (*HLA-A, HCG4P5, MOG, TRIM26 , IFITM4PI*) involved in the association between JIA and specific autoimmune diseases, such as Crohn's disease, asthma, and rheumatoid arthritis. Additionally, we found a distinct association to Hodgkin lymphoma through a set of genes in 6p21.3 (*FKBPL, PBX2, AGER*), as well as chronic lymphocytic leukaemia through the *BAK1* gene. Genes like *PBX2* and *BAK1* have been implicated in the regulation of cell cycle and apoptosis. **Discussion:** Our findings suggest that an individual's JIA phenotype is influenced in part by their genetic risk for co-occurring conditions. The identification of regulatory mechanisms linking JIA and comorbid traits enhances our understanding of disease origins and enables the identification of shared therapeutic targets, ultimately improving outcomes for patients with multimorbidity.

Primary Supervisor: Prof. O'Sullivan, J

C13

Uncovering the developmental intersection between autism and co-occurring traits

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Background: Autism is a complex neurodevelopmental condition that manifests in various ways. It is often accompanied by other neurological disorders, such as ADHD and anxiety, which can complicate diagnosis and management. The role of specific genes in autism have been investigated but their relationship with co-occurring traits is not fully understood. **Objectives:** To identify traits genetically associated with autism and to compare this with the New Zealand autistic population. **Methods:** In this study, we integrated genetic information at various levels (expression quantitative trait loci [eQTLs], genes, and proteins) to investigate the connectivity between autism and co-occurring traits. We then used the New Zealand health records to find conditions autistic individuals had either an increased or decreased risk for. **Results:** We discovered that the 17q21.31 locus contributes to the intersection between autism and other neurological traits and conditions in fetal cortical tissue. We also identified an additional distinct cluster of co-occurring traits, including cognition and worry, linked to genetic loci at 3p21.1. These distinct genetic loci had developmental windows (e.g. fetal development) in which they had the potential to influence trait combinations. From our epidemiological study, we found an overlap in co-occurring conditions with we had identified in our network analysis. **Discussion:** Our results support the hypothesis that an individual's autism phenotype is partially determined by their genetic risk for co-occurring conditions. Overall, our findings provide insights into the relationship between autism and co-occurring traits, which could be used to develop predictive models for better clinical management.
Primary Supervisor: Prof. O'Sullivan, J

Oral Presentation Room D - 505-007

D1

Non-invasive Mapping Of Post-Pancreaticoduodenectomy Gastric Function Using Gastric Alimetry®

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Background: Pancreaticoduodenectomy (PD) is an operation performed for pancreaticobiliary malignancies. A common post-operative complication is delayed gastric emptying. Emerging evidence suggests gastric myoelectrical abnormalities may underlie these problems. A non-invasive body surface gastric electrical mapping device was recently developed to evaluate gastric electrical activity and function. **Objectives:** This world's first study will assess the feasibility of the Gastric Alimetry device on the stomach following PD, to identify any changes in gastric activity and their correlation with symptoms. **Methods:** PD patients from Auckland between 2017-2022 were recruited. Gastric Alimetry® (Auckland, New Zealand) was employed, comprising a stretchable array and cloud-based analytics platform. 30 minutes of baseline recording was performed, followed by a meal challenge and 4 hours of post-prandial recordings. Quantitative analysis included gastric frequency, amplitude, Gastric Alimetry Rhythm Index (GA-RI, measuring rhythm stability) and symptom burden score. Adverse events were recorded. **Results:** 16 patients were recruited. Spectral abnormalities were more common in patients with moderate-severe symptoms(3/5) vs mild-minimal symptoms(1/11); p=0.029. Abnormalities in symptomatic patients encompassed low GA-RI in 2 patients; and low amplitude in 1 patient, indicating gastric neuromuscular dysfunction. Symptom phenotypes included sensorimotor(3), post-gastric(2) and continuous(2); 2 had mixed profiles. There were no adverse events. **Discussion:** Gastric Alimetry is a feasible technique to non-invasively assess gastric function following PD. A third of patients developed moderate-severe gastric symptoms with a range of phenotypes, indicating gastric sensory, post-gastric and continuous contributions. There is now a role for Gastric Alimetry testing in evaluating the causes of chronic gastric symptoms after PD.
Primary Supervisor: Prof O'Grady, G

D2

Using EEG to Assess Neural Effects of Estradiol:Progesterone Ratio in Females with and without Epilepsy

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Background: Catamenial epilepsy is a menstrual cycle-specific exacerbation of seizures. Literature suggests changes in the ratio of sex steroids across the menstrual cycle may affect seizure frequency. Visual gamma (VG) is an inducible brain oscillation that can be measured with electroencephalography. Studies have found VG varies in frequency across the menstrual cycle in healthy women (HC), reflecting changes to GABA-related inhibition. GABAergic inhibition is protective against seizures. **Objectives***:* Measure VG as a reflection of changes in GABAergic inhibition, determining if sex steroids alter neural signaling across the menstrual cycle in females with and without epilepsy. **Methods:** Electroencephalography recorded induced VG in HC (n=49) and a pilot sample (n=12) of females with epilepsy (EC). Absolute sex steroid concentration in blood samples of participants across mid-luteal, mid-follicular and peri-menstrual phases were also collected. **Results:** Mean estradiol (E2) was relatively similar in HC (*M*=297.48, SD=216.01, range 60-1169 pmol/L) compared to EC (*M*=352.86, SD=277.01, range 92-1088 pmol/L). As was progesterone (P4) in EC (*M*=12.74, S=15.93, range 0.2-45.9 nmol/L) compared to HC (*M*=15.01, SD= 19.83, range 0.2-116 nmol/L). Mean ratio of E2:P4 may be higher in EC (426.08) compared to HC (170.35) though this was only marginally significant ($F_{(1,67.6)}$=3.97, *p*=0.05). **Discussion:** E2 has excitatory neural effects and allopregnanolone (metabolite of P4), enhances GABAergic inhibition. E2:P4 may relate to a difference in excitatory to inhibitory balance in the brain. Analysis of VG aims to uncover if there are associated changes in GABA-driven inhibition. Knowledge provided by this research may help uncover the pathophysiology of catamenial seizures.
Primary Supervisor: Dr Sumner, R

D3

The Effect of the Menstrual Cycle on Normal Gastric Electrophysiology Using Gastric Alimetry

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Background: The stomach has a pacemaker and electrical system analogous to that of the heart which can become disrupted in disease states, resulting in non-specific gastric symptoms such as nausea, vomiting and abdominal pain. Functional gastroduodenal diseases are defined by this symptom group in the absence of structural or organic disease and occur at higher rates in females. The menstrual cycle's natural progesterone and estrogen fluctuations have been hypothesized as a driver of functional gastroduodenal symptoms. **Objectives:** To establish the effect of the menstrual cycle on normal female gastric electrophysiology using a validated Body Surface Gastric Mapping (BSGM) device (similar to an electrocardiogram (ECG) but for the stomach) and validated metrics. **Methods:** Healthy control subjects underwent non-invasive BSGM recording using the Gastric Alimetry device, comprised of a high-resolution 64-channel electrode array and wearable reader. Pre-menopausal participants were divided into follicular and luteal phases depending on menstrual cycle day and their BSGM metrics were retrospectively analysed in comparison to post-menopausal women and males. **Results:** Menstrual cycle phase and menopausal status were associated with significant variances in gastric physiology. Pre-menopausal women in the luteal phase had significantly higher principal gastric frequencies (PGF; the sustained frequency at which the stomach oscillates) than males (mean 3.21 cpm, SD (0.17) vs. mean 3.01 cpm, SD (0.2), $p < 0.001$) and pre-menopausal women in the follicular phase (mean 3.21 cpm, SD (0.17) vs. mean 2.94 cpm, SD (0.17), $p < 0.001$). **Discussion:** Normal gastric electrophysiology appears to differ in pre-menopausal women during the luteal phase.
Primary Supervisor: Prof. O'Grady, G

D4

Exploring the Role of Extracellular Vesicles in Endometriosis Patients in Aotearoa

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Background: Endometriosis is a chronic, painful gynaecological condition affecting at least 10% of menstruating people born with a uterus. The pathophysiology of endometriosis is vastly under-researched, and treatments are often ineffective. We urgently need to understand the molecular crosstalk between cells in endometriosis before more effective diagnostic and treatment methods can be developed. Extracellular vesicles (EVs) are nano-sized intercellular communication factors released by all cell types. Dysregulated EV production and packaging has been implicated in the pathogenesis of many diseases, but their role in endometriosis is underexplored. **Objectives:** To compare methods of EV isolation from peritoneal fluid (PF) of endometriosis patients. **Methods:** Established connections with clinicians to recruit and collect samples from endometriosis patients. Compared ultracentrifugation (UC), size exclusion chromatography (SEC), and 20-nanometre filters (S20) to optimise a method for isolation of EVs from PF. **Results:** Collected and stored PF from 10 endometriosis patients. The SEC method yielded the highest concentration of nanoparticles ($5.04 \times 10^8 – 2.15 \times 10^{10}$ particles/mL) and lowest concentration of co-isolated proteins (45.3 – 172.5 µg/mL) compared to the UC ($9.15 \times 10^7 – 1.74 \times 10^{10}$ particles/mL; 44.0 – 599.6 µg/mL) or S20 methods ($4.85 \times 10^8 – 1.33 \times 10^{10}$ particles/mL; 432.9 – 1723.1 µg/mL). **Discussion:** Using the highest yield method (SEC), EVs isolated from PF of a further 40 endometriosis patients will be utilised in cell line experiments to determine their effects on proliferation, migration, invasion, and macrophage polarisation – typical endometriotic behaviours. Understanding the role of EV-mediated cellular crosstalk will provide valuable insights into endometriosis pathophysiology and progression.
Primary Supervisor: Assoc Prof. Blenkiron, C; Dr Cree, L.

D5

Working with a global healthcare community to define, conceptualise and measure kindness in healthcare

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Background: Kindness as a concept in healthcare remains poorly defined in existing literature, but is increasingly recognised as a key tenet of healthcare quality improvement. To measure it as a component of quality improvement, we must first agree on a definition of kindness. **Objectives:** To establish a definition of kindness in healthcare using both literature review and qualitative research methodology and design a measurement tool exploring how healthcare professionals conceptualise and identify conditions for kindness inside their work environments. **Methods:** Triangulate data from existing literature exploring how kindness is defined and measured, with data gained from a survey of healthcare professionals (n=77), and an interview series (n=15) with global experts in healthcare policy, research and practice, immersed in advancing the concept of kindness in healthcare. Using a participatory action research framework, develop a measurement tool for kindness in healthcare, implemented at 2-3 test sites including a kaupapa Māori primary care service, mainstream general practice, and a large Womens' Hospital. **Results:** Early results show a unification of key concepts that could define kindness in healthcare across data sources. The interview series with global healthcare experts indicate strong support and desire for a measurement tool for kindness that could inform action and organisational cultural change. **Discussion:** We believe we can establish a working definition of kindness, that will be used to aid development of a prototype measurement tool that could inform change actions at an organisational level, enabling conditions for kindness, based on data received from an organisation's own unique healthcare workforce.
Primary Supervisor: Dr Wilkinson-Meyers, L

D6

"I didn't want to go home" – Modifiable risk factors associated with hospital readmissions

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Background: One out of every eight people will be readmitted to hospital after leaving, yet some of these readmissions could be prevented. Identifying modifiable risk factors for preventable readmissions could help identify patients who are at high risk of readmission and identify reasons why they are at high risk, to inform prevention strategies. However, no studies have explored modifiable readmission risk factors in New Zealand (NZ). **Objectives:** To identify factors associated with preventable readmissions from the perspectives of patients and healthcare professionals (HCP). **Methods:** Patients who had been readmitted to Te Toka Tumai Auckland, between June 2021 and April 2022 were invited to participate in semi-structured interviews. HCPs with experience looking after readmitted patients were recruited from several NZ hospitals from February 2023. Data were analysed using inductive thematic analysis to identify factors associated with readmissions. **Results:** Of the 46 patients invited to participate, 30 were included (53% female; 17% Māori; 20% Pacific; mean (SD) age 50(17) years). Several themes related to hospital readmissions were identified by patients, including communication, misalignment between patient illness perceptions and treatment, unclear or missing information, poor health literacy, poor medication management and health system factors. We conducted 16 interviews and one focus group with HCPs. Preliminary findings from HCPs identify factors including treatment expectations and poor medication adherence. **Discussion:** Of these factors identified by patients and HCPs, several are potentially modifiable. These factors could help identify who and why patients are at risk of readmissions and provide practical insights to reduce readmission risk.
Primary Supervisor: Dr Chan, A

D7

Neither Pacific nor Asian: Investigating intersectionality of ethnicity and identity among Fiji-Indian youth in Aotearoa

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Background: Ethnic identity is a key part of an adolescents' life. However, for population groups whose identities are cultural blends, ethnic identity is harder to define. The construction of a sense of identity becomes more difficult when they are excluded by the very groups they seek to identify with. Fiji-Indians, given their complex histories of migration, are subject to 'dual-exclusion', i.e., they are perceived as neither Pacific nor Asian by these respective communities. These exclusions can lead to potential gaps in healthcare and wellbeing. **Objectives**: To explore the implications of dual-exclusion on Fiji-Indian secondary school students in their construction of identity and sense of wellbeing. **Methods:** Secondary quantitative and qualitative Youth'19 Rangatahi Smart Survey data was used for analyses. Data analysis, including logistic regressions were conducted on quantitative data to examine the relationship between ethnicity, connectedness and healthcare use. Thematic analysis was conducted on qualitative short-text responses. **Results:** While there are similarities in discourses of identity, wellbeing and health between Fiji-Indian, Indian and Fijian groups, there are also stark differences that set Fiji-Indian experiences apart. For example, the odds for a student not accessing healthcare services because they didn't know how to was 0.50 times lower for Fiji-Indians students compared to Fijian students. **Discussion:** Due to their intersectional identities, Fiji-Indian students are currently experiencing poorer health and wellbeing outcomes when compared to their Pacific and Asian counterparts. More research must be done to explore intersectional ethnic identities, dual-exclusion and the impact on health and wellbeing for dual-identity population groups.
Primary Supervisor: Assoc Prof Peiris-John, R

D8

Comparison of outcomes of a randomised trial assessed by study questionnaire and by data linkage

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Background: Self-report questionnaires are used to obtain data on participants' health status after randomised trials, but can be time-consuming, and costly. Administrative datasets may provide potentially cost-efficient and bias free health information, but there is a need to determine how administrative data and self-report data compare and whether they could be used interchangeably to identify the occurrence of the chronic conditions. **Objective:** To determine whether questionnaire data can be replaced with data from routinely collected administrative datasets to identify chronic diseases for the follow-up of participants in a randomised controlled trial conducted in New Zealand. **Methods**: 424 surviving adult children of mothers recruited to the Auckland Steroid Trial (1969-1974) were asked to complete a questionnaire and consent to access New Zealand health data, including Testsafe laboratory data. The proportion of participants with diabetes mellitus, pre-diabetes, total diabetes, hyperlipidaemia, hypertension, mental health disorders, and asthma was calculated with the information available in each data source. **Results**: The proportion of cases identified by both questionnaire and administrative data ranged from 1% for pre-diabetes to 24% for mental health disorders. The number of cases identified solely by administrative data was notably higher than the number of cases identified solely by questionnaire for all conditions except high blood pressure and mental health disorders. Combining all data sources increased the number of participants detected for all outcomes. **Discussion**: A combination of self-reported questionnaire, pharmaceutical and laboratory data was required to identify participants with the chronic conditions of interest in this follow-up of a randomised trial.
Primary Supervisor: Distinguished Professor. Harding, J

D9

EPIC PLEFF Study: Exploring the Prognostic ImpaCt of PLeural EFFusion in the Intensive Care Unit

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Background: Pleural effusion (PLEFF) is a common finding in patients in the intensive care unit. However, it's significance to patients' outcomes remains severely understudied. **Objectives:** Our study aims to elucidate the prognostic value of PLEFF on clinical outcomes for adult ICU patients. **Methods:** The Medical Information Mart for Intensive Care (MIMIC)-IV de-identified ICU patient database was utilised to access health records of over 80,000 patients over a 10-year span. Diagnosis codes, radiology reports and laboratory results were utilised to discern the presence of PLEFF within an ICU patient cohort to compare against a non-PLEFF cohort following propensity score matching. Outcomes reported include length of stay (LOS), mortality, need for invasive mechanical ventilation, and sequential organ failure assessment (SOFA) scores over time. Further analysis was conducted for the five diseases most associated with PLEFF and treatment status. **Results:** PLEFF significantly elevated all measured outcomes ($p<0.0001$; all) compared to the non-PLEFF cohort (n=7540 each cohort). On subgroup analysis, variation arose with no significance in ICU mortality and SOFA over time for other subcategories ($p>0.05$). Diverging patterns in mortality timing and invasive mechanical ventilation could be observed in the study. **Discussion:** Our study provides impactful findings to inform clinical trials and clinical decision-making regarding PLEFF in the ICU by depicting prognostic significance across crucial clinical outcomes. The disease subcategories results provide detailed and specific areas of opportunity for timely interventions to reduce mortality in PLEFF patients.
Primary Supervisor: Prof. Windsor, J

D10

A systematic review of nutritional guidelines for preterm infants

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Background: There is no consensus on optimal nutrition for preterm infants, leading to substantial practice variation. Variation may prevent clinicians from providing optimal care. **Objectives:** We aimed to assess the quality of nutritional guidelines for preterm infants, the consistency of recommendations, and the gaps in recommendations. **Methods:** We searched databases and websites for nutritional guidelines for preterm infants before first discharge, endorsed, prepared, or authorised by a regional, national, or international body, written in English, and published between 2012-2023. Two reviewers independently screened articles and extracted the recommendations. Four reviewers appraised the included guidelines using AGREE II. Gaps in recommendations were either identified by the guidelines or when recommendations were based on very low certainty evidence. **Results:** 7051 records were identified, and 27 guidelines included, 26% of which were high in quality. We found considerable variation in recommendations, many of which lacked details of certainty of evidence and strength of recommendation. Recommendations for feeding types and breastmilk fortification were consistent among high quality guidelines, but recommendations varied for intakes of almost all nutrients and monitoring of nutritional adequacy. Most gaps in recommendations were based on a very low certainty of evidence. **Discussion:** This review offers an up-to-date summary of major nutrition recommendations for preterm infants and areas needing further research. The recommendations are mostly inconsistent and lack of robust evidence base. Future development of nutritional guidelines for preterm infants should improve the guideline development process, involve stakeholders/consumers, and focus on comprehensive guidelines which cover all nutrition components for preterm infants.
Primary Supervisor: Distinguished Prof Harding, J

D11

Fetal growth restriction and fetal sexes: brain versus brawn?

King V[1], Dhillon S[1], Lear B[1], Beacom M[1], Lear C[1], Stone P[2], Gunn A[1], Bennet L[1]
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Background: Sex differences in fetal brain development have been reported. Late-onset fetal growth restriction (FGR) is a leading cause of adverse outcomes in pregnancy including impaired neurodevelopment. **Objectives:** This preliminary study examined the effect of late-onset FGR on fetal growth and sleep state development. **Methods:** Preterm fetal sheep at 0.7 gestation were surgically instrumented with catheters and electrodes and a silicone occluder was placed around one umbilical artery. 5d post-surgery the UA occluder was gradually inflated over 3-4d to reduce blood flow to the placenta, and sustained for 21d. Fetal physiology was continuously recorded. **Results:** Sleep-state cycling emerged earlier in FGR fetuses compared with controls (115d gestation vs 122d). Overall, FGR males spent a greater proportion of time in non-rapid eye movement (NREM) sleep compared to FGR females, while FGR females spent more time in REM sleep. Brain:bodyweight ratios were equivalent between sexes in controls. FGR female fetuses had a larger ratio compared with males, with heavier brains. **Discussion:** Emergence of discrete sleep-state cycling reflects maturing neural network development and represents a period where energy demands for fetal growth and fetal activity can be balanced. Cerebral energy demands are lower in NREM sleep. Our pilot data suggest that in later-onset FGR, an earlier onset of sleep-state cycling may be required to ensure a greater overall proportion of time in REM, a state critical for development of neural connectivity. FGR females appear to prioritise energy use for brain growth and development, while males may prioritise more time to somatic growth.

Primary Supervisor: Prof Bennet, L

D12

Fetal plasma-derived extracellular vesicles as biomarkers of hypoxia-ischaemia-mediated preterm brain injury.

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[1] Department of Physiology, University of Auckland, [2] Department of Obstetrics and Gynaecology, University of Auckland

Background: Perinatal hypoxia-ischaemia (HI) can have devastating consequences on cerebral development in preterm infants (<37 weeks gestation). Impactful interventions to reduce the extent of brain injury are impeded due to the inability to diagnose preterm infant brain injury accurately and rapidly. Extracellular vesicles (EVs) are released from all cells of the body (including the brain) and can be isolated from biofluids. Previously, EVs have shown biomarker potential in adult brain injury. **Objectives:** We aimed to establish whether EVs could be isolated and characterised in fetal plasma as the first step towards investigating their diagnostic potential of preterm brain injury. **Methods:** Fetal plasma samples were collected 6 hours following either umbilical cord occlusion (n=12) or sham occlusion (n=8) from a sheep HI model of preterm brain injury. Samples underwent EV isolation by size-exclusion chromatography (SEC) and enriched fractions, determined using nanoparticle tracking analysis (NTA) and BCA, were pooled. The pooled samples were further characterised according to MISEV 2018 guidelines including NTA. **Results:** SEC fractions 1-6 were pooled for further characterisation. NTA analysis showed the occlusion cohort has significantly higher particle concentration ($4.32e^{+10}$ particles/mL ±$4.80e^{+9}$ particles/mL (SEM) vs $2.97e^{+10}$ particles/mL ±$3.00e^{+9}$ particles/mL (SEM), *p=0.0298*) and smaller particle size (125.5nm ±4.971nm (SEM) vs 168.0nm ±3.297nm (SEM), *p<0.0001*) compared to the sham-occlusion cohort. **Discussion:** Successful isolation and characterisation of plasma EVs from preterm fetal sheep allow for further investigation as to whether the fetal plasma EVs themselves or the protein cargo offers a useful clinical biomarker for the identification of preterm brain injury.

Primary supervisors: Assoc Prof. Fraser, M; Dr Gamage, T

D13

Assessing the Efficacy of Fetal Heart Rate Variability Measures as Biomarkers for mild Fetal Brain Injury

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Background: Hypoxia-ischemia (HI) is a significant contributor to perinatal brain injury. Early identification and treatment during pregnancy may improve neural outcomes. Fetal heart rate variability (FHRV) is a valuable measure of fetal well-being, yet its effectiveness in identifying antenatal brain injury remains to be determined. **Objectives:** This project examined the biomarker utility of different FHRV indices after an HI insult leading to mild-moderate brain injury. **Methods:** 0.7 gestation fetal sheep were surgically instrumented with catheters, electrodes, and a silicone occluder placed around the umbilical cord. 5d post-surgery fetuses underwent sham-HI (n=8) or 15-min umbilical cord compression to induce brain injury (HI, n=11). Evolving injury was classified into phases: latent (0-6h) and secondary (6h-4 days). Time, frequency and non-linear FHRV domains: standard deviation of normal-to-normal R-R intervals (SDNN), root-mean-square of successive differences (RMSSD), very-low-frequency (VLF), heart-rate fragmentation (HRF), detrended-fluctuation analysis (DFA)-α1 were assessed. **Results:** The latent phase was characterised by initial suppression in time and frequency domain measures, which resolved to baseline levels for the duration of the study. The secondary phase was only denoted by suppressed HRF and elevated DFA-α1, indicating a decrease in short-term signal complexity during this period. These changes closely aligned with suppression of circadian oscillations in all FHRV measures, which progressively re-established in ~4-5 days post-HI. **Discussion:** The findings suggest that a subset of non-linear FHRV measures may be potential biomarkers for detecting mild-moderate HI and identifying early stages of injury. Early disruption to circadian rhythmicity suggests that HI injury may change circadian clock gene expression.
Primary Supervisor: Prof. Bennet, L

D14

Erythropoietin improved recovery of brain activity after mild hypoxia-ischemia in the term-equivalent fetal sheep

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Background: Infants with mild hypoxic ischemic encephalopathy have significant risk of brain injury and adverse neurodevelopmental outcomes but there are no treatments available. Erythropoietin (EPO) has been shown to have neuroprotective and neurorestorative effects in preclinical studies. **Objectives:** The aim of this study was to determine whether EPO treatment would reduce perinatal brain injury after mild hypoxia-ischemia (HI). **Methods:** Term-equivalent chronically instrumented fetal sheep were randomized to sham-control (n=7), HI-vehicle (n=8) and HI-EPO (n=7). Mild cerebral HI was induced by 10 minutes of bilateral carotid artery occlusion. EPO was infused from 2-74 h after occlusion. **Results:** HI was associated with a significant decrease in EEG power, which remained significantly below sham-control until 120 hours post-HI ($P<0.05$). EPO was associated with more rapid recovery of EEG power to sham-control levels within 10 hours. HI was associated with a significant decrease in spectral edge frequency, which remained significantly less than sham-controls until 10 hours post-HI ($P<0.05$). EPO was associated with a more rapid recovery of spectral edge frequency to sham-control levels by 6 hours. HI was associated with a transient loss of sleep state cycling between high power, low frequency activity and low power, high frequency activity. The HI-vehicle group had significantly more crossings into both high voltage and low voltage states and had more fragmented cycling behaviour 12-24 h post-HI than the EPO group. **Discussion:** EPO improved recovery of EEG, spectral edge and sleep state cycling suggesting that it may be an effective treatment for mild HI injury.
Primary Supervisor: Assoc Prof Davidson, J

D15

Five-year vs ten-year predicted cardiovascular disease risk in Aotearoa New Zealand

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Background: There is no consensus on the optimal time window for cardiovascular disease (CVD) risk prediction equations. Most countries recommend a '10-year' prediction window, whereas Aotearoa New Zealand (NZ) and Australia recommend predicting 5-year CVD risk. **Objectives:** To describe predicted 5-year and 10-year CVD risk distributions in the NZ population and examine whether they identified different high-risk populations. **Methods:** Encrypted individual-level linkage of NZ administrative health datasets identified 1,746,665 participants without CVD or heart failure, aged 30-74 years in 2006, with follow-up linkage to hospitalisations and mortality until 2018. We described the distribution of predicted 5-year and 10-year CVD risks and compared characteristics of high-risk participants selected by 5-year and 10-year equations. **Results:** A total of 155,924 CVD events occurred during 19,728,636 person-years of follow-up. The median 5-year and 10-year CVD risks were 1.0% and 2.5% in women and 2.4% and 5.8% in men. Most participants in the highest two deciles of 5-year risk were also found in the highest two deciles of 10-year risk (96.9% and 95.8% of women and men). Participants only identified in the top two deciles of 5-year risk were younger, more likely to be from groups with high incidence of CVD and from deprived areas, and much more likely to be dispensed CVD preventive medications. **Discussion:** Five-year and 10-year equations demonstrated substantial overlap in groups defined as 'high risk', although 5-year equations identified slightly more people from populations known to be at increased CVD risk, highlighting an advantage of 5-year over 10-year CVD risk assessment.

Primary Supervisor: Prof. Jackson, R

Oral Presentation Room E - 505-010

E1

Understanding risk factors for pharmacists' complaints through a nationwide database: a qualitative content analysis

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Background: Pharmacists play a crucial role in the healthcare system, significantly influencing the provision of medication services and ensuring patient safety. **Objectives:** This study aims to analyse opinions from the New Zealand Health and Disability Commissioner (HDC) pertaining to pharmacists in order to gain comprehensive insights into the characteristics and risk factors associated with pharmacist complaints. **Methods:** This study utilises a retrospective, qualitative approach. An inductive content analysis technique was employed to analyse 37 reports of pharmacist complaints cases sourced from the HDC publicly available database. The narrative reports were divided into meaning units, then condensed and labelled into codes. By comparing the similarities and differences, risk factors and final categories emerged. **Results:** The content analysis identified a total of 20 categories of risk factors, which were subsequently grouped into five overarching themes: pharmacist factors, organisational factors, system factors, medication-specific factors, and external environmental factors. **Discussion:** Pharmacists bear primary responsibility for complaints as the principal providers of pharmacy services. Moreover, within complex environments, systems, and organisations, multiple factors impact pharmacists' behaviour and the occurrence of complaints. It is recommended to adopt a holistic approach that considers individual pharmacist's actions and the broader context in which they practice. These findings provide valuable insights that expand the understanding of risk management in pharmacist practice, serving as a valuable resource for regulatory bodies, policymakers, educators, and practitioners.
Primary Supervisor: Assoc Prof. Shane, S

E2

Pharmacovigilance-related regulatory obligations for the natural health products (NHPs) industry: a scoping review

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Background: Pharmacovigilance is the science and practice of safety monitoring for marketed medicinal products, including natural health products (NHPs). Pharmacovigilance systems involve several stakeholders, including the pharmaceutical and NHPs industry. While industry obligations regarding pharmacovigilance for conventional medicines are well-documented, there is limited information internationally on regulatory obligations for the NHPs industry with respect to pharmacovigilance for NHPs. **Objectives:** To describe regulatory obligations and requirements for the NHPs industry regarding pharmacovigilance for NHPs. **Methods:** A list was created of the top 30 countries/regions, plus New Zealand, from the World Health Organization list of nations with the highest Current Health Expenditure in 2020. For these countries, publicly accessible regulatory instruments describing pharmacovigilance obligations for the NHPs industry and available in English at official governmental websites were identified. **Results:** Regulations for ten countries/regions (Australia, Canada, EU, India, New Zealand, Republic of Korea, South Africa, Switzerland, UK, USA) were included. Of these, all have general and/or specific regulations covering NHPs and their definitions, though these definitions vary. Regulations from seven of these countries/regions specified timelines for mandatory reporting of suspected adverse reactions by industry for their products, usually requiring the NHPs industry to report serious adverse events within 15 days of becoming aware. Three countries/regions (EU, India, UK) specified set timelines for submissions of Periodic Safety Update Reports. **Discussion:** Regulatory obligations for the NHPs industry regarding pharmacovigilance for NHPs differed by country/region and emphasized the reporting of serious adverse events. Regulatory obligations also varied *within* certain countries/regions for different categories of NHPs.
Primary Supervisor: Prof. Barnes, J

E3

Can Cysteamine and Everolimus combination treatment prevent kidney dysfunction in cystinosis rats?

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Background: Nephropathic cystinosis is a rare lysosomal storage disorder caused by mutations in the cystine transporter cystinosin (*CTNS*), resulting in cystine accumulation in all cells of the body. The kidney is the first organ affected and despite long-term treatment, patients still progress to kidney failure with the need for transplant inevitable. We have shown that a combination treatment of cystine-depleting drug, cysteamine and the mTOR inhibitor, everolimus, can rescue the cystinotic phenotype in *in vitro* models. To evaluate this therapy *in vivo,* we performed pre-clinical testing in our rodent model of cystinosis which faithfully recapitulates the human disease within 3-6 months as seen by: failure to gain weight, excessive thirst (polydipsia) and urination (polyuria), cystine accumulation, Fanconi syndrome and kidney dysfunction. **Objectives:** To determine if combination treatment is a better therapy than cysteamine monotreatment and can preserve kidney function in *Ctns* knockout (KO) rats. **Methods:** Six-week-old *Ctns* KO rats were dosed with either vehicle, cysteamine or combination (cysteamine and everolimus) via jelly pills for 6 months. Plasma and urine were collected monthly for in-depth analysis and body weights were measured weekly. At the end of study, tissues were harvested for cystine measurements, immunohistochemistry and histology. **Results:** Cysteamine monotreatment was efficacious in ameliorating the disease phenotype however, combination treatment resulted in a greater reduction in tissue cystine levels, polydipsia, polyuria and a superior improvement in gross kidney morphology and histology compared to monotreatment. **Discussion:** These results demonstrate the potential of a cysteamine/everolimus dual therapy to improve the treatment of cystinosis.
Primary Supervisor: Dr Hollywood, J

E4

The recreational use of natural health products/substances for psychoactive effects in New Zealand: a review

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Background: Natural substances, such as certain species of plants and mushrooms, have been used for their psychoactive effects since prehistory. However, their patterns and prevalence of use, and those of contemporary natural health products (NHPs) used in this context, are not known. **Objectives:** To map the published literature documenting the recreational use of NHPs for psychoactive effects in New Zealand (NZ). **Methods:** Biomedical databases (Medline, Embase, AMED, PsycINFO) were searched systematically up to August 2021. Grey literature sources (NZ government and relevant organisations' websites) were also searched systematically for relevant documents up to August 2021. Original research studies reporting on the prevalence and/or exploring the recreational use of natural substances/NHPs for psychoactive effects were included in this review. **Results:** In total, 26 studies met inclusion criteria. Few studies specifically asked about natural substances/NHPs use in this context. A range of natural substances/NHPs are used recreationally in NZ to obtain psychoactive effects. Hallucinogenic mushrooms and *Salvia divinorum* were the most frequently reported substances across all studies. Specific patterns of use were described among individuals from certain ethnic backgrounds and age groups. Different data collection methods and unclear NHP and substance use definitions were used across studies. **Discussion:** There is a limited number of studies/reports on the recreational use of natural substances/NHPs for psychoactive effects in NZ. Large, nationally representative studies are required to obtain comprehensive data on the prevalence and patterns of use of NHPs for psychoactive effects.
Primary Supervisor: Prof. Barnes, J

E5

Clozapine-Induced Cardiotoxicity: Investigating reactive species associated with metabolite cycling.

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Background: Clozapine is an antipsychotic, limited in its prescription by adverse drug reactions, including cardiotoxicity. While one of its circulating metabolites (*N*-desmethylclozapine) is routinely studied, the other (clozapine-*N*-oxide) is drastically under-investigated. **Objectives:** To identify if Cytochrome P450 (CYP) isoforms, including those expressed in the heart, catalyse oxidation and reduction of clozapine and clozapine-*N*-oxide and to assess whether these metabolic pathways correlate with the production of reactive species. **Methods:** Clozapine, *N*-desmethylclozapine and/or clozapine-*N*-oxide were incubated with hepatic and cardioselective CYP isoforms with cofactor NADPH in the presence of 2'-7'-dichlorofluorescein diacetate (DCF-DA). Clozapine metabolites were quantified using liquid chromatography-mass spectrometry, and their rate of formation by each isoform was assessed relative to the formation of reactive species (measured indirectly via DCF-DA oxidation by free radicals). **Results:** CYP3A4 predominately catalysed clozapine-*N*-oxide formation and was associated with concentration-dependent reactive species production. Those isoforms favouring the *N*-desmethylclozapine pathway (CYP1A2, CYP2C19) or that catalysed *N*-desmethylclozapine and clozapine-*N*-oxide formation equally (CYP1B1) were not. The reduction of clozapine-*N*-oxide to clozapine was catalysed by all isoforms studied. The cardioselective isoform CYP1A1 catalysed the reduction of clozapine-*N*-oxide back to clozapine but not the oxidation of clozapine to clozapine-*N*-oxide. This process was associated with DCF-DA oxidation. **Discussion:** Unique to this investigation is the finding that various CYP isoforms catalyse clozapine-*N*-oxide reduction back into clozapine. This has allowed us to explore the relative contribution of oxidation and reduction pathways to the production of reactive species. Identifying such species connects metabolism and oxidative stress as a potential mechanism behind clozapine-induced cardiotoxicity.

Primary Supervisor: Prof. Tingle, M

E6

Faecal microbiota transplant-mediated alteration of the phageome composition in a clinical trial for obesity

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Background: Faecal microbiota transplant (FMT) is an experimental medical procedure used to treat diseases associated with the gut microbiome through the introduction of donor faecal microbiome. Gastrointestinal phages are implicated with human health and successful engraftment of donor phages has been correlated with FMT treatment efficacy. Phages can impact the environment they inhabit by modulating bacterial communities, either through predation or by enhancing their fitness. **Objectives:** In this study, we have investigated the effects of FMT on the phageome composition of participants within the Gut Bugs Trial (GBT), a placebo control clinical trial that investigated the efficacy of FMT in the treatment of adolescent obesity-related symptoms. **Methods:** Stool samples in the GBT were collected at baseline (prior to the transplant) and up to six months after the transplant (*i.e.,* 6 weeks, 12 weeks, and 26 weeks). Microbial DNA was sequenced using Illumina technology, and phage sequences were identified and characterised *in silico*. **Results:** Donor phages engrafted stably in recipients following the FMT for the entire study time course. Phage engraftment was donor specific, and engraftment efficacy was positively correlated with donor phageome diversity. Engraftment of donor phages increased the abundance of temperate phages within FMT recipients and their phageome variability and diversity. An increase in variability and diversity was also observed in the bacteriome, suggesting that FMT altered microbial dynamics. **Discussion:** FMT proved effective in modulating the gastrointestinal environment of the GBT obese adolescents by altering their phageome composition in a donor-specific manner and by promoting shifts in microbial dynamics.

Primary Supervisor: Prof. O'Sullivan, J

E7

Activated yet in-active; the paradoxical effect of dasatinib on Lymphocyte Specific Kinase

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Background: Lymphocyte specific kinase (Lck) plays a crucial role in T-cell mediated immune responses and is an important drug target for controlling T-cell based autoimmunity. Lck is recruited to the T-cell receptor (TCR) where it performs early phosphorylation events in the TCR signalling pathway. The multi-target kinase inhibitor dasatinib is a potent Lck inhibitor and blocker of T-cell function. While studying dasatinib, we discovered unexpectedly dasatinib has a bimodal effect on the Lck phosphorylation state. **Objectives:** To study the molecular pharmacology of dasatinib by investigating Lck activity in cells. **Methods:** Jurkat and CCRF-CEM T-cells were treated with dasatinib at concentrations from 0.01 to 100nM with Lck phosphorylation at the activating (Y394) and inhibitory (Y505) sites and markers of TCR signalling monitored by western blot analysis. **Results:** In both Jurkat and CCRF-CEM cells, 1nM dasatinib consistently causes hyperphosphorylation of Lck Y394 but not Y505 and at this concentration signalling downstream of Lck was inhibited. At 100nM, dasatinib decreases Lck phosphorylation at both sites and completely blocks TCR signalling. **Discussion:** This study has identified paradoxical activation of Lck as a novel mechanism of action of an Lck inhibitor occurring at ultra-low concentrations. The paradoxical increase in activated Lck is not unique to Jurkat T-cells and does not rely on TCR stimulation indicating dependency on drug binding. Understanding how dasatinib promotes the phosphorylation state change and what binding mode is involved has important implications for the design of new compounds as well as providing insight into drug induced changes in the TCR signalosome.
Primary Supervisor: Assoc Prof. Flanagan, J

E8

Overcoming Barriers to Drug Checking Research in Illicit Drug Consumption

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[1]School of Pharmacy

Background: Legal controls in investigating illicit drug consumption pose one of the most significant barriers. Typically, only those authorised to possess and work with illicit drug materials are those working in law enforcement or the criminal justice system. Researchers investigating risks or harms need to work within the law, and in many jurisdictions, this inhibits access to drugs for research. Furthermore, drug samples obtained from legal sources (police or customs) may not be representative of drug forms available on the illicit market. **Objectives:** To facilitate laboratory research with drug samples sourced directly from consumers, using legislation that was passed in New Zealand in 2022 to enable 'drug checking' by licensed providers. **Methods:** Application to be a licensed provider and to use this legislation to collect and analyse drug samples. **Results:** The application process was thorough and time-intensive. The legislation requires that all University of Auckland Council members were subject to criminal record checks. The legislation also requires that all clients must receive results outlining the drugs contained in their samples with tailored harm reduction advice, requiring the development of advice and researcher training. A licence was issued following a twelve-month application process. **Discussion:** The ability to use this legislation to enable research into illicit drugs in New Zealand has enabled this project and future research into illicit drug material. Analysis of drug samples paired with individualised advice is now a gold standard in harm reduction. This research builds on existing drug checking systems to include dosage analysis and associated advice.
Primary Supervisor: Dr Rhys Ponton

E9

Structure guided poly-pharmacology targeting the bacterial GHKL proteins to overcome antibiotic resistance

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Background: The shortage of antibacterial agents caused by increasing drug resistance of bacterial pathogens is a global concern. Bacterial two-component systems (TCS) are signalling proteins involved in the development of antibiotic tolerance. Recent studies using *E. faecalis* showed deleting the CroRS TCS histidine kinase (HK) gene can overcome antibiotic tolerance. The data identify the HK in TCS as a promising target for re-sensitising bacteria to existing antibiotics. **Objectives**: To discover small molecule inhibitors of the E. faecalis CroS HK ATP-binding site. **Methods:** Molecular docking based virtual screening against publicly available HK structures using known HK inhibitors was undertaken. A new virtual fragment hot-spot method was developed to improve the predictive power of HK structures generated by AI. Enrichment calculations were employed to characterise the predictive ability of the protein structures. **Results:** Enrichment calculations indicate that existing HK structures are capable of identifying some HK inhibitors. A molecular modelling workflow that includes fragment-hotspot mapping and capability for processing hundreds of different protein conformations was able to develop a binding model for the CroS ATP-binding site that explained substrate binding and also exhibited some predictive ability for known HK inhibitors. **Discussion:** In the absence of crystal structures for many TCS HK proteins methods based on AI predictions of protein structure can be used to develop molecular models relevant for drug discovery, although functional models may not be possible for all HKs. Models of the CroS protein with a substrate analogue bound showed similar interactions to other HK enzymes crystallised with the substrate.
Primary Supervisor: Assoc Prof. Flanagan, J

E10

Group A Streptococcus vaccine development: Exploring M75 AP1 protein to expand pilus-based vaccine coverage.

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Background: Group A *Streptococcus* (GAS) causes pharyngitis, impetigo, toxic shock syndrome, and autoimmune diseases, contributing to high morbidity and mortality in New Zealand (NZ) and worldwide. The GAS pilus is an important virulence factor that contributes to bacterial adhesion. Each GAS strain carries a particular pilus type encoded in a variable genomic region, and little is known about the pilus from the M75 611024 (GAS M75) strain. **Objectives:** To characterise the GAS M75 pilus with a focus on the AP1 subunit. **Methods:** The GAS M75 AP1 gene was cloned into an *Escherichia coli* expression vector for protein expression and purification. GAS M75 was made bioluminescent by inserting a pLZ12-km2-P23R TA ffn reporter plasmid, and growth curves were generated by measuring the optical density (OD_{600nm}), bioluminescence and colony forming units (CFU). Flow cytometry was used to test pilus expression in different growth conditions. Adhesion assays using the HaCaT and Detroit 562 (human skin and human pharyngeal, respectively) cell lines tested the adhesion properties of AP1. **Results:** Colony PCR of ten *E. coli* colonies showed the expected band at around 1300 bp. Growth kinetics showed that GAS M75 Wt had the highest OD_{600nm}. However, the strain containing the reporter plasmid and no kanamycin showed the highest bioluminescence. **Discussion:** The colony PCR suggests cloning of the GAS M75 AP1 gene into pPROEX htb was successful. Purified AP1 protein used in adhesion assays would show the role of AP1 as an adhesin. The information from this study will assist research around vaccines for GAS.
Primary Supervisor: Dr Loh, J

E11

Exploring the Immunostimulatory Properties of GAS Pili

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Background: Despite Group A Streptococcus (GAS) infections/complications posing a global health burden, there is no available vaccine. One potential vaccine candidate is GAS pilus, a hair-like cell surface structure key during initiation of infection. GAS pili have been observed to induce the production of protective antibodies but the innate immune response involved has not been defined. **Objectives:** Investigate the interaction between GAS pili and components of the innate immunity to characterise the implication of pili-based vaccines on the immune system. **Methods:** Recombinant forms of pilus proteins and *L. lactis* gain-of-function strains were generated and used in immunoassays/flow cytometry experiments to investigate the interaction with toll-like receptors (TLRs), cytokine production, and immune cell activation. Pili induced inflammation was also studied in moth larvae and a pilus-based vaccine was tested in mice. **Results:** Pili/pilus proteins induced upregulation of proteins and inflammatory cytokines associated with immune activation. The TLR reporter cell assays indicated pilus specificity to TLR2 in its TLR2/6 heterodimeric form. This was confirmed by cytokine measurement, where production of downstream cytokine was inhibited in the presence of a TLR2 antagonist. Pili mediated inflammation stimulate antibody production in mice and did not correlate with disease severity in wax worms. **Discussion:** Our results showed that GAS pili are ligands of TLR2 with the ability to prime the immune system for enhanced antibody production, as well as induce cytokines associated with immune activation. This helps emphasise the pilus proteins potential as a GAS vaccine candidate and as an adjuvant.

Primary Supervisor: Dr Tsai, C

E12

Spatial Analysis of Dendritic Cell Subsets in Human Lymph Nodes

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[1] School of Biological Sciences

Background: Dendritic cells (DCs) are antigen-presenting cells that present antigen to naive T cells in the lymph node, generating an antigen-specific T cell response. While human DCs have been extensively characterised in the blood, understanding of the DCs found in lymphoid tissues is still incomplete. A particular population to be investigated is the CD208+ DCs previously identified in our lab, a population absent in blood but found in many human tissues. **Objectives:** Establish the identity of these CD208+ cells and characterise their spatial relationship with T cell populations in the lymph node. **Methods:** Sections of human lymph node were stained using multiplex Immunofluorescence to examine the localisation of each immune cell population using protein markers and RNA scope to examine the localisation of specific chemokine transcripts. Single cell RNA sequencing was used to examine gene expression profiles of different DC subsets. **Results:** CD208+ DCs were found to exclusively express certain chemokines involved in the trafficking of particular T cell subsets. These DC were spatially associated with these T cell subsets in lymph node. **Discussion:** This study has increased our understanding of human DCs and how they contribute to the generation of immune responses. Knowledge of the specific roles of each DC subpopulation will be important for the development of DC-based immunotherapy treatments (eg. DC-based vaccines).

Primary Supervisor: Prof. Dunbar, R

Oral Presentation Room F - 503-024

F1

Treating Impetigo with Antiseptics, Replacing Antibiotics (TIARA): a randomised controlled trial comparing topical impetigo treatments

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Background: New Zealand has a high incidence of the superficial bacterial skin infection impetigo. Frequent prescribing of topical antibiotic fusidic acid (FA) in NZ has led to widespread FA resistance and selection of methicillin resistant *S. aureus* (MRSA). In response, antiseptics are replacing antibiotics, despite limited evidence. **Objectives:** To compare the effectiveness of topical FA with topical antiseptic hydrogen peroxide (HP) and basic wound care in the treatment of impetigo and to examine potential changes in the antimicrobial resistance following treatment**. Methods:** Children presenting to school health clinics in Auckland with mild-to-moderate impetigo were randomised to receive either FA, HP or wound care for five days. Primary outcome was based on analysis of photographs taken before and after treatment, by graders blinded to treatment arm. Bacterial swabs were taken before and after treatment. **Results:** 84% (132/157) and 79% (134/169) of impetigo improved with FA and HP respectively. 64% (48/74) of those treated with wound care improved. Overall non-inferiority of antiseptic was not shown. Stratified-analysis of impetigo limited to discrete body-parts, demonstrated non-inferiority of HP compared to FA. Wound care was not non-inferior to FA. Higher rates of residual bacteria were seen following antiseptic and wound care compared to FA. **Discussion:** Antiseptic cream is non-inferior to topical antibiotic for mild-to-moderate impetigo limited to a single region of the body. Although antiseptic produced clinical resolution for most, higher rates of bacteria remain following treatment with antiseptic. Questions remain over whether this has clinical impact, e.g. recurrence or risk of post streptococcal phenomena.
Primary Supervisor: Dr Best, E

F2

WITHDRAWN

F3

Antibiofilm activity of a commercial antiseptic agent compared to antibiotics commonly prescribed for sinonasal disease

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Background: Chronic rhinosinusitis (CRS) is a sinonasal disease associated with a low quality-of-life and high economic burden. Antibiotics are prescribed widely for its treatment, however, the evidence supporting its efficacy is poor. This may be due to biofilms which are multicellular assemblages of microbes embedded in an extracellular matrix. Bacteria residing in biofilms are inherently more resistant to antibiotic activity than their planktonic counterparts. Furthermore, the subinhibitory antibiotic concentrations can lead to the development of antimicrobial resistant strains of bacteria. This necessitates the search for a novel antimicrobial agent (not an antibiotic) for the treatment of sinus disease. **Objectives:** To assess the antibiofilm activity of doxycycline, roxithromycin and a commercial antiseptic on clinically relevant strains of bacteria. **Methods:** Laboratory strains of clinically relevant bacteria were grown as biofilms in the Calgary Biofilm Device. The biofilms were exposed to the commercial agent and the antibiotics at different time points. After treatment, colony forming units were enumerated. **Results:** Using the clinically relevant concentration of antibiotics, no significant change in biofilm presence relative to saline was recorded. In comparison, the commercial agent demonstrated rapid antibiofilm activity with there being species-dependent variation. **Discussion:** This study has demonstrated that oral antibiotics commonly prescribed for sinonasal diseases are likely insufficient at eradicating biofilms. Therefore, treating these patients with oral antibiotics will only predispose them to adverse drug reactions and the potential emergence of antimicrobial resistant bacteria. Alternative approaches for antibiofilm treatment such as the tested commercial agent could be a potential way forward.
Primary Supervisor: Dr Biswas, K

F4

Antibiofilm activity of novel polymyxin B analogues

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Background: Antimicrobial resistance poses a serious threat to global health. The growing prevalence of multi-drug resistant organisms necessitates the development of new antimicrobials to combat this. Polymyxin B (PMB) is currently a last-line antibiotic used for infections caused by Gram-negative bacteria. These infections are difficult to treat due to their ability to form biofilms, which are communities of cells within a protective extracellular matrix. The work leading up to this project has produced three novel polymyxin analogues, which have a better safety profile than PMB in kidney organoid models, but unproven antibiofilm efficacy. These compounds are JW-9K, JW-9G, and AC4.120. **Objective:** To assess the antibiofilm efficacy of three novel polymyxin analogues compared to native PMB. **Methods:** Laboratory strains of *Pseudomonas aeruginosa* 27853, *Klebsiella pneumoniae* 35596, and *Acinetobacter baumannii* 19606 were grown as biofilms using the Calgary Biofilm Device. These biofilms were then treated at different concentrations of the polymyxin analogues for 24 hours. The minimum biofilm eradication concentration (MBEC) was established by culture on tryptic soy agar. **Results:** All three novel compounds demonstrated non-inferior efficacy against *P. aeruginosa* biofilms when compared to standard PMB. Against biofilms formed by *K. pneumoniae* and *A. baumannii*, only AC4.120 demonstrated similar efficacy. It was most effective against *P. aeruginosa* biofilms, with a median MBEC of 48 µg/mL vs. 32 µg/mL for PMB (p = 0.314). **Discussion:** This study has highlighted one of the analogues as having similar antibiofilm efficacy to native PMB. This analogue warrants further investigation using clinical isolates of Gram-negative bacteria.
Primary Supervisor: Dr Biswas, K

F5

Ocular surface in health and diabetes: from young children to young adults

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Background: Diabetic neuropathy is one of the most common complications of diabetes. *In vivo* confocal microscopy (IVCM) of the cornea is a non-invasive tool that can detect small nerve fibre changes. These changes in corneal nerves occur prior to clinical peripheral neuropathy. Corneal nerve alterations have been observed in adult patients with diabetes using confocal microscopy, but limited research has been conducted in the paediatric and adolescent population. **Objectives:** To assess ocular surface health, corneal nerve microstructure, corneal sensitivity, and peripheral neuropathy, in children and young adults with type 1 diabetes. **Methods:** Participants from paediatric and adolescent diabetes clinics and age-matched controls were recruited. Neurological tests - Michigan Neuropathy Screening Instrument questionnaire (MNSI) and biothesiometry; and ophthalmologic assessments including the dry eye questionnaire (DEQ-5), non-contact corneal aesthesiometry (NCCA), keratography, and IVCM. **Results:** Twenty-four participants (8 to 26 years old, 7M, 6F), including 5 controls and 8 of those with type 1 diabetes were examined. Preliminary results of 13, show no signs of peripheral neuropathy and no statistically significant difference in ocular surface health. Corneal nerve fibre length was 15.52 ± 2.95 mm/mm^2 in controls compared to 14.52 ± 3.77mm/mm^2 in those with diabetes (p=0.32). No statistically significant differences were noted in corneal sensitivity threshold (p= 0.35) and tear meniscus height (p= 0.63). **Discussion:** The difference in ocular surface health, corneal nerve microstructure and corneal sensitivity between children and young adults with and without diabetes is not statistically significant. A larger participant cohort is required to confirm these findings.
Primary Supervisor: Dr Misra, S

F6

Parents' and professionals' experiences of diagnosis and decisions for critical congenital heart disease in Aotearoa

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Background: Critical congenital heart disease (CCHD) requires urgent intervention. In Aotearoa, survival for one CCHD subtype is lower for Māori and Pasifika infants compared to Europeans, consistent with global ethnic disparities in health outcomes. Providing equitable healthcare to an ethnically diverse population is challenging. However, limited evidence exists about personal experiences of the diagnostic and decision pathways for CCHD in Aotearoa. **Objectives:** To understand parents' and healthcare professionals' experiences of a CCHD fetal diagnosis and decision making in Aotearoa. **Methods:** We generated qualitative data using semi-structured interviews during 2022-23. Parents (n=25) with a fetal diagnosis of CCHD and specialist midwives, doctors and nurses (n=20) involved with cardiac families of Māori, Pasifika, Asian and European ethnicities participated. Data were analysed using inductive thematic analysis. **Results**: Parents undergoing a CCHD diagnosis reported culturally dissonant world views, impacting their level of healthcare engagement. Parents of all ethnicities reported responses of grief and gratitude. Healthcare professionals described systemic barriers to delivering equitable healthcare in a culturally hegemonic setting and displayed a growing awareness of, and attempts to improve, culturally sensitive practice. **Discussion:** Disparate cultural world-views of parents and professionals, along with healthcare system barriers, likely contribute to different survival outcomes in CCHD by ethnicity in Aotearoa. Training healthcare professionals to optimise culturally sensitive practice and deconstruct cultural barriers may improve engagement and equitable healthcare provision for ethnic minority families. Insights from this study can be used to inform future healthcare policies, training, and practice to reduce ethnic inequities.
Primary Supervisor: Prof. Bloomfield, F

F7

Adolescent understanding of the developmental origins of health and disease concepts: a Pacific perspective

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Background: The developmental origins of health and disease (DOHaD) framework highlights the role of maternal and paternal health on disease risk in offspring and across generations. The period of adolescence, where lifestyle behaviours become entrained and track into adulthood, has gained increasing recognition as a key DOHaD window where interventions may have the greatest impact in breaking the cycle of non-communicable diseases (NCDs). However, data around recognition of DOHaD concepts in Pacific adolescents remains limited. **Objective:** This study aimed to identify, for the first time, the baseline level of understanding of DOHaD concepts in adolescents aged 16-19 years living in Aotearoa New Zealand, focusing on Pacific adolescents. **Method:** A validated "Public Understanding of DOHaD" questionnaire utilising Likert attitude scales and closed items was used to explore adolescents' knowledge of DOHaD concepts. Data are also stratified to examine differences in DOHaD awareness across genders and between Pasifika and non-Pasifika. **Results:** Data analysis is still underway. Preliminary analysis (n=171) suggests that DOHaD awareness is low overall (14%) and lower in Pasifika adolescents (4%) as compared to non-Pasifika (10%). Of those with awareness of DOHaD concepts, rates were higher in females as compared to males and gender diverse (83%, 13% and 4% respectively). **Discussion:** Preliminary evidence suggests that awareness of DOHaD concepts remains poor across all adolescent demographics. Increasing such awareness through improved adolescent health literacy is of particular relevance for Pasifika where there is a disproportionately higher burden of NCDs and where there may be a relatively poor understanding of DOHaD concepts.
Primary Supervisor: Prof. Vickers, M

F8

Poloxamer 188-modified pH-sensitive liposomes for enhanced anti-tumour drug delivery.

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Background: Liposomes have emerged as versatile drug carriers, offering tumour-targeted distribution and controlled release, thus improving therapeutic efficacy and minimising damage to healthy tissues. In addition, pH-sensitive liposomes are superior for intracellular drug delivery. Incorporating poly(ethylene)glycol (PEG) on the surface of liposomes (PEGylation) which acts as a steric barrier to opsonisation can prevent liposome clearance in vivo. However, PEGylation reduces liposome internalisation and may induce anti-PEG antibody production, resulting in diminished efficacy and adverse reactions. **Objectives**: This study aims to develop pH-sensitive liposomes grafted with poloxamer 188 (P188) to overcome some limitations of PEGylation and prevent drug leakage. Bufalin (BUF), a poorly soluble anticancer agent was used as a model drug. **Methods:** PEGylated or poloxamer 188-modified liposomes (BUF-PEG-pSL, BUF-P188-pSL) were developed and HP-β-cyclodextrin was employed as a solubility enhancer for BUF. The liposomes were characterised in terms of morphology, size, pH-responsive release properties, and in vitro cytotoxicity against breast cancer (BT474) cells. **Results**: BUF-P188-pSL exhibited superior drug loading (1.5% w/w) and a release profile devoid of drug leakage compared to BUF-PEG-pSL. In contrast to PEGylation, P188-coating favourablly slow down the drug release at pH 7.4 but did not affect the pH-sensitivity of the liposomes (rapid release in endosome and cytosol). **Discussion**: Post-insertion of poloxamer 188 to the liposomes appeared to be able to restore drug retention, possibly by increasing the packing density of phospholipids bilayers. Consequently, P188-pSL has the potential to stabilise pSL as an alternative to PEG and holds great promise for enhancing treatment efficacy and reducing side effects.
Primary Supervisor: Prof. Wu, Z

F9

What enablers and barriers influence successful breastmilk feeding in very preterm pēpi (infants) in Aotearoa?

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Background: Breastmilk is crucial for the optimal nutrition and development of preterm pēpi (infants). The volume of milk expressed in the first week after birth is a determining factor in the infant's feeding journey and health outcomes. Some parents are unable to express enough to meet their infant's requirements, and a recent trial conducted in Aotearoa revealed unexplained ethnic disparities in breastfeeding outcomes, particularly for Māori. **Aims**: To determine what factors influence successful breastmilk feeding in very preterm pēpi (born before 37 weeks) within Aotearoa Neonatal Intensive Care Units. **Methods:** Qualitative semi-structured interviews will be conducted with parents/whānau who intend to breastfeed their pēpi and healthcare professionals involved in their care. Demographic data and feeding practices will be obtained from medical records. Recruitment will continue until thematic data saturation is reached, indicating that further interviews are unlikely to generate new themes. **Results:** This study builds upon the findings of our previous trial, in which Māori pēpi transitioned from intravenous fluids to enteral feeds faster (p=0.007) and were less likely to receive breastmilk exclusively at discharge (p=0.0006) compared to other ethnicities. **Discussion:** This research will explore the lived experiences of whānau of very preterm pēpi and the healthcare professionals involved in their care and the reasons for variation in breastmilk provision. This will allow us to empower whānau in their breastmilk feeding journey, improve preterm health outcomes and ensure equitable neonatal nutrition practices across the country. Our findings will feed into developing national nutrition guidelines for preterm pēpi in Aotearoa.

Primary Supervisor: Prof. Bloomfield, F

F10

F11

Paediatric osteomyelitis: Identification of bacterial genes and phenotype that predispose to adverse health outcomes

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Background: Paediatric acute hematogenous osteomyelitis (PAHO) occurs in children with bacterial infection of the bone, easily treated with antibiotics. Some patients (primarily Māori and Pacific Islander) experience complications such as multi-focal sepsis, despite the same treatment approach and no delay in presentation. Methicillin sensitive staphylococcus aureus (MSSA) is primarily identified, with little known about specific strains influence on adverse outcomes. **Objectives:** To identify bacterial genes and phenotype in MSSA strains collected from children with PAHO that correlate with adverse outcomes. **Methods:** 95 bacterial isolates from children with PAHO treated in Auckland were genotyped, antibiotic sensitivity assays conducted, and compared with complicated (MSSA, chronic or recurrent disease, ≥8 weeks of antibiotics) and uncomplicated (MSSA, no relapse, ≤6.5 weeks of antibiotics) clinical outcomes. **Results:** Preliminary analysis identified 85 as MSSA by genotype; 29 complicated, 47 uncomplicated, 9 required intensive care. 31 unique strains were identified; 7 complicated, 17 uncomplicated, 7 overlapped. Two phylogenetic tree clusters contained a predominant grouping of complicated strains. 100% of MSSA isolates were sensitive to flucloxacillin, however 33% of strains demonstrated a minimum bactericidal concentration discordant with its inhibitory concentration, reaching the threshold for antibiotic resistance. **Discussion:** This study demonstrates the practical application of bacterial genotyping and antibiotic sensitivity to yield clinically relevant information. While this study is in its infancy, the dual analysis of bacterial genome sequencing and in-vitro phenotyping holds promise and paves the way for understanding the link between the bacterial pathogen and its ability to cause severe infection in children with PAHO.
Primary Supervisor: Prof. Cornish, J

F12

Discovery of novel autoantigen biomarkers for Acute Rheumatic Fever

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Background: Acute Rheumatic Fever (ARF) is a serious post-infectious sequela of a Group A Streptococcus (GAS) infection. ARF can progress to chronic rheumatic heart disease and is associated with significant burden in Aotearoa NZ and globally. During a GAS infection, immune dysregulation can result in the generation of immune cells and antibodies that bind to human proteins and contribute to ARF disease. The current dogma is that mimicry exists between GAS and human heart proteins providing a basis for cross-reactivity. However, there has been a lack of contemporary technologies applied to profile autoantibodies in ARF. **Objectives:** To discover and validate novel autoantibody biomarkers for ARF elucidate pathogenesis. **Methods:** High-throughput antigen discovery techniques were employed to identify novel human antigens reactive in ARF patient sera compared with matched controls. These newly discovered autoantigens were validated by ELISA and a Luminex multiplex bead-based assay incorporating these peptides is undergoing optimisation. **Results:** This approach identified both novel and historical antigens associated with ARF, proteins found in heart tissue and the extracellular matrix. The novel autoantigen peptides had significantly ($p < 0.0001$) increased reactivity in children with ARF compared to healthy matched controls and GAS pharyngitis.**Discussion:** A panel of promising autoantibody biomarkers has been identified. Future work will include expansion of bead-based assays for these autoantigens for measurement of different antibody isotypes and subclasses. Characterising autoantibodies against both novel and historical ARF antigens will aid validating biomarkers and elucidating pathogenesis.
Primary Supervisor: Assoc Prof. Moreland, N

F13

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

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Background: Breast cancer is the leading cause of death in women under 65 in Aotearoa, New Zealand. Breast tumours exist as a heterogenous collection of cancerous cells and non-malignant cells, including immune cells such as tumour-associated macrophages (TAMs), collectively termed the tumour microenvironment (TME). TAMs can polarise into a pro-inflammatory or pro-tumour state and may influence treatment responses. However more physiologically relevant models are required to better understand their role in breast cancer. **Objectives**: To establish a novel 3D cancer-immune model using primary breast tumour organoids and macrophages, analyse tumour-immune interactions and investigate the influence of macrophages on cancer cell growth, survival and drug responses. **Methods**: Organoid-macrophage model optimisation is being performed using primary murine mammary tumour organoids from the MMTV-PyMT mouse model and bone-marrow derived macrophages. Organoids are either cultured alone, or with macrophages, along with chemotherapy, to analyse the tumour-immune cell interactions and their effect on drug sensitivity. Cell death is assessed via confocal 3D microscopy and flow cytometry. **Results**: Preliminary data from co-culture experiments have demonstrated profound heterogeneity in macrophage-organoid interactions and suggested macrophages provide a protective effect from chemotherapy-induced cytotoxicity. Experiments are underway to further characterise these interactions and determine the influence of different TAM polarisation states. **Discussion**: Our model may offer new insights into tumour heterogeneity and the pro-tumorigenic role of the breast tumour microenvironment. Our long-term goal is to set up the complimentary patient-derived organoid-macrophage model to investigate these interactions in patient tumour tissue and their implications for variable patient-drug responses.

Primary Supervisor: Dr Nolan, E

F14

A Kaupapa Māori Critique of Māori Food and Nutrition Data in Aotearoa

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Background: This study reveals a kaupapa Māori analysis of Māori nutrition data sovereignty and governance issues among Māori food and nutrition data collected at a National level. A Kaupapa Māori framework was developed and used to review six national health surveys/ studies which collect food and nutrition data from Māori. **Objectives:** To develop a Māori food and nutrition data sovereignty framework and use this to highlight the failings of national surveys/studies in respecting Māori data sovereignty and governance. **Methods:** An analysis framework was developed on the basis of Māori data sovereignty principles as set out by Te Mana Raraunga. The framework was used as a guiding tool when reviewing publicly available survey documents, results and methodology reports. This tool gave each of the six surveys analysed a score for Māori data sovereignty and governance out of 12. **Results:** Overall, the mean total score of Māori nutrition data sovereignty and governance across all the surveys/studies was 2.8. With Te Kupenga scoring the highest (9/12) and the lowest score (1/12) being shared by the NZ Health Survey, the HPA lifestyle survey and the 2008/09 Adult Nutrition Survey. **Discussion:** Issues identified across the six surveys include a lack of Māori leadership and true power sharing under Te Tiriti. The absence of Māori input and control across national surveys and Māori data results in the homogenisation of Māori as a people and individual blame for public health issues.

Primary Supervisor: Assoc Prof. Cormack, D

F15

Rangatiratanga o te Kai - Reconceptualising Food Security in Aotearoa

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Background: Transformative change is urgently needed in food security research and data advancement in Aotearoa New Zealand. Māori communities face disproportionate challenges in achieving food security, while outdated monocultural assessment frameworks and definitions challenge food security equity. **Objectives:** To challenge existing approaches to food security and offer pathways towards realising Māori aspirations for an inclusive future food system. To incorporate the rich mātauranga, tikanga, traditions and values of Te Ao Māori to inform the development of a more equitable food security model in Aotearoa. **Methods:** Kaupapa Māori qualitative interviews were undertaken with 18 participants across the motu. The interviews explored participants' perspectives on food security, food sovereignty and mātauranga Māori. The data was analysed thematically through NVIVO to identify key themes. The findings informed the development of a new food security definition and assessment framework that incorporates Māori values and aspirations. **Results:** Three scales of potential food security transformation have been identified, each with specific recommendations. Firstly, to reconceptualise definitions and assumptions of food security that are currently rooted in colonial ideals. Secondly, broaden indicators and cultural considerations in the assessment framework used in New Zealand's food security literature. Lastly, incorporate Māori understandings of food security and food sovereignty in the application of definitions and assessment frameworks to enhance effectiveness. **Discussion:** This study highlights the importance of incorporating the dynamic and diverse knowledge of Te Ao Māori to address food security inequities in Aotearoa New Zealand and promote a fair and inclusive food system.

Primary Supervisor: Dr Anderson, A

Poster Presentations - Grafton Atrium

P1

Developing Equipment for Rat Ocular Biometry Measurement

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Background: Myopia associating with high risk of sight-threatening ocular complications is reaching epidemic levels worldwide. Research has identified that a higher level of ambient illuminance offers protection against the myopia onset, with dopamine playing a role in this protective effect. The level of dopamine is regulated by its uptake by the dopamine transporter (DAT). In the DAT knock-out (DAT-KO) rats' brain, high dopamine levels had been confirmed. Considering the potential relationship between dopamine and myopia, DAT-KO rats could serve as a valuable animal model for myopia research. However, ocular parameters of these animals have not been studied yet. **Objectives:** To develop equipment for reliably measuring biometry parameters in the rat eye. **Methods:** DAT-KO rats and wild-type (DAT-WT) rats were employed. The rat was placed on an animal stand after anaesthetising and a streak retinoscope and trial lens were utilized to measure the refractive state. An infrared webcam, positioned at the centre of a cone placido disc topographer featuring two concentric rings of infrared LED was employed to capture images for corneal curvature analysis. A-scan ultrasound with a 15 MHz ultrasound probe was used to obtain the anterior chamber depth (ACD), lens thickness (LT) and vitreous chamber depth (VCD). **Results:** The refractive state, infrared imaging system and A-scan ultrasound was appropriate for measuring ocular parameter in rat. **Discussion:** The combined biometry techniques probed to be reliable tools for ocular parameters measurement in the rat eye. These quantitative assessments confirm differences between WT and DAT-KO that can be used for myopia research.

Primary Supervisor: Assoc Prof. Acosta, M

P2

Objective modalities of delayed gastric emptying following pancreaticoduodenectomy- a systematic review

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Background: Delayed gastric emptying (DGE) is a frequent complication after pancreaticoduodenectomy (PD). The diagnosis of DGE is based on International Study Group for Pancreatic Surgery (ISGPS) clinical criteria, however, concerns exist and objective assessments of DGE may be more valuable. **Objectives:** This literature review aimed to identify objective measures of DGE following PD and determine whether these measures correlate with the clinical definition of DGE. **Methods:** A systematic search was performed using the MEDLINE Ovid, EMBASE, Google Scholar and CINAHL databases for studies including pancreatic surgery, delayed gastric emptying and gastric motility until June 2022. The primary outcome was objective modalities undertaken to assess DGE following PD and correlation between objective and clinical diagnosis of DGE. **Results:** 4881 records were identified; 46 studies were included in the final analysis. There were 4 objective modalities of DGE assessment: gastric scintigraphy (n= 28), acetaminophen/paracetamol absorption test (n= 10), fluoroscopy (n=6) and the 13C-acetate breath test (n=3). Protocols were inconsistent, and reported correlations between clinical and objective measures of DGE were variable. However, amongst these measures, at least one study inferred a correlation with the greatest evidence accumulated for gastric scintigraphy. **Discussion:** Several objective modalities assessing DGE following PD have been identified and evaluated, however, are infrequently used. Substantial variability exists in the literature regarding indications and interpretation of these tests. There is now a need for a real-time objective modality which correlates with ISGPS DGE definition after PD, to ultimately inform future research and treatment.

Primary Supervisor: Professor O'Grady, G

P3

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

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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 leads to a timelier and more specific response to alleviate cell stress caused by accumulation of mHTTS.

Primary Supervisor: Assoc Prof. Young, D

P4

P5

Beat-to-beat regulation of the coronary arteries by the cardiac vagus nerve.

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Background: The heart is regulated by the autonomic nervous system. The parasympathetic nervous system decreases heart rate (HR) and increases coronary blood flow (CoBF) via the cardiac vagus nerve. Previously, this has been indirectly studied using pharmacological blockade. **Objectives:** To investigate the beat-to-beat regulation of HR and CoBF by the cardiac vagus nerve using directly recorded cardiac vagus nerve activity (CVNA). **Methods:** Sheep were instrumented to record CVNA, CoBF and HR in conscious conditions. The level of CVNA per cardiac cycle was quantified and grouped into quartiles. For each quartile of CVNA, changes in hemodynamic variables were measured for the subsequent 5 cardiac cycles. The sheep were then administered atropine (0.8 mg/kg/min) to block the actions of the primary vagal neurotransmitter, acetylcholine, to study changes in this regulation. **Results:** Following high levels of CVNA, there was a decrease in HR (0.64±0.28 bpm) and CoBF (0.78±0.21 ml/min) 2 cardiac cycles after the initial beat. In contrast, cardiac cycles containing the lowest quartile of activity were associated with increases in HR (0.59±0.34 bpm) and CoBF (1.01±0.21 ml/min). These changes were attenuated in the presence of atropine. **Discussion:** Higher levels of directly recorded CVNA decrease HR, 2 cardiac cycles after the initial beat. This is consistent with the idea that the vagus is involved in beat-to-beat reductions in HR**.** An increase in CoBF during high CVNA was not demonstrated, potentially due to confounding effects by reductions in HR or factors known to influence CoBF.

Primary Supervisor: Dr Shanks, J

P6

Towards the development of an assay for urinary uracil for prediction of severe 5-fluorouracil toxicity

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Background: The anticancer drug 5-fluorouracil (5-FU) causes life-threatening toxicity in some people, mainly due to a deficiency in the dihydropyrimidine dehydrogenase (DPD) enzyme. Uracil is also metabolised by this enzyme to its metabolite dihydrouracil (DHU). Measurement of endogenous uracil in plasma is recommended by the European Medicines Agency (EMA) for pre-therapeutic screening of DPD deficiency. Post-collection analytical issues have recently been identified, which may be due to enzymatic conversion of uracil to DHU in leucocytes. We want to determine if measuring uracil in urine is a feasible alternative since urine does not contain the DPD enzyme. **Objectives:** To establish an assay for quantification of uracil in urine. **Methods:** Spot urine samples were previously collected from two patient cohorts (n = 37 and n = 166) prior to receiving 5-FU-based chemotherapy. Uracil and DHU were prepared as standard solutions or spiked into randomly selected urine samples and examined by high-performance liquid chromatography (HPLC) with UV detection. Possible endogenous interfering compounds were also assessed, including uridine and pseudouridine (Ψ). **Results:** Chromatographic separation of uracil and DHU was not possible, and Ψ also co-eluted with uracil. **Discussion:** HPLC with UV detection is not able to quantify uracil or DHU in urine, thus a mass-based approach is required. We are now investigating mass spectrometry (MS). Once the quantitative method has been established and validated, uracil and DHU concentrations in all urine samples will be determined, contributing to the evaluation of whether urinary uracil is a potential biomarker of DPD deficiency and 5-FU toxicity prediction.

Primary Supervisor: Dr Helsby, N

P7

Diagnosis of Young-Onset Dementia in New Zealand

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Background: Young onset dementia (YOD) is defined as dementia with symptom onset before 65 years of age. The life expectancy at diagnosis is longer for these patients; thus, the financial and social burden of dementia is increased. Timely diagnosis of YOD is crucial for future planning and accessing support services. **Objectives:** This study aimed to identify factors that increase the time to diagnose YOD in New Zealand. **Methods:** This retrospective observational study recruited participants via clinical referrals and independent advertising. The sample included dementia patients diagnosed between 1 January 2015- 1 January 2023. Multiple choice questionnaire data was obtained from YOD patients, their care partners, and the care partners of deceased YOD patients. Additionally, clinical patient records were analyzed independently by two researchers. **Results:** The participant pool included 40 people with YOD and 39 care partners. The mean time to diagnosis of YOD was 3.5 ± 2 years, the mean time from symptom onset to first clinical visit was 16.3 ± 16.5 months, and the mean time from first clinical visit to diagnosis of YOD was 27.15 ± 22.10 months. An indication of depression/anxiety at presentation correlated with increased diagnosis time. **Discussion:** This study is the first to describe the time to diagnose YOD in New Zealand and provides insight into factors that prolong the diagnostic time for YOD.
Primary Supervisor: Dr Ryan, B

P8

A Scoping Review of Healthy Nutrition Interventions among University Students: Exploring the Socio-Ecological Landscape

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Background: An unhealthy diet is a risk factor for many chronic diseases, particularly, university students, whose lifestyle and eating habits could influence their future health status. **Objective:** To describe the characteristics of healthy nutrition interventions aimed at university students according to the socio-ecological model. **Methods:** A scoping review was conducted following the PRISMA guidelines. Search strategies were developed using the SPIDER framework. Relevant studies published from January 2015 until May 2023 were retrieved from four databases: Embase, Medline, Scopus, and Google Scholar. An amended version of the socio-ecological model, which interplays between various factors including micro-level (intrapersonal, interpersonal), meso-level (setting), and macro-level (societal) nutrition interventions was used as a framework to report findings. **Results:** 28 studies were included; 15/28 studies were conducted in the US and 16/28 were randomized controlled trials. Interventions targeting the micro-level factors were most frequently applied (n=19). A small number of studies combined factors from different levels; however, no studies reported interventions combining micro- and macro-level factors. The educational interventions were the most common at the micro-level: providing health information through classes (n=10) and enhancing hands-on cooking skills (n=3). While providing healthier choices with promotional signs were common at the meso-level, nutritional labelling and pricing and marketing strategies were deployed at the macro-level. **Discussion:** The socio-ecological model could provide a clear and consistent framework for understanding healthy nutrition interventions among university students on campus. Further research is required to design macro-level interventions to promote healthy dietary behaviour at the population level.
Primary Supervisor: Dr Chen, Y

P9

Development and validation of a stability indicating HPLC method for tonabersat assay

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Background: Tonabersat is a novel cis benzopyran derivative with potential applications in managing ocular diseases like uveitis and diabetic retinopathy. However, its poor solubility poses formulation challenges for ocular drug delivery. Additionally, the chemical stability of Tonabersat within dosage forms is poorly understood.**Objective**: The present study aimed to develop and validate a rapid stability indicating HPLC method for the assay of Tonabersat. **Methods:** A reverse-phase HPLC method was developed using a Kinetex® C18 column equilibrated at 50 °C with gradient elution of acetonitrile and water at a flow rate of 0.5 mL/min. Tonabersat and its degradation products were detected at 275 nm. The analytical method was used to analyze Tonabersat forced degradation samples and was validated for specificity, accuracy, precision, linearity, limit of quantitation (LOQ), limit of detection (LOD), and robustness as per the International Conference for Harmonization's guidelines.**Results:** The method showed good linear regression (R2=0.99995) in the range of 0.5-200 µg/mL, with the LOD and LOQ being 0.8 µg/mL and 5 µg/mL, respectively. Intra-day and inter-day precision was less than 2% and 5%, respectively, while method accuracy was 97.0% to 102.2%. Significant drug degradation was observed in acidic, alkaline, and oxidative conditions, while on exposure to photolytic, thermal, and hydrolytic stress, the drug remained stable. **Discussion**: The developed assay method is rapid and stability-indicating with adequate precision and accuracy. This method will now be used to measure drug stability in eyedrop formulations. The degradation studies provide useful information for the formulation development of Tonabersat.

Primary Supervisors: Assoc Prof. Rupenthal, I and Dr Agarwal, P

P10

Genetic determinants of sensitivity and resistance to HER2-targeting antibody drug conjugates

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Background: Trastuzumab deruxtecan (T-DXd, Enhertu) and trastuzumab duocarmazine (SYD985) are HER2-targeting antibody drug conjugates (ADC) that have demonstrated high antitumour activity in HER2-positive and HER2-low metastatic breast cancer. TDXd and SYD985, both being second-generation ADCs have demonstrated their 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. The lack of research on the mechanisms of resistance to T-DXd and SYD985 necessitates further exploration in this area. **Objectives:** To identify genetic determinants of sensitivity and resistance to HER2-targeting ADCs and understand the bases underlying these resistance mechanisms. **Methods:** We performed a whole-genome Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)/Cas9 screen in HER2+ breast cancer cell lines transduced with the MinLibCas9 library. Transduced cells were exposed to T-DXd, SYD985 biosimilar and their respective cytotoxic payloads for 30 days. Genomic DNA was extracted and subjected to Next-generation sequencing (NSG). **Results:** Sequencing identified gene knockouts enriched or depleted in response to ADC or payload treatment in each cell line. **Discussion:** The response genes responsible for ADC sensitivity and resistance can act as predictive biomarkers to identify patients most likely to benefit from ADC therapy. Additionally, the proteins encoded by the response genes and their downstream pathways present novel drug targets, providing an effective approach to overcome resistance to HER2-targeting ADCs.

Primary supervisor: Assoc Prof. Jamieson, S

P11

In vivo imaging of developmental neural activity in postnatal mice

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Background: During the first three postnatal weeks the mouse brain undergoes major developmental rewiring that establishes the neural circuitry seen in the adult brain. Alterations during this period contribute to the miswiring of neural connections and lead to circuit dysfunction. Therefore, studying neural activity during this period is important for understanding the mechanisms of circuit dysfunction associated with neurodevelopmental disorders such as autism spectrum disorder. Recent advancement in widefield *in vivo* calcium imaging have paved way for a novel method to study neural activity in developing neonatal mice. **Objectives:** To record widespread spontaneous neural activity in the developing cortex of postnatal mice using mesoscopic *in vivo* calcium imaging. **Methods:** Mice at postnatal day 1 were transfected with the genetically encoded calcium indicator, GCaMP7 by injection into the transverse sinus. Fluorescence intensity changes that reflect neuronal activity, were recorded from sedated neonatal mice at postnatal day 8-10 under a custom-built mesoscope. **Results:** The method of injecting GCaMP into the transverse sinus to transfect neurons and imaging under the mesoscope showed clear cortex wide neural activity. At this age, distinct activity patterns associated with neural circuitry refinement was observed in different regions of the neonatal brain. **Discussion:** We demonstrate that the use of a recently established imaging technique is capable of *in vivo* calcium imaging of developing neural activity in neonatal mice. This novel method for visualising neural activity has enabled our current investigation into mechanisms of neural circuit dysfunction in a mouse model of autism spectrum disorder.

Primary Supervisor: Dr Cheyne, J

P12

The power of words and its effect on older people

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Background: Negative media coverage of older people has been consistently observed and was exacerbated during the Covid-19 crisis. Older people were consistently designated as a high-priority, at-risk group for Covid-19. **Objectives:** We will examine the portrayal and representation of older people in the media during the Covid-19 pandemic, with a specific focus on vulnerability. We explore the potential consequences of labelling older individuals as vulnerable during the pandemic. **Methods:** A qualitative media analysis approach was employed to achieve the research question which is to understand how older people and vulnerability is deployed and conceptualised within media discourses. A Critical Discourse Analysis (CDA) also served as the framework for the analysis, allowing for a critical examination of language use in the media and exploring power dynamics and the relationship between language and ageism. **Results:** We have identified four prominent themes through which vulnerability was portrayed in the media: risk, protection, caution, and resources. **Discussion:** These findings have implications for age-inclusive practices, policy development to combat ageism, and further research on media influences on ageing. Understanding how media messages contribute to ageist attitudes and stereotypes enables practitioners to develop strategies to challenge negative perceptions and promote positive ageing narratives. By challenging negative stereotypes and promoting more nuanced representations of older people, this research contributes to the creation of a more inclusive and age-friendly society.

Primary Supervisor: Assoc Prof. Wiles, J

P13

WITHDRAWN

P14

Development of Vaccines against Gonococcal Disease using the PilVax Platform

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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 in particular 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), adhesin complex protein (Ng-ACP), Transferrin binding protein A (TbpA), the uncharacterized protein NGO2054 and a peptidomimetic of LOS have previously raised interest as potential vaccine targets for gonorrhoea. Those peptides were genetically engineered into two different exposed loop regions of the backbone protein of the *Streptococcus pyogenes* pilus (a hair-like surface structure) and expressed in the food-grade bacterium *Lactococcus lactis*. BalbC mice will immunised intranasally with the modified *L. lactis* bacteria. Antibody responses (serum IgA/IgG) and IgA responses in BAL fluid and saliva will be evaluated by 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 both loop regions of the pilus backbone protein and expression in *L. lactis* was confirmed by Western blot and flow cytometry. **Discussion:** PilVax is a promising novel vaccine platform to induce mucosal responses against selected peptides or short proteins. If successful, this project might lead to a vaccine candidate that could be further evaluated in clinical trials.

Primary supervisor: Prof. Proft, T

P15

Investigating the Neurosteroid Withdrawal Hypothesis of Pericatamenial Epilepsy using Visual Long Term Potentiation

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Background: Fluctuations in sex steroids across the menstrual cycle are associated with cyclic functional brain changes in health and disease. The withdrawal of neuroprotective progesterone/allopregnanolone around menstrual onset is thought to be implicated in seizure exacerbation in 40% of females with epilepsy, a disorder termed pericatamenial epilepsy (PCE). **Objectives:** Measure changes in visually induced long-term potentiation (LTP) across the menstrual cycle to investigate changes in oestradiol-related excitation versus progesterone-related inhibition. **Methods:** Visually induced LTP was recorded using electroencephalography in 25 healthy females during the perimenstrual, mid-follicular, and mid-luteal phases. Visual LTP was assessed as changes in visual evoked potential (VEP) amplitude after high-frequency stimulation (tetanus). This will later form the comparison group of the main analysis between females with epilepsy with and without catamenial exacerbation. **Results:** LTP occurred in the P2 VEP component in the late post-tetanus condition ($p < 0.001$ FWE-c). P2 modulation was greater during the mid-follicular phase, where both sex steroid levels are the lowest, than the perimenstrual phase, which also has low hormone levels but is associated with neurosteroid withdrawal. **Discussion:** Lower LTP modulation during the perimenstrual phase could be attributed to dominating effects of allopregnanolone-related GABAergic inhibition. Rodent literature suggests PCE might be driven by reduced GABAergic inhibition. Thus, we expect the opposite change in LTP in the PCE cohort, where LTP modulation will be greater during the perimenstrual phase than the mid-follicular and/or mid-luteal. This will be the first direct investigation of the neurosteroid withdrawal theory of PCE in humans.

Primary Supervisor: Dr Sumner, R.

P16

Dopaminergic Retinal Neurons in a Dopamine Transporter Knockout (DAT-KO) Model

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Background: Attention-Deficit Hyperactivity disorder (ADHD) is a neurodevelopmental disorder with neurotransmitter activity alterations. Although its pathophysiology is not fully understood, dysfunctional dopamine transporters and impaired neurotransmission have been implicated. The Dopamine Transporter Knockout (DAT-KO) model shows disrupted dopamine levels, which represents ADHD-related neurochemical changes. The retina contains dopaminergic cells that produce dopamine that can be measured to proxy the diagnosis of ADHD. **Objectives:** To investigate dopaminergic retinal neurons by measuring dopamine production and assessing neurochemical changes. **Methods**: Fast- Scan Cyclic Voltammetry (FSCV) was used to measure and compare retinal dopamine levels in the DAT-KO and DAT-Wildtype (WT) retinal tissues. The rat eyes were enucleated and retinal tissues placed in artificial cerebrospinal fluid solution bubbled with carbogen gas. Carbon Fiber microelectrodes (CFM; 100 µm) for the FSCV study, were produced and calibrated to identify electrode sensitivity for dopamine levels measurement. The CFM was slowly lowered into central and peripheral regions of the retina tissue at different depths, A nearby stimulating electrode was used to evoke dopamine release that was recorded. **Results:** In DAT-KO rats, retinal dopamine levels were found to be considerably higher in the central retinal region (1848 ± 185 nM) than the peripheral region (89 ± 27 nM). Interestingly, in DAT-WT, dopamine levels in the central region were reduced (1251 nM). **Discussion:** Dopamine measured in the retinal tissues using FSCV shows difference between DAT-KO and DAT-WT, and may provide objective parameters that serve as a biomarker for ADHD.

Primary Supervisors: Assoc Prof. Acosta, M and Dr Freestone, F

P17

Faecal microbiome transplants leave footprints in the plasma metabolome.

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Background: Gut microbes affect processes in their hosts far beyond the organ they inhabit. The mechanisms allowing them to do so are diverse and often poorly understood. Many microbes metabolise compounds fed to them through the host or from the exogenous environment and form small (<1500 AMU) metabolites distinct from the host's endogenous metabolome. Many microbially derived metabolites [MDMs] are produced by different microbiota. Many MDMs are found in circulation and have effects, positive or negative, upon host appetite, metabolism and adipogenesis. Faecal microbiota transfer [FMT] is a procedure where microbiota isolated from a healthy donor stool is transplanted into a recipient to partially replace and remediate problems associated with a dysbiotic gut microbiome. The GutBugs Trial is a double-blinded, randomised, controlled trial investigating the effects of FMT treatment on obese adolescents. **Objectives:** To identify metabolites that correlate with resolution of metabolic syndrome (high waist circumference, blood pressure, plasma lipids and glucose) and weight loss following FMT. **Methods:** We used liquid-chromatography with mass spectrometry to apply an untargeted-metabolomic approach to the serum of trial participants to investigate changes in the abundance of MDMs with phenotypic changes seen in participants. **Results:** At four years post-FMT, treatment was associated with weight loss, reduction in fat mass and improvement in metabolic syndrome. We identified 3,258 (ms^2 acquired) metabolites and annotated 656. Sixty-one metabolites varied significantly with FMT-treatment over four years. **Discussion:** These findings may provide mechanistic links between metagenomic and taxonomic changes in the microbiome and clinical outcomes of the GutBugs Trial.

Primary Supervisor: Dr Pook, C.

P18

How the primary cilium influences chondrocyte phenotype and energy metabolism

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Background: The primary cilium is an important mechanochemical sensory organelle of the cell. Defects in primary cilium results in systemic growth and metabolic disorders, but effects on energy metabolism at the cellular level are less well studied. **Objectives:** To characterise differences in energy metabolism and phenotype between *Tg737^{ORPK}* (primary cilia-mutant murine chondrocyte cell line) and wild type (WT) in 2D culture. **Methods:** *Tg737^{ORPK}* and WT cells were cultured in serum-free media for two days to encourage primary cilium expression on the cell surface. primary cilium expression was confirmed with fluorescence microscopy. Cell lysates were collected for mRNA and protein expression analysis and compared via qPCR and western blot. OCR (oxygen consumption rate) and ECAR (extracellular acidification rate) were assessed by dual TR-FRET. **Results:** *Tg737^{ORPK}* cells were ciliated at approximately half the frequency of WT cells. qPCR showed *Tg737^{ORPK}* cells expressed significantly lower *Col2a1, Col10a1* and *Adamts5* than WT ($p < 0.001$, $p = 0.006$, and $p = 0.005$). *Sox9,* expression was lower in *Tg737^{ORPK}* cells at the mRNA level ($p = 0.023$), but higher in *Tg737^{ORPK}* cells at the protein level ($p = 0.004$). Preliminary data suggests reduced ECAR in *Tg737^{ORPK}* cells. **Discussion:** *Tg737^{ORPK}* cells are phenotypically different from WT cells. Preliminary ECAR suggest that WT murine chondrocytes with an intact primary cilium favour glycolysis over oxidative phosphorylation. As chondrocytes have adapted to grow in cartilage which is avascular, the results imply that the primary cilium is important for a chondrocyte's ability to metabolise energy independent of oxygen availability.

Primary Supervisor: Dr Poulsen, R

P19

A cell-based platform for studying the effects of ultrasound on neurons following stretch injury

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Background: Ultrasound has the potential to promote neuronal regeneration following injury. However, experimental setups evaluating ultrasound in cell models face difficulty in being translated *in vivo*. This is because conventional cell culture vessels lack acoustic transparency, making it challenging to determine how the used ultrasound parameters will perform *in vivo*. Setups using immersible acoustically transparent cell culture vessels address these issues and confer ready extrapolation of findings to *in vivo* models. **Objectives:** To develop and characterise an immersible acoustically transparent chamber for exposing injured neuronal cells to ultrasound. **Methods:** A polydimethylsiloxane (PDMS) chamber for neuronal cell culture was designed. The acoustic transparency of the chamber was evaluated using a hydrophone and oscilloscope. The suitability of the chamber for sterile cell culture was evaluated using a leakage assay. Finally, SHSY5Y cells were cultured in PDMS microchannel wells, housed in the PDMS chamber to induce strain injury for future analyses of ultrasound effects on nerve injury. **Results:** An acoustically transparent chamber was developed with ultrasound traveling through the system, unperturbed, which was in stark contrast to conventional cell culture vessels. The chamber demonstrated no evidence of leakage and could successfully grow neuronal cells with no contamination. **Discussion:** We have successfully developed a chamber suitable for culturing cells and studying ultrasound effects in neuronal injury. Ongoing studies aim to induce strain injury within the cultured cells and subsequently evaluate axonal regeneration in the absence and presence of ultrasound. The designed device will provide valuable insights into establishing appropriate ultrasound parameters for neuronal regeneration.

Primary Supervisor: Dr Thakur, S

P20

Factors influencing the development of metabolic syndrome in patients prescribed a second-generation antipsychotic: Systematic review/Meta-analysis.

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Background: The relative risk of metabolic syndrome in patients with serious mental illness is ~2-3 times higher than that of the general population. The psychosocial factors most responsible for this relationship are poorly understood. **Objectives:** To identify the main contributory factors in the metabolic syndrome and serious mental illness relationship, in those patients who are on second generation antipsychotics, which is currently the first line treatment for said condition. **Methods:** We conducted a systematic review using the PRISMA guidelines [PROSPERO registration (CRD42023426231)]. We searched the following databases; MEDLINE, EMBASE, PsycINFO and the Cochrane library. We included studies that reported at least one of our prespecified outcomes. Studies were only eligible for inclusion if: ≥70% were on a second generation antipsychotic(s) and ≥70% had a diagnosed serious mental illness. **Results:** The search yielded 4202 total records, 25 articles were able to be used for final analysis. We have found that there is no consistent way to measure the main psychosocial variables associated with the development of metabolic syndrome in patients on second generation antipsychotics. There is weak evidence to suggest that engaging in physical activity reduces your risk of developing metabolic syndrome [OR=-0.34; 95% CI -0.54,-0.14]. Whilst not being in a relationship increases your risk of developing metabolic syndrome [OR=1.39; 95% CI 1.14,1.69]. **Discussion:** We believe that the Health Promoting Lifestyle Profile-II tool has the best evidence for identifying the psychosocial factors affect the development of metabolic syndrome in patients with serious mental illness.

Primary Supervisor: Dr Djurkov, A

P21

The Patient Experience of Gout Remission: A Qualitative Study

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Background: Preliminary remission criteria for gout have been developed. However, the patient experience of gout remission has not been described. **Objectives:** This qualitative study aimed to understand the patient experience of gout remission and views about the preliminary gout remission criteria. **Methods:** Semi-structured interviews were conducted. All participants had gout, had not had a gout flare in the preceding six months, and were on urate lowering medication. Participants were asked to discuss their experience of gout remission and views about the preliminary remission criteria. Interviews were audio recorded and transcribed verbatim. Data were analysed using a reflexive thematic approach. **Results:** Twenty participants with gout (17 male participants, median age 63 years) were interviewed. Four key themes of the patient experience of remission were identified: 1) minimal or no gout symptoms (absence of pain due to gout flares, good physical function, smaller or no tophi); 2) freedom from dietary restrictions; 3) gout is 'not on the mind'; and 4) multifaceted management strategies to maintain remission (regular urate lowering therapy, exercise, healthy eating). Participants believed that the preliminary remission criteria contained all relevant domains but considered that the pain and patient global assessment domains overlapped with the gout flares domain. Participants regarded 12 months as a more suitable timeframe than six months to measure remission. **Discussion:** Patients experience gout remission as a return to normality with minimal or no gout symptoms, dietary freedom, and absence of mental load. Patients utilize a range of management strategies to maintain gout remission.

Primary supervisor: Prof. Dalbeth, N

P22

Strategies for delaying diabetic cataracts: Developing a bovine model to understand changes associated with hyperglycaemia

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Background: In diabetic cataracts, hyperglycaemia-induced oxidative stress is proposed to damage ion transporters that regulate cell volume, resulting in characteristic cell swelling and cortical opacity. Evidence indicates that excess glucose metabolism via the polyol pathway generates sorbitol and fructose and is the source of this oxidative stress. Drugs that target polyol activity are used successfully in canines to prevent diabetic cataract, but do not work in humans, most likely due to differences in polyol pathway enzyme activity between species. An animal model more similar to humans, such as bovine, could help lead to development of successful treatments. **Objectives:** To assess the suitability of bovine lenses incubated in high glucose as a model for human diabetic lenses. **Methods:** Reverse Transcriptase-Polymerase Chain Reaction and subsequent DNA sequencing using targeted primers against key volume regulatory ion transporters, including KCC1-4, NKCC1-2, was performed on RNA isolated from human and bovine lenses. Gas chromatography-mass spectrometry determined levels of glucose, sorbitol, fructose and the antioxidant glutathione in the different regions of control or high glucose incubated bovine lenses. **Results:** Bovine and human lenses both contain KCC1, 3 and 4, and NKCC1. High glucose incubated lenses contained elevated levels of glucose, sorbitol and fructose and decreased levels of glutathione in the outer regions of the lens compared to control lenses. **Discussion:** These findings mimic changes observed in human diabetic cataracts suggesting that this bovine model may be useful for the study of hyperglycaemia-induced oxidative stress and loss of cell volume regulation in diabetic lenses.

Primary Supervisor: Assoc Prof. Lim, J

P23

Characterising the obese osteoarthritic phenotype: Developing a novel protocol for spatial lipidomics analysis of cartilage

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Background: Obesity is a major risk factor for osteoarthritis (OA) due to joint loading and systemic inflammation. A characteristic of obesity is lipid accumulation although the role of lipids related to obesity and inflammation in OA remains poorly understood. This study aims to use un-targeted MALDI-IMS (matrix-assisted laser desorption/ionisation-imaging mass spectroscopy) to spatially and quantitatively profile lipids in human knee OA cartilage. **Objectives**: 1) Develop a protocol for sectioning non-decalcified human OA cartilage suitable for MALDI-IMS and histology 2) Optimise section preparation (matrix sublimation testing) and imaging parameters that yield the greatest lipid ionisation in the range of 100–2000Da. **Methods:** Human tibial plateau were obtained with consent from patients undergoing knee replacement. Tape-stabilised tissue cryosectioning was optimised for temperature and tissue thickness and applied to two types of slides compatible with MALDI-IMS and histology. Ammonium formate (AmF) pre-treatment, three matrices, and ion-polarity modes were optimised and compared for lipid ionisation using MALDI-IMS. Qualitative data analysis with five criteria and bioinformatics were used to determine which combination provided the greatest lipid ionisation with the lowest signal-to-noise ratio. **Results:** A combination of cryofilm-stabilised sections on copper slides yielded flat sections stable for MALDI-IMS. Normharmane matrix/AmF improved lipid ionisation in negative-ion mode. Matrices - 1,5-diaminonapthalene (DAN), 2,5-dihydroxybenzoic acid (DHB) without Amf improved ionisation in both ionisation modes. DAN was more favourable for lipid ionisation and downstream lipidomics analysis. **Discussion:** A protocol was developed that allows native cartilage-on-bone to be sectioned to allow optimal ionisation for spatial lipidomic imaging and analysis using MALDI-IMS.
Primary Supervisor: Assoc Prof. McGlashan, S

P24

Development of hypoxia-activated prodrugs of second generation analogues of bedaquiline for treatment of latent Tuberculosis

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Background: Latent tuberculosis (TB) is one of the mechanisms of TB virulence. Granulomas are the pathological hallmark of latent TB that are formed when the adaptive immune system contains *Mycobacterium tuberculosis* (Mtb). These granulomas are hypoxic, affecting delivery of TB drugs. This highlights the need to target Mtb in hypoxic granulomas. Bedaquiline is a novel drug approved in 2012 for resistant TB. While it demonstrates potency against Mtb, bedaquiline may not penetrate granulomas. Other adverse effects have led to the development of better second generation analogues TBAJ-587 and TBAJ-876. However, these compounds may also not penetrate granulomas due to structural similarities to bedaquiline. **Objectives:** To develop and explore hypoxia activated prodrug (HAP) strategy to deliver bedaquiline, TBAJ-587, and TBAJ-876 selectively to hypoxic granuloma regions. **Methods:** Protocols for the synthesis of HAPs of bedaquiline, TBAJ-587, and TBAJ-876 are developed through exploring different synthetic routes. **Results:** Various reaction conditions were screened and optimized to synthesise nine HAPs of TBAJ-587. **Discussion:** A synthetic route was established for the synthesis of HAPs. This strategy can be applied to other TB drugs to form HAPs for extending their utility in treating latent TB. Anti-TB activity testing of the compounds will be carried out on Microplate Alamar Blue Assay (MABA) and Low-Oxygen Recovery Assay (LORA). Comparing susceptibility data for bedaquiline, TBAJ-587, and TBAJ-876 with that of corresponding HAPs will facilitate measurement of the effectiveness of hypoxia-mediated release. If the prodrugs show selectivity towards hypoxic regions, this will provide insights into using HAP strategies for TB treatment.
Primary Supervisor: Dr Choi, P

P25

Developing Novel Therapeutics for Glioblastoma

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Background: Glioblastoma (GBM) is the most common and malignant primary brain tumour in adults. The prognosis is poor, with various barriers impeding the development of effective therapies to improve patient survival. A class of near-infrared heptamethine cyanine dyes (HMCD) can cross the blood-brain barrier and selectively target tumour cells, showing promising potential as a brain-drug delivery molecule to increase therapeutic bioavailability in the brain. This allows the potential repurposing of anticancer agents that previously lacked efficacy in treating GBM. **Objectives:** To screen and identify potent HMCD conjugate compounds and explore HMCD's photo-active properties for aiding development of novel GBM therapies. **Method:** Several HMCD compounds attached to different tyrosine kinase inhibitors (HMCD-TKI conjugates) were synthesised and screened on patient-derived primary GBM cells and commercially available GBM cell lines. Concentration-response curves for cell count, proliferation, and cell death were generated via *in vitro* assays. Additionally, the possibility of near-infrared photo-activation-induced cytotoxic activity was tested. **Results:** In most cases, HMCD-TKI conjugates had enhanced cytotoxic activity, with some producing a 200-fold increase in potency (nanomolar EC_{50} values) compared to their parent HMCDs or TKIs. We also have data showing that 6 hours of near-infrared light activation of a lead HMCD-TKI compound could double the cytotoxic activity compared to the no-light control. **Discussion:** HMCDs are a promising molecule for improving TKI cytotoxicity in GBM cells and show photo-activation properties that could further enhance their potencies and effectiveness. Therefore, investigating the potential of HMCD conjugation with light activation could provide novel approaches to developing GBM treatments.

Primary Supervisor: Dr Park, T

P26

Predicting cardiovascular risk across whole populations using administrative data, laboratory results and deep learning

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Background: Risk prediction equations are an established tool to inform clinical decisions about preventing cardiovascular disease (CVD). Certain equations can be applied across entire populations to inform population-based CVD prevention efforts. Our team have employed deep-learning approaches to create powerful equations trained entirely on national administrative datasets. However, the performance of these models is limited by the number of predictors available at a population level. A recent data-sharing effort means all laboratory test results in Auckland and Northland have become available to help train better-performing risk prediction models. **Objectives:** Determine the impact of adding routinely collected laboratory tests to deep-learning-based administrative-data-based risk prediction equations. **Methods:** Estimated glomerular filtration rate, haemoglobin A1C and total cholesterol: high-density lipoprotein ratio results were extracted for all individuals aged 30-75 years in Auckland and Northland (23,467,297 tests across 819,281 people). Results were individually linked to administrative CVD risk predictor data and demographic information. Sex-specific deep learning models were trained to estimate 5-year and compared to similar models trained without biochemical variables. **Results:** The addition of biochemical predictors moderately improved model performance across all assessed measures of calibration and discrimination. Subpopulation analysis also showed improved calibration in certain ethnic and age-based subpopulations. **Discussion:** These results show that using laboratory test results improves the performance of administrative-data-based equations, notably for certain ethnic subpopulations in which previous models underperformed. This demonstrates the untapped potential of several available but currently unlinked databases and will help inform future data extraction and model development efforts.

Primary Supervisor: Prof. Jackson, R

P27

Unlocking the Secrets of Shark Cartilage

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Background: Cartilaginous fishes (sharks, rays, and skates) have thrived for over 400 million years with skeletons composed purely of cartilage. Research has focused on the mineralised layer overlying the unmineralized cartilage as a biomaterial, however, the unmineralised core and its resident cells have received less attention, despite indications that this tissue exhibits self-regeneration, continuous growth, and anti-cancer properties. **Objectives:** To understand the biology of the unmineralized cartilage, the study aims to: (1) to optimise novel chondrocyte culture methods (2) to perform histological and proteomic analysis of shark cartilage. **Methods:** Cartilage was removed from the pectoral girdle of a dogfish shark, *Squalus Acanthias* (n=1). To isolate chondrocytes from the extracellular matrix, the cartilage was digested in collagenase overnight. Isolated cells were either cultured on plastic or seeded in 3D agarose gels then cultured in media supplemented with urea and NaCL at 24°C in hypoxic conditions. Viability was assessed using Trypan Blue exclusion assay or LIVE/Dead assay. Histology and MALDI imaging development are currently ongoing. **Results:** Isolated chondrocytes remained viable (>96%) following isolation and adhered to plastic after 72h. Cells remained viable for 3 passages over 12 weeks and exhibited a fibroblast-like morphology. Interestingly, cells accumulated extensive intracellular vesicles with each passage. Chondrocytes cultured in agarose showed a reduced viability despite being a more phenotypic culture model. **Discussion**: This is the first study to isolate and maintain shark chondrocytes in culture. This work lays the foundation for investigating the properties of shark chondrocytes and their potential unique properties related to cartilage repair.
Primary Supervisor: Assoc Prof. McGlashan, S

P28

Examining structural plasticity within human heart neurons and its role in Atrial Fibrillation

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Background: Atrial fibrillation (AF) is the most prevalent pathological atrial arrhythmia, raising the risk of stroke, heart failure and dementia. Neuronal clusters termed ganglionated plexi (GP) located in epicardial adipose tissue on the myocardium have been implicated in AF arrythmogenesis. How GP are linked to AF is unknown. **Objectives:** To examine structural neuronal changes occurring in GP with AF. **Methods:** Epicardial adipose tissue samples containing the right atrial GP were resected AF and non-AF patients undergoing open heart surgery. Samples were fixed for large tissue custom line scanning stage confocal imaging to enable visualisation of entire human GP for the first time. CUBIC, hydrophilic, and hydrophobic clearing methods, followed by immunohistochemistry were used to visualise GPs. **Results:** Structural heterogeneity was observed at tissue, cellular and subcellular levels, with GP varying in volume and number of neurons (95.5±91.6 cell bodies [mean±SD]). GP neurons from AF and non-AF patients could be distinguished by the differential distribution of both neuronal area (*p=0.0051*; non-AF 877±10 μm^2; AF 836±11 μm^2 [mean±SEM) and synapse volume (*p<0.0001*; non-AF 2.57±0.034μm^3; AF 2.82±0.032 μm^3 [mean±SEM]), suggesting AF-related changes in synaptic structure and cell morphology that could reflect differences in neuron communication both within and between GP. Multiple GP cellular phenotypes were detected, including predominant cholinergic neurons, noradrenergic neurons (12.1±11.1% [mean±SD]), small intensely fluorescent cells, and a novel sensory neuron population (39.0±20.9% [mean±SD]). **Discussion:** Phenotypic and synaptic changes occur with AF, together identifying structural plasticity occurs in GP neurons in AF patients that could link to potential causation pathways.
Primary supervisor: Prof. Montgomery, J

P29

Exploring chronic low-grade inflammation-associated white matter alterations in major depressive disorder

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Background: Chronic low-grade inflammation is thought to play a role in worsening the symptoms of major depressive disorder (MDD) and hampering the response to antidepressant treatments. Diffusion kurtosis imaging (DKI) has been shown to provide sensitive measures of inflammation inside the brain and be lowered in MDD compared to controls. **Objectives:** This pilot study examines differences in DKI metrics in the white matter of individuals with major depressive disorder, stratified by the presence or absence of chronic low-grade inflammation, and healthy controls. **Methods:** Ten patients with MDD and CRP≤1 mg/L (low-inflammation group), four with MDD and CRP ≥3mg/L (high-inflammation group), and nine healthy controls with CRP ≤1mg/L underwent DKI. DKI metrics in white matter tracts were analysed using tract-based spatial statistics. A one-way ANOVA test was applied across the three groups to reveal clusters of significant group effects. **Results:** Clusters of significant group effects for radial and mean kurtosis were identified in areas including the left anterior corona radiata and left inferior fronto-occipital fasciculus. Post-hoc t-tests indicated that within these areas, there was lower radial kurtosis in the high-inflammation MDD group compared to the low-inflammation MDD group. **Discussion:** This study highlights the role of DKI as a marker of the effects of chronic low-grade inflammation on the brain in MDD. These findings warrant further investigation in larger cohorts to assess their clinical implications; DKI metrics like mean kurtosis and radial kurtosis may potentially be able to identify patient subgroups and target those who may benefit from anti-inflammatory treatment in MDD.
Primary Supervisor: Dr Lin, J

P30

Assessing the dynamics of horizontal gene transfer after faecal microbiota transplantation in obese adolescents

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Background: Horizontal gene transfer (HGT) describes the transmission of DNA outside of direct ancestral lineages. The process is best characterised within the bacterial kingdom and can enable the acquisition of genetic traits that support bacterial adaptation to novel niches. The adaptation of bacteria to novel niches has particular relevance for faecal microbiota transplantation (FMT), a therapeutic procedure which aims to resolve gut-related health conditions of individuals, through transplanted gut microbiota from healthy donors. **Objectives:** Assess the impact of HGT in the gut microbiomes of FMT recipients from The Gut Bugs Trial (Liggins Institute), before and after treatment. **Methods:** HGT events across FMT and placebo recipient metagenomic samples were assessed using two complementary methodologies. First, all tentative HGT events, including historical HGT signatures, were quantified using the bioBakery tool WAAFLE. Second, metagenomic assembly and gene clustering were used to assess and quantify donor-specific genes transferred to recipients following the intervention. **Results:** Both methodologies found no difference between the level of tentative HGT events in the gut microbiomes of FMT and placebo recipients, post-intervention. **Discussion:** Quorum sensing molecules produced by bacteria are known to influence the efficiency of HGT. The pre-intervention bowel cleanse administered in the Gut Bugs Trial may have reduced the host bacterial population below a threshold, that subsequently hindered quorum sensing mediated HGT. Therefore, we hypothesise that analysis of an additional FMT trial dataset with no participant bowel cleanse will show a disparity in the levels of HGT between FMT and placebo recipients, post-intervention.
Primary Supervisor: Prof. O'Sullivan, J

P31

The Acute Effects of Clozapine and Valproate on the Heart

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Background: Clozapine (CLZ) is the only available treatment for treatment-resistant schizophrenia. Although highly effective, CLZ is also associated with adverse effects like cardiotoxicities, including myocarditis and cardiomyopathy. CLZ-induced cardiotoxicities occur in 1 to 4 % of patients but are among the most deadly of CLZ's adverse effects. Adjunct sodium valproate (VPA) treatment has been identified as a risk factor in the development of cardiotoxicity. The mechanism(s) behind CLZ-induced cardiotoxicities are largely unknown although there are suggestions of altered mitochondrial function. **Objective:** To assess the acute effects of CLZ and VPA on mitochondrial function in human heart tissue. **Methods:** Right atrial samples from consenting patients undergoing surgery at Auckland Hospital were obtained. Bundles (~5 mg) of cardiac muscle fibres were dissected and permeabilised for direct mitochondrial exposure to treatments, including high doses of CLZ (5000 ng/mL) and VPA (1000 µg/mL). Oxygen consumption alongside hydrogen peroxide production from the fibres was measured using high resolution respirometry and fluorometry with sequential titration of substrates, uncouplers, and inhibitors to determine the effect of each treatment on various respiratory states and pathways. **Preliminary findings:** Both acute CLZ and VPA seem to decrease oxygen flux during oxidative phosphorylation through complexes I and II (CLZ: 38.08 pmol/s/mg, SEM=4.72, n=7; VPA: 40.60 pmol/s/mg, SEM=1.048, n=6) compared to control (54.32 pmol/s/mg, SEM=7.34, n=7) though this is not statistically significant (CLZ: $p = 0.06$, VPA: $p = 0.20$). **Discussion:** While further investigation is necessary, these findings provide some insights into the effects of CLZ and VPA on mitochondrial function.
Primary Supervisor: Dr Ward, M

P32

The Contraceptive Conundrum: The Influence of Systemic Hormonal Contraception on Functional Gastroduodenal Symptoms

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Background: Patients with functional gastroduodenal (FGD) diseases experience nausea, vomiting, bloating, without evidence of organic or structural causes. Females with FGD diseases are more likely to use systemic hormonal contraception (SHC); however, the effect of progesterone and estrogen on their symptoms remains controversial. **Objectives:** To evaluate the influence of systemic hormonal contraceptives on FGD symptoms. **Methods:** Patients used 0-10 Likert scales on a validated symptom logging App to continuously report symptoms during non-invasive gastric mapping (Gastric Alimetry). Analysis was performed using a large, collaborative database of patients who met ROME IV criteria for chronic nausea and vomiting syndrome or functional dyspepsia. **Results:** 120 patients were included; pre-menopausal women were divided into SHC users (n = 23) and non-SHC users (n = 43). Post-menopausal (n = 30) and male (n = 24) patients were controls. On preliminary analysis, SHC and non-SHC users exhibited significantly higher symptom burdens than post-menopausal females and males ($p = 0.001$). Subgroup analysis and stratification by type of SHC revealed those on combined oral contraceptives (COC) with hormone-free intervals (HFI) had significantly higher nausea scores compared to continuous COC users (5.04 vs. 2.87, $p = 0.023$). The COC with HFI group demonstrated higher scores than contraceptive-free pre-menopausal women for nausea (5.04 vs. 3.61, $p = 0.022$) and reflux (4.0 vs. 1.19, $p = 0.007$). **Discussion:** Pre-menopausal women experience a disproportionate burden of FGD symptoms. COC's with HFI may exacerbate reflux and nausea; alternatively, continuous COC's could be evaluated to minimise symptom burden.
Primary Supervisor: Prof. O'Grady, G

P33

Microglial and astrocytic responses in the human midcingulate cortex in Huntington's disease

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Background: Huntington's disease (HD) is a neurodegenerative disorder that can cause motor, mood, and cognitive symptoms. Neuronal death in the cingulate cortex correlates with mood symptomatology. However, the contributors to pathology in this brain region and symptom presentation are not well understood. **Objectives**: To quantify the density of mutant huntingtin protein (mHTT) and neuroinflammatory glial changes in the midcingulate cortex of post-mortem Huntington's disease patients and determine if either correlates with the presentation of mood, motor, or mixed symptomatology. **Methods:** Using immunohistochemistry, post-mortem midcingulate cortex (MCC) tissue from HD and control cases were stained with fluorescent markers for mHTT, microglia, and astrocyte proteins: Connexin 43 and excitatory amino acid transporter 2 (EAAT2). Glial marker and mHTT density, alongside microglia morphology were quantified. **Results:** The results show microglia do not proliferate in HD, but transition from ramified states into activated morphologies in HD compared to controls ($p=0.001$). Activated microglia display close contacts with mHTT aggregates and the proportion of activated microglia positively correlate with mHTT burden ($p=0.001$). Astrocytes labelled with EAAT2 show decreased density ($p=0.0012$), size ($p=0.0054$), and percent area coverage ($p=0.0015$) in HD cases, particularly those associated with mood symptoms. **Discussion:** This data demonstrates the presence of glial changes and their association with both mHTT burden in the MCC and the presentation of symptomatology in HD. These findings are significant as they highlight the importance of glia in the presentation of HD, which can inform research into therapeutics addressing symptom management.

Primary Supervisor: Dr Mugisho, L

3-Minute Elevator Pitch - 505-011

EP1

Gastric electrical activity and histological effects of gastrointestinal anastomosis- a chronic animal study

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Background: Formation of a gastrointestinal anastomosis is a common technique performed in gastrointestinal surgery. While most patients recover well, some unfortunately develop gastric dysfunction without an obvious cause. Emerging evidence suggests gastric electrophysiological abnormalities, propagated by cells in the lumen of the gastrointestinal tract named Interstitial Cells of Cajal (ICC), may underlie these problems. **Objectives:** This study will assess electrophysiological changes across a gastrointestinal anastomosis and determine whether ICC regrowth occurs through the anastomotic scar tissue in a chronic pig model. **Methods:** 8 female weaner pigs underwent general anaesthesia, laparotomy and formation of gastrointestinal anastomosis. The pigs were then recovered for 2 weeks and a further laparotomy and high resolution gastrointestinal mapping was performed with specimens collected for histology. Gastric and intestinal slow wave direction, frequency, amplitude and velocity were obtained. Histology was also performed using ANO1 stains for ICC for the anastomosis. **Results:** Preliminary results confirm the presence of gastric slow waves present at 2 weeks post-operatively. Intestinal slow waves were observed, propagating retrograde through the anastomosis and into the stomach in at least 1 case. Histology also confirms the presence of ICC regrowth at the anastomosis. Full results to come. **Discussion:** Gastric dysfunction can occur following the formation of a gastrointestinal anastomosis. This study has now found retrograde intestinal waves travelling into the stomach through the anastomosis with presence of ICC at the anastomosis, thereby providing both an electrophysiological and histological explanation of the dysfunction. The research can now inform future research and treatment in this field.
Primary Supervisor: Prof. O'Grady, G

EP2

Dual Action Preservative Free Non-Aqueous Eye Drop: Revolutionizing Dry Eye Disease Treatment

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Background: Dry eye disease (DED) requires a comprehensive approach to address lubrication and inflammation. Conventional aqueous eye drops often fall short, as they may contain preservatives that can further irritate the eyes of DED patients. **Objective:** This study aimed to develop a dual-action, clear, non-aqueous, preservative-free eye drop formulation to treat dry eye disease. **Methods:** A non-aqueous solution of Tonabersat was prepared using different non-aqueous solvents. An HPLC method was developed and validated to detect Tonabersat and assess its stability. The optimised formulation was characterised through description and assay. Additionally, an ex vivo tissue penetration study was conducted using a whole eye globe with a flow model at a 15-minute time point. **Results:** Tonabersat demonstrated solubility of 7.1 mg/mL in medium-chain triglycerides, suitable for the desired therapeutic strength of 1 mg/mL. In the ex vivo tissue penetration study, the highest drug concentration was observed in the conjunctiva, followed by the eyelid and cornea, while no drug was detected in the retina and sclera-choroid after 15 minutes of exposure. **Discussion:** The developed clear, non-aqueous, preservative-free eye drop formulation addresses the limitations of traditional aqueous eye drops for DED treatment. Tonabersat solubility in medium-chain triglycerides allows for appropriate formulation strength. The validated HPLC method ensures accurate detection and stability assessment. The ex vivo tissue penetration study confirms the effective delivery of Tonabersat to target ocular tissues while minimising systemic exposure. This formulation shows promise for treating dry eye disease, but further studies are necessary to establish efficacy and safety.
Primary Supervisors: Assoc Prof. Rupenthal, I and Dr Agarwal, P

EP3

Decoding the non-coding genome in Parkinson's disease

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Background: Parkinson's disease (PD) is a complex neurodegenerative disease, characterized pathologically by the loss of dopaminergic neurons and the presence of Lewy bodies. One major challenge in PD research is the sporadic and complex nature of the disease. However, recent studies have identified variants associated with the risk of sporadic PD. We have further used Mendelian Randomisation (MR), a statistical tool, to identify putatively causal variants and their target genes. Understanding the mechanisms by which these variants, especially those in non-coding regions, contribute to PD risk is crucial for developing diagnostics, clinical interventions, and therapies. **Objectives:** To determine the target gene effects of PD-associated variants in pairs of isogenic clones containing either the major (Ref) or minor (Alt) allele at each variant site. **Methods:** CRISPR/Cas9 will be used to introduce single base changes (reflective of the PD variants) to the KOLF2.1J induced pluripotent stem cell (iPSC) line, creating isogenic pairs that differ only by the single base we are interested in. Genotypes will be confirmed using Sanger sequencing and off-target events will be checked using PCR and Sanger sequencing. The edited iPSC lines will then be differentiated towards PD-relevant cell types, such as cortical neurons. The allele-specific impact of these variants on gene expression will be investigated using total RNA sequencing. **Results:** We are currently producing the first CRISPR/Cas9 edited clones. **Discussion:** This study will elucidate the function and target genes of these variants in PD-relevant cells, bringing us closer to precision medicine for people with PD.

Primary Supervisor: Prof. O'Sullivan J

EP4

Optimising a protocol for the isolation and characterization of plasma extracellular vesicles

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Background: Extracellular vesicles (EVs) are small lipid membrane vesicles present in various biological fluids such as blood, urine, and plasma. EVs play crucial roles in various physiological and pathological processes. One of their essential functions is facilitating intercellular communication, allowing cells to exchange proteins, lipids, and genetic material. Potentially EVs hold significant promise as biomarkers for diagnosis and prognosis because of their stability and accessibility. However, an advancement is required to improve isolation techniques and standardisation of EVs. **Objectives:** This study aims to develop an optimal method to isolate and characterise EVs from blood samples. **Methods:** Plasma samples obtained by venous cannulation underwent pre-processing, EV isolation, and characterisation as per the guidelines of MISEV 2018. **Result:** Ultracentrifugation followed by size exclusion chromatography was employed to isolate EVs. The protein content of the isolated EVs was determined using a high-sensitivity BCA assay for which the EV protein concentration was determined as 20.30 ug/ul concentrated from Size Exclusion Chromatography fractions 15 and 16. The concentration of isolated EVs, were measured using nano-sight 300., a nanoparticle tracking analysis system. Furthermore, the isolated EVs were visualised through transmission electron microscopy. EV samples were characterised using western blot to identify EV markers such as CD9, CD81, and CD63 in contrast to non-EV markers like calnexin, GAPDH and GRP64. **Conclusion:** We foresee this work of optimising isolation and characterisation protocol to be used in large scale functional studies to understand EVs therapeutic potential.

Primary Supervisor: Prof. Mithen, R

EP5

Decoding Autoimmune Disease: Playing Detective with DNA Mutations

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Background: An autoimmune disease is a condition in which the immune system mistakenly attacks and damages healthy cells in the body. Although its exact cause remains unknown, studies have shown that genetics play a key role in its development. **Objectives:** To understand the biological mechanism of how some DNA mutations can lead to the development of autoimmunity. **Methods:** We examine the genetic makeup of autoimmune patients and compare it with that of healthy controls. We systematically identify potential causal mutations and try to understand their functions. **Results:** We found 71 DNA mutations that changed the expression of genes enriched in immune-related functions including antigen processing and presentation, and pro-inflammatory cytokine signalling. **Discussion:** The genes and biological pathways we identified as potentially causal for the disease can serve as targets for future drug development.

Primary Supervisor: Prof. O'Sullivan, J

EP6

The effectiveness of an internet-delivered intervention for gaming disorder

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Background: Around 3% of gamers have gaming disorder – an addiction to video games where people play up to 70 hours a week. Gaming disorder treatment is predominantly psychotherapeutic, provided in person, and targeted towards severe symptoms. Though most help-seekers with low to moderate severity indicate a preference for a brief internet-delivered intervention, its effectiveness has not been adequately examined. **Objective:** This randomised controlled trial aimed to determine the effectiveness of a brief website-based program for developing new habits to support gaming reduction (Gaming Habit Hacker) compared to an assessment-only comparison group. **Methods:** The study recruited 215 participants from New Zealand and Australia who were 16 years or older and had self-identified problems with gaming. Participants were randomly assigned to Gaming Habit Hacker or a comparison group. Gaming Habit Hacker delivered a range of behaviour change techniques across 28 days, including feedback on assessment, goal setting, action planning, coping planning, and feedback on outcomes of behaviour by an online coach. The comparison group received assessments only. Participants completed surveys at baseline and 4-week post-intervention. **Results:** At post-intervention, Gaming Habit Hacker participants reported significant improvements to the primary outcome of gaming hours and a range of other variables. Most participants found the website engaging and reported that access to a coach was especially helpful. **Discussion:** A brief internet-delivered intervention appears to have an impact on gaming and could be made readily available to health services. Gaming Habit Hacker could also be further developed into a mobile app to improve accessibility.

Primary Supervisor: Dr Wilkinson-Meyers, L.

EP7

Optimisation of corneal tissue engineering to facilitate epithelial wound healing

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Background Development in corneal tissue engineering is critical in aiding donor tissue shortages to treat corneal disease, particularly in developing countries. Cornea epithelial cells provide the protective barrier for the underlying stroma to maintain its transparent properties. Epithelial wound healing occurs primarily through basal cell migration, derived from limbal stem cells. Corneal epithelia have been shown to elongate and align along surface topographical features, however, there have been few clinical translations of enhanced epithelial biological structure and function. Post-operative corneal haze has been observed and attributed to incomplete monolayers. Thus, optimising the time required for complete epithelial monolayer coverage of the stroma is of clinical interest. **Objectives** Develop a cell-based *in-silico* model to investigate wound closure time over varying topographical patterns. **Methods** Ring-barrier monolayer cell culture assays were used to study wounded and non-wounded cell behaviour. Image analysis of *in vitro* time-lapse data provided parameters to inform *in-silico* model development. Agent-based modelling tools CompuCell3D and PhysiCell were assessed for capability in replicating *in vitro* assays. Coverage time of a two-dimensional *in-silico* wound was assessed with identical image processing. **Results** PhysiCell sufficiently captures time scaling behaviours of density changes during wound healing. This differs between large and small experimental wound configurations. **Discussion** The CompuCell3D and PhysiCell models enable reasonable estimations of the cells' dynamic morphology and mechanical interactions, respectively. Neither model sufficiently represents both fundamental cell behaviours, critical in accurately replicating response to topography. The recommended model for modelling *in vitro* assays will require identification of the critical parameters of interest.
Primary Supervisor: Assoc Prof. Clarke, R.

EP8

Hyaluronic Acid Biology and its Significance in Pancreatic Ductal Adenocarcinoma

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Background: Hyaluronic acid (HA) is a major component of the stroma in pancreatic ductal adenocarcinoma (PDAC) and its high abundance is negatively correlated with patient survival. The biology of HA tells us that it can be a triple threat in cancers: by activation of receptors, by acting as a source of energy, or by creating a barrier preventing chemotherapies from entering the tumour. In 2019, despite initial promise, a HA depleting drug failed in phase III clinical trials. **Objectives:** To understand the role of HA in PDAC using *in vitro* models. **Methods:** Bioinformatics tools such as Ingenuity Pathway Analysis were used to identify 53 genes that play a role in HA biology. Using large genomic datasets, the abundance of the genes and relative survival association in PDAC was catalogued, suggesting a subset to warrant further investigation. Additionally, the effect of HA on PDAC cells and its mechanism of action, the effect of exogenous HA on 3D *in vitro* models was evaluated. **Results:** RNA-sequencing of these 3D models showed that exposure to HA causes changes in important Gen Set Enrichment Analysis (GSEA) pathways, such as hypoxia, hedgehog signalling, and oxidative phosphorylation, as well as HA-dependent up-regulation of genes such as *VEGFA*. **Discussion:** These enriched pathways are upregulated in PDAC tumours, demonstrating the function of HA in this context. Given that up-to 80% of PDAC tumours consist of cancer-associated fibroblasts, immune cells, and extracellular matrix components, our next step is to use *in-situ* spatial transcriptomics to further investigate the role of HA.
Primary Supervisor: Professor Print, C; Assoc Prof. Blenkiron, C

EP9

Kiwi Preemies: What's the crunch?

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Background: Preterm birth is a significant global issue with far-reaching implications for infants and society. Fifteen million newborns worldwide are born prematurely, and 1 million of those babies die due to preterm birth complications. In New Zealand, about 8% of babies are born preterm. This is higher than the rate in many other developed countries. Maternal nutritional status has consistently been proven to contribute to the probability of preterm birth. Sociodemographic factors, such as education level, age, ethnicity, culture, parity, and income, contribute to maternal nutritional status and diet patterns a pregnant woman follows. **Methods:** The geographic distribution of preterm births and the variables/factors mentioned above will be illustrated through a map with layers created in Geographic Information System (GIS). The associations between preterm births, nutrition, micronutrient supplementation, climate factors, and other sociodemographic factors will be done using multiple logistic regression and mixed effects logistic regression models. Our cohort consists of over 6000 women. **Objectives:** We need to investigate how nutrition before and during pregnancy is associated with preterm births and how this association is mapped throughout NZ. This will help us understand what areas of NZ are disproportionately affected and why. **Results:** We hypothesise that we'll see regional differences in the number of preterm births that could be due to access to healthcare, diet, rural vs urban, income, education, and climate factors such as natural disasters. **Discussion:** Our study will provide the results to develop evidence-based recommendations that optimise nutrition so we can reduce preventable preterm births in NZ.
Primary Supervisor: Prof. Bloomfield, F

EP10

Inflammation in Diabetic Retinopathy

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Background: Diabetic retinopathy (DR) is a sight-threatening disease that affects individuals with diabetes, disrupting vascular integrity of retinal blood vessels. Current treatments only offer limited delay but do not halt DR progression entirely. **Objectives:** As chronic inflammation has been identified as a key characteristic of DR, this study aims to investigate the potential of targeting inflammation as a therapeutic strategy for DR. **Methods:** Immunohistochemistry and western blotting were employed to assess inflammation in post-mortem retina from non-diabetic controls and donors with diabetes with and without DR. A systematic review was also conducted to examine changes in systemic and ocular inflammation in the progression of DR. Furthermore, blood biomarker levels and DR screening results were evaluated before and after bariatric surgery to examine the impact of systemic inflammation on DR progression. **Results:** Our findings demonstrate that inflammation is present in the retina even before DR onset in individuals with diabetes, and systemic inflammation correlates with intraocular inflammation as DR severity increases. Moreover, we discovered that measuring inflammatory markers through blood tests could be used as a predictive tool for determining DR progression. **Discussion:** Collectively, these findings provide strong evidence supporting the targeting of inflammation as a promising therapeutic approach for the treatment of DR.
Primary Supervisor: Dr Mugisho, O (Lola)

EP11

Utilizing 3D hydrogels to promote survival and maturation of directly reprogrammed human-induced oligodendrocyte precursor cells

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Background: Multiple Sclerosis (MS) is an autoimmune, demyelinating disease of the central nervous system characterized by the loss of oligodendrocytes (OLs) and the myelin sheath, impairing neuronal signal transduction. The transplantation of oligodendrocyte precursor cells (OPCs) has emerged as a potential therapy to replace oligodendrocytes, restoring the myelin sheath and signal transduction. However, these studies have reported issues with long-term survival, maturation, integration and functionality of transplanted cells. To overcome this, we propose the encapsulation of OPCs into 3D hydrogels to provide a more permissible environment that protects cells, achieving enhanced survival, maturation and functionality. **Objectives:** To compare the survival and maturation of directly reprogrammed human oligodendrocyte precursor cells (hiOPCs) in 3D hydrogels and traditional 2D cell culture surfaces. **Methods:** Human fibroblasts were directly reprogrammed to hiOPCs and seeded onto poly-o-laminin coated glass coverslips or encapsulated into three hydrogel formulations: gelatin methacryloyl (GelMA), Laminink or GelMA + 10μg/mL laminin. At various timepoints, survival and maturation of hiOPCs were assessed via a LIVE/DEAD assay and oligodendrocyte marker expression, respectively. **Results:** hiOPCs can survive and mature within 3D hydrogels for up to 2 weeks in culture, expressing oligodendrocyte markers O4 and O1. **Discussion:** This study demonstrates for the first time that reprogrammed hiOPCs can survive and mature into oligodendrocytes within 3D hydrogels. The ability for 3D encapsulated hiOPCs to remyelinate the demyelinated brain will next be investigated using (1) an *ex vivo* organotypic slice culture system and (2) the cuprizone mouse model of demyelination.
Primary Supervisor: Dr McCaughey-Chapman, A

EP12

Sensitisation of radiation resistant colon cancer: The oxygenated microbubble hydrogel approach

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Background: "Hypoxia" - a state of reduced oxygen that develops within the tumour microenvironment due to its irregular vasculature, could result in treatment resistance. Reoxygenation of the tumour in a sustained manner, using oxygenated lipid microbubbles (OMB) loaded in a temperature sensitive gel could alleviate this condition. The OMB would carry the oxygen while the gel would sustain its release into the tumour microenvironment. **Objectives:** To formulate a gas based therapeutic composed of OMB dispersed in a temperature sensitive poloxamer hydrogel for intratumoural administration. **Methods:** OMB were generated by first preparing a liposomal mixture-DSPC:DSPE-PEG(Distearoylphosphatidylcholine:1,2-Distearoyl-sn-glycero-3-phosphoethanolamine-polyethylene glycol), which was dispersed in a thermosensitive poloxamer hydrogel mixture (P407:P188). This was pressurised with oxygen and vortexed in a gas-tight vial. Characterisations included – OMB size distribution, injectability, thermosensitivity, oxygen loading and release, and impact on efficacy of radiotherapy against a colon cancer cell line (HCT116). **Results:** DSPC:DSPE-PEG liposomes at a molar ratio of 94:6 dispersed in 21:6.5 (% w/w) of P407:P188 generated OMB with a size distribution in the acceptable limit of 0.8-8 μm. Formulations gelled near physiological temperatures and were deemed to be within established limits of injectability (12N<F<38N). The hydrogel component enabled a sustained release of oxygen. Cell-culture studies under hypoxia are ongoing and this would shed light on the effect of the formulation on the treatment resistant hypoxic cells. **Discussion:** This study involved the development and characterisation of OMB dispersed in a thermosensitive poloxamer hydrogel. It is expected that such a formulation will sensitise radiation therapy of hypoxic resistant cancer cells.
Primary Supervisor: Dr Thakur, S

EP13

Analysing Vitamin status and early Intravenous Nutrition in the NICU (The AVIatioN Study)

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Background: Vitamins are essential nutrients that have important and diverse biochemical functions. Vitamin deficiency can be fatal. Little is known about the actual vitamin status or requirements of extremely low birthweight babies (< 1000 g, ELBW) at birth, and how vitamin deficiencies affect mortality and clinical outcome. Following a previous investigation (ProVIDe cohort), neonatal intensive care unit (NICU) feeding guidelines and IV solutions have changed to contain increased vitamins. **Objectives:** To determine whether the change in vitamin administration results in fewer infants with plasma vitamins below the reference range and whether it affects neonatal morbidities. **Methods:** ELBW babies are being recruited at Te Whatu Ora Te Toka Tumai and Waikato NICUs within the first week of life. A blood sample is taken on the seventh day of life and analysed for concentrations of fat- and water-soluble vitamins, alongside samples from the ProVIDe cohort. Vitamin concentrations will be compared between the previous and present cohort. Incidence of hypophosphataemia, refeeding syndrome, mortality and presence of common neonatal morbidities will be compared between infants with one or more plasma vitamin concentrations below the reference range and infants within the reference range. **Results:** Recruitment is ongoing, aiming to finish with a cohort of 106 babies across both hospitals by the end of the year. **Discussion:** The outcomes of this study will show whether the new nutrition protocol and reformulation of IVs are effective in providing adequate vitamins to ELBW babies. The findings will be integrated into the Aotearoa preterm nutrition guidelines that are currently being developed.
Primary Supervisor: Prof. Bloomfield, F

EP14

Who develops gestational diabetes mellitus in New Zealand and what are the health risks?

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Background: Gestational diabetes mellitus (GDM) is a global health issue with significant implications for affected women and their infants. Knowledge of sociodemographic information associated with GDM in New Zealand remains limited. Addressing this knowledge gap may help develop effective strategies against New Zealand's increasing GDM prevalence. **Objectives:** To assess sociodemographic and medical characteristics of pregnant women with and without GDM in New Zealand using a contemporary dataset and investigate immediate health outcomes of mothers and their infants. **Methods:** Data from the Gestational Diabetes Mellitus Study of Diagnostic Thresholds Trial will be analysed, encompassing maternal sociodemographic and medical characteristics, and maternal and infant health outcomes until hospital discharge. Logistic regression will assess risk factors associated with GDM. Log binomial regression, log Poisson models, and linear regression will assess associations between GDM and immediate maternal and infant health consequences. **Results:** Preliminary analysis revealed the following risk factors associated with GDM: maternal ages ≥40 years [adjusted odds ratios (aOR) 2.53(1.07-5.99), p=0.03], overweight [aOR 2.20 (1.45-3.33), p=0.0002] and obese [aOR 3.55 (2.29-5.50), p<0.0001] using body mass index (BMI) classifications, family history of diabetes mellitus [aOR 1.38 (CI 1.02-1.86), p=0.03] and Asian ethnicity [aOR 2.44 (CI 1.66-3.59), p<0.0001]. **Discussion:** This study aims to provide insights to help inform future health practices and improve outcomes for women at risk of developing GDM in New Zealand. Findings may potentially reduce the burden and cost of GDM in New Zealand, identify modifiable factors for targeted interventions, and support efforts to increase maternity screening for high-risk populations.
Primary Supervisor: Prof. Crowther, C

EP15

Androgens in the endometrium: A forgotten piece of the puzzle

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Background: Androgens and the androgen receptor (AR) have mainly been studied as part of ovarian pathologies in female reproduction. The presence of AR in the endometrium suggests potential roles in its biology. Androgens display anti-proliferative functions, combating estrogen action in the endometrium. However, existing knowledge on androgen steroidogenesis pathways and regulation of androgen signalling in the endometrium is scarce and conflicting.**Objectives:** To characterise and determine the regulation of AR and steroidogenic enzymes in the endometrium. **Methods:** Effects of estrogen and progesterone on gene and protein expressions of members of androgen signalling pathway were examined in endometrial explants, epithelial (HES) and stromal (HESC) cell-lines. **Results:** While *AR* mRNA decreased significantly following 72h combined estrogen-progesterone and 24h estrogen treatments in HESCs, AR protein significantly increased following 48h and 72h of combined estrogen-progesterone treatment. No variations were seen in explants in response to treatments, suggesting cell-specific regulation. We report 11β-hydroxysteroid dehydrogenase (*11β-HSD*) type 1 and 2 mRNA expressions in endometrial tissues, with significantly increased *11β-HSD2* expression in response to 24h combined estrogen-progesterone treatment. Genes of other enzymes involved in androgen synthesis pathways were not present in endometrial tissues. **Discussion:** Our data show AR and some enzymes involved in androgen synthesis are regulated by estrogen and progesterone in the endometrium, begging the question whether there is local androgen production and what the potential roles could be. A more integrative approach to androgens in the female reproductive tract is necessary to improve understanding of its role in endometrial biology.

Primary Supervisor: Dr Ponnampalam, A


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