




Healthex 2022

Celebrating Student Research

CONFERENCE PROGRAMME BOOKLET
FRIDAY, 2ND SEPTEMBER



MEDICAL AND HEALTH SCIENCES



Auckland Medical Research Foundation
est. 1955



LIGGINS INSTITUTE



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 HealthX 2022, the sixteenth 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.

HealthX 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 talent 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.

HealthX 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 HealthX 2022 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 HealthX 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 HealthX 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, HealthX 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 HealthX 2022.



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

On Behalf of the 2022 HealtheX Organising Committee

Dear Colleagues,

On behalf of the 2022 HealtheX organising committee, we are honoured to welcome you to the 16th anniversary of the FMHS HealtheX conference, the Health Exposition celebrating student research.

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 2021, we maintained a 'smart' and digitally secure abstract submission, judging, and administration portal. All of these avenues were built on and improved this year through the dedicated application of the extensive expertise of our beloved faculty staff member, and FMHS Staff Special Achievement award winner, Ian Sayer. His help aids 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.

HealtheX 2021 embraced the Zoom video conferencing platform to seamlessly allow presenters, judges, and attendees to attend and compete despite the ongoing COVID-19 pandemic. We sought to build upon this success by ensuring a hybrid physical and digital conference this year for HealtheX 2022 to invite and encourage the wider community to attend the event and learn of the breakthrough scientific research being done by students at the University of Auckland. 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. Through avenues of oral, poster, and 3-Minute Elevator Pitch communication categories, HealtheX imparts a colourful appreciation for the varied approaches taken by scientists to work towards the common goal of improving global health, and demonstrates the true scope and caliber of the ability of students.

HealtheX is a conference organised by the students for the students. The success of HealtheX 2022 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. Last, but certainly not the least, the entire team of HealtheX 2022 is grateful for the trusted, continuous and generous support of the Auckland Medical Research Foundation, the Maurice and Phyllis Paykel Trust, FMHS Postdoc Society, FMHS Postgraduate Student Association, and the Liggins Institute. HealtheX is also grateful to the new collaborations with, and sponsorships by Abacus dx, and New England BioLabs.

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



Kyrah Thumbadoo and Conor Nelson
Co-Chairs, HealtheX 2022

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 (eg., judging packs), and relevant HealtheX merchandise.

Lunch - 11:30 am - 13:00 pm

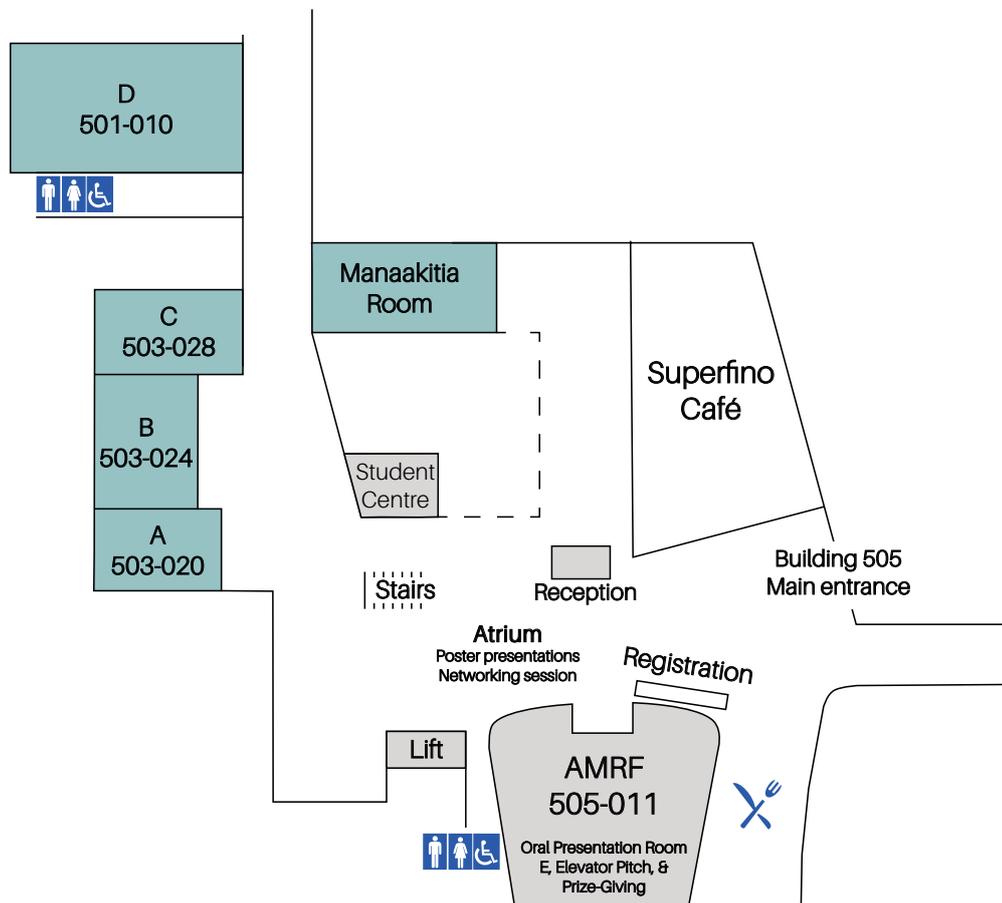
We cater for multiple dietary requirements for all registered judges, competitors, and invited guests. Please ensure your name tag is visible as you enter the main lunch area.

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 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 13 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 \$15,000 in prize money.

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



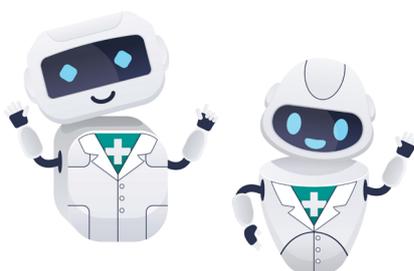
Conference Schedule

Date: Friday, 2nd September

Time: 8:30 am - 6:00 pm

Location: Grafton Atrium, Grafton Campus, University of Auckland, Auckland 1023

Time	Programme				
8:30 am	Registration - <i>Grafton Atrium</i>				
8:55 am - 10:15 am	Oral Presentation Session 1				
	Room A <i>503-020</i> A1 - A5	Room B <i>503-024</i> B1 - B4	Room C <i>503-028</i> C1 - C5	Room D <i>501-010</i> D1 - D3	Room E <i>505-011</i> E1 - E4
Break					
10:40 am - 12:00 pm	Oral Presentation Session 2				
	Room A <i>503-020</i> A6 - A10	Room B <i>503-024</i> B5 - B9	Room C <i>503-028</i> C6 - C10	Room D <i>501-010</i> D4 - D8	Room E <i>505-011</i> E5 - E9
11:30 am - 13:00 pm	Lunch for all Judges, Presenters, and Participants - <i>Grafton Atrium</i>				
12:15 pm - 13:15pm	Poster Viewing Session - <i>Grafton Atrium</i>				
13:25 pm - 15:00 pm	Oral Presentation Session 3				
	Room A <i>503-020</i> A11 - A16	Room B <i>503-024</i> B10 - B15	Room C <i>503-028</i> C11 - C15		
Break					
15:30 pm - 18:30 pm	3-Minute Elevator Pitch Competition - <i>AMRF Lecture Theatre (505-011)</i>				
	Prize-Giving Ceremony - <i>AMRF Lecture Theatre (505-011)</i>				
	Networking Session - <i>Grafton Atrium</i>				
Event Closes					



Zoom Links

Oral Presentation Room A

<https://auckland.zoom.us/j/91687287082?pwd=VDIZODIYTIBNY3dOL0ZtakpJRUYxQT09>

Meeting ID: 916 8728 7082

Passcode: 438791

Oral Presentation Room B

<https://auckland.zoom.us/j/93320457538?pwd=RXZPb2hEZDQwSCs5L2ZJalJQQ0s3UT09>

Meeting ID: 933 2045 7538

Passcode: 726034

Oral Presentation Room C

<https://auckland.zoom.us/j/97965489022?pwd=WVNrMWNTtMlBTMDI3Q0tUTjFGTFNmZz09>

Meeting ID: 979 6548 9022

Passcode: 165126

Oral Presentation Room D

<https://auckland.zoom.us/j/93607362706?pwd=WTByWjJVR0tpK25SMXU0YW0wMGNPUT09>

Meeting ID: 936 0736 2706

Passcode: 960036

Oral Presentation Room E

<https://auckland.zoom.us/j/98179441615?pwd=bEtwKzE1UHJoTW5vWWN0aXdBcHBZQT09>

Meeting ID: 981 7944 1615

Passcode: 757497

3-Minute Elevator Pitch and Prize Giving Ceremony

<https://auckland.zoom.us/j/91985448420?pwd=U1RxN0xkQkhXUGVqalNubmt2VUYxQT09>

Meeting ID: 919 8544 8420

Passcode: 190088

Time	Oral Presentations Room A - 503-020
8:55 am	Introduction by Chairperson
9:00 am	A1 - Wenxuan Chen Supervisor: Dr Jonathan Astin Pappa2 and igf signalling regulates lymphatic vessel growth
9:15 am	A2 - Zena Al-Ani Supervisor: Professor Maxim Petrov Associations of Imaging Biomarkers in the Progression of Pancreatitis, and the Role of Gut Hormones
9:30 am	A3 - Julia Plank Supervisor: Dr Joanne Lin Brain temperature as a measure of neuroinflammation: assessment using whole-brain magnetic resonance spectroscopy
9:45 am	A4 - WITHDRAWN
10:00 am	A5 - Senilaite Tautuiaki Supervisor: Dr Farha Ramzan The effects of kawakawa (Piper Excelsum) consumption on markers of inflammation.
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	A6 - Sam McCullough Supervisor: Dr Scott Graham Development of an iPSC-derived model of brain pericytes to investigate their role in neuroinflammation
11:00 am	A7 - Zahra Laouby Supervisor: Dr Simon J O'Carroll See-through the ailment: chronic imaging to study nerve cell activity following spinal cord injury
11:15 am	A8 - Bronwyn Riley Supervisor: Dr Peter Freestone Regional differences in striatal dopamine transmission between DAT-KO and wildtype rats
11:30 am	A9 - Yuting Xiao Supervisor: Dr Jie Zhang Identification of stem cells in the posterior limb
11:45 am	A10 - Lance Martinez Supervisor: Dr Malvinder Singh-Bains Characterising Tau Pathology in the Huntington's Disease human brain
12:15 pm	Break and Poster Viewing Session
1:25 pm	Introduction by Chairperson
1:30 pm	A11 - Olivia Mills Supervisor: Professor Laura Bennet Cardiovascular and cerebral perfusion changes during post-asphyxia seizures in preterm fetal sheep
1:45 pm	A12 - Benjamin Lear Supervisor: Professor Laura Bennet Predicting long-term outcomes after Hypoxia-ischemia in preterm fetal sheep
2:00 pm	A13 - Holly Wilson Supervisor: Associate Professor Justin Dean Characterising the nature of inflammation-induced cerebellar injury in the preterm-equivalent rat
2:15 pm	A14 - Alice McDouall Supervisor: Associate Professor Joanne Davidson Detrimental effects of slow rewarming after therapeutic hypothermia for cerebral ischemia in near-term fetal sheep
2:30 pm	A15 - Michael Beacom Supervisor: Professor Laura Bennet Embracing the chaos of fetal heart variability: a biomarker for evolving fetal hypoxic-ischaemic brain injury
2:45 pm	A16 - Fatima Faroze Supervisor: Associate Professor James P. Fisher To vape or not to vape that's the question: A state of the artery investigation.
3:00 pm	Break
3:30 pm	3-Minute Elevator Pitch Competition - <i>AMRF Lecture Theatre (505-011)</i> Prize Giving Ceremony - <i>AMRF Lecture Theatre (505-011)</i> Networking Session - <i>Grafton Atrium</i>
6:30 pm	Event Closes

Time	Oral Presentations Room B - 503-024	
8:55 am	Introduction by Chairperson	
9:00 am	B1 - Jay Gong Persistent opioid use after hospital admissions for surgery and trauma in New Zealand	Supervisor: Dr Amy Chan
9:15 am	B2 - Estelle Miller Psychedelic Microdosing in Reality: exploring what people who microdose are consuming and effects experienced	Supervisor: Dr Rhys Ponton
9:30 am	B3 - Rachael Yelder Changing medication mindsets: A brief intervention to improve patients' experience of methotrexate	Supervisor: Professor Keith Petrie
9:45 am	B4 - Tessa Pocock Developing an evidence-based model of meaningful mobility in the context of positive ageing	Supervisor: Professor Melody Smith
10:15 am	Break	
10:40 am	Introduction by Chairperson	
10:45 am	B4 - Joseph Chen Scopolamine's effect on heart rate variability and electroencephalography measures in participants with and without depression	Supervisor: Dr Suresh Muthukumaraswamy
11:00 am	B6 - Queenie Yong Seeking genetic modifiers to the drug trastuzumab emtansine (T-DM1) to advance HER2-targeted therapy	Supervisor: Dr Barbara Lipert
11:15 am	B7 - Kelly Peterken Investigating ligand and adjuvant combinations for development of a polyvalent Staphylococcus aureus vaccine	Supervisor: Dr Fiona Radcliff
11:30 am	B8 - Grace Tawhai The Development and Testing of a Novel Solute for Nasal Irrigation in CRS	Supervisor: Professor Richard Douglas
11:45 am	B9 - Ray Ong Delivery of bovine lactoferrin to osteoblasts in vitro using niosomes	Supervisor: Professor Jillian Cornish
12:15 pm	Break and Poster Viewing Session	
1:25 pm	Introduction by Chairperson	
1:30 pm	B10 - Abbey Lissaman Regulation of Estrogen Receptors by DNA Methylation and Hydroxymethylation in Human Endometrium	Supervisor: Dr Anna Ponnampalam
1:45 pm	B11 - Victoria King Small and squishy: growth restriction in the chronically instrumented fetal sheep	Supervisor: Professor Laura Bennet
2:00 pm	B12 - Yi Zhang Proliferation and invasion-associated miRNAs in first-trimester and term placental extracellular vesicles: inspirations for cancer-regulation	Supervisor: Professor Larry Chamley
2:15 pm	B13 - Xinyi Sun Proteomic analysis of placental extracellular vesicles on inhibiting the growth of ovarian cancer	Supervisor: Professor Larry Chamley
2:30 pm	B14 - Tayla Wickman Characterising haematopoietic progenitors within the placental villous core	Supervisor: Associate Professor Joanna James
2:45 pm	B15 - Luam Ghebream Predictors of injury among young children in New Zealand: a longitudinal trajectory approach	Supervisor: Professor Bridget Kool
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 - 503-028
8:55 am	Introduction by Chairperson
9:00 am	C1 - Joevy Lim Supervisor: Professor Charles McGhee The Epidemiology of Eye Melanoma in New Zealand - A 20-year Study
9:15 am	C2 - Finley Breeze Supervisor: Dr James McKelvie Predicting ophthalmic clinic non-attendance using machine learning
9:30 am	C3 - Judith Glasson Supervisor: Dr Laura Domigan Crystallin Clear: Improving Bioengineered Corneal Stromal Materials
9:45 am	C4 - Avik Shome Supervisor: Associate Professor Ilva Rupenthal Comprehensive grading system for experimental autoimmune uveitis in mice
10:00 am	C5 - Vicky Wen Supervisor: Professor Trevor Sherwin Optimising Umbilical Cord Mesenchymal Stem Cells for the Treatment of Keratoconus
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	C6 - Zainab Noori Supervisor: Dr Manisha Sharma Are we Compromising the Dabigatran Product Stability by Using Adherence Packaging?
11:00 am	C7 - Shima Mohammadi Moghadam Supervisor: Dr Julie Choisne Intra-subject and inter-subject accuracy in predicting gait parameters using wearable sensors and Random Forest
11:15 am	C8 - Dingchang Shi Supervisor: Dr George Guo Developing a bioinformatics tool to identify stable isotope incorporated compounds in imaging mass spectrometry data
11:30 am	C9 - WITHDRAWN
11:45 am	C10 - Pang Ying Cheung Supervisor: Dr Juliette Cheyne Go big: the power of the mesoscope
12:15 pm	Break and Poster Viewing Session
1:25 pm	Introduction by Chairperson
1:30 pm	C11 - Lydia Aa-Young Shim Supervisor: Associate Professor Rachael Parke When Death becomes Life: determinants of deceased organ donation consent
1:45 pm	C12 - Muayad Al-Kamyani Supervisor: Professor Greg O'Grady Functional dyspepsia association with retrograde slow waves detected by a body surface gastric mapping device
2:00 pm	C13 - Isabella Pickering Supervisor: Dr Elizabeth Broadbent An evaluation of digital humans in delivering relaxation for wound healing and stress reduction
2:15 pm	C14 - Tim Hsu-Han Wang Supervisor: Professor Greg O'Grady Investigations of post-operative gastric dysfunction using novel technologies
2:30 pm	C15 - Luke Boyle Supervisor: Professor Thomas Lumley Using Days Alive and Out of Hospital to measure inequities after cardiovascular surgery
3:00 pm	Break
3:30 pm	3-Minute Elevator Pitch Competition - <i>AMRF Lecture Theatre (505-011)</i> Prize Giving Ceremony - <i>AMRF Lecture Theatre (505-011)</i> Networking Session - <i>Grafton Atrium</i>
6:30 pm	Event Closes

Time	Oral Presentations Room D - 501-010
8:55 am	Introduction by Chairperson
9:00 am	D1 - Alyona Oryshchuk Two in One: Killing Leukaemia Stem Cells while Supporting Normal Haematopoietic Stem Cells Supervisor: Professor Stefan Bohlander
9:15 am	D2 - WITHDRAWN
9:30 am	D3 - Annika Anderson Understanding Transforming Growth Factor Beta signalling family's relationship with endometrial cancer through novel mutations. Supervisor: Dr Anassuya Ramachandran
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	D6 - Jae Yoon Rhee Identification of genes involved in lymphatic vessel development through forward genetic screening Supervisor: Dr Jonathan Astin
11:00 am	D7 - Lauren Watson Understanding the role of IL-6 -174 G/C (rs1800795) promoter variant in metabolic responses to exercise Supervisor: Associate Professor Troy Merry
11:15 am	D8 - Rachel Jaros Comorbidity genetic risk and pathways impact SARS-CoV-2 infection outcomes Supervisor: Professor Justin O'Sullivan
11:30 am	D9 - WITHDRAWN
11:45 am	D10 - Roan Zaied De novo identification of asthma multimorbidities Supervisor: Professor Justin O'Sullivan
12:15 pm	Break and Poster Viewing Session
3:00 pm	Break
3:30 pm	3-Minute Elevator Pitch Competition - <i>AMRF Lecture Theatre (505-011)</i> Prize Giving Ceremony - <i>AMRF Lecture Theatre (505-011)</i> Networking Session - <i>Grafton Atrium</i>
6:30 pm	Event Closes

Time	Oral Presentations Room E - AMRF Lecture Theatre (505-011)
8:55 am	Introduction by Chairperson
9:00 am	E1 - Dilsha Gimhani Investigating cardiac sympathetic transduction and its effects on vascular function Supervisor: Dr Rohit Ramchandra
9:15 am	E2 - Jingyuan Liang Cardiovascular medication drop-in during 12-year follow-up and insights for risk prediction equations Supervisor: Professor Rod Jackson
9:30 am	E3 - Bruno Batinica Addition of Biochemical Markers to Population-Level Cardiovascular Disease Risk Prediction Equations Supervisor: Professor Rod Jackson
9:45 am	E4 - Olivia Gold Components underlying synaptic plasticity in the carotid body Supervisor: Dr Audrys Pauza
10:15 am	Break
10:40 am	Introduction by Chairperson
10:45 am	E5 - Vidit Satokar Fish oil supplementation in pregnant mothers with overweight/obesity to improve infant body composition and metabolism. Supervisor: Dr Ben Albert
11:00 am	E6 - Marco Annandale Cardiac fructose inhibition is a promising therapeutic target for treating diastolic dysfunction in diabetes. Supervisor: Dr Kim Mellor
11:15 am	E7 - Jerusha Gojer Impact of kawakawa on the postprandial levels of circulating microRNA's related to insulin sensitivity Supervisor: Dr Farha Ramzan
11:30 am	E8 - Zahlee Buckley Fish oil supplementation increases omega-3 content of human milk, in women with overweight and obesity. Supervisor: Dr Ben Albert
11:45 am	E9 - Manpreet Singh Potential Impact of fast-food sodium reduction targets on the consumption of sodium in New Zealanders. Supervisor: Dr Helen Eyles
12:15 pm	Break and Poster Viewing Session
3:00 pm	Break
3:30 pm	3-Minute Elevator Pitch Competition - AMRF Lecture Theatre (505-011) Prize Giving Ceremony - AMRF Lecture Theatre (505-011) Networking Session - Grafton Atrium
6:30 pm	Event Closes

Poster Session - *Grafton Atrium*

P1 - Anmol Sandhu	Supervisor: Professor Trevor Sherwin
Investigating umbilical cord stem cells for the treatment of corneal endothelial dysfunction	
P2 - Anna Pilaar	Supervisor: Professor Rod Dunbar
Ex vivo T cell re-stimulation protocol for adoptive cell therapy	
P3 - Anna Worthington	Supervisor: Dr Andrea Braakhuis
Development of eHealth-Based Behavior Change Support for Young Adults Using the Nine Principles Framework	
P4 - Brittany Hazelgrove	Supervisor: Associate Professor Darren Svirskis
Uncovering neural activity in the spinal cord recorded by a novel bioelectronic implant	
P5 - Cameron Heyman	Supervisor: Professor Lynette Tippett
Investigating White Matter Hyperintensities in the Context of Cognitive Decline and Alzheimer's Disease	
P6 - Daiana Yedgy	Supervisor: Professor Maurice A. Curtis
Phosphorylated tau and α -synuclein presentation in the human olfactory epithelium	
P7 - Emily Gould	Supervisor: Dr Peter Freestone
Regional variation of dopamine transmission in the caudolateral (tail) striatum	
P8 - Emily MacFarlane	Supervisor: Dr Gus Grey
Presbyopia and Water Regulation in the Human Lens: The Relationship Between Syneresis and Protein Structure	
P9 - WITHDRAWN	
P10 - Gabriela Bantas	Supervisor: Dr Lola Mugisho
The potential involvement of Benzalkonium Chloride in inflammasome activation	
P11 - Issy Cowlshaw	Supervisor: Dr Laura Domigan
Optimisation of Corneal Tissue Engineering	
P12 - Julia Newland	Supervisor: Dr Andrea Kwakowsky
K ⁺ -Cl ⁻ co-transporter 2 (KCC2) expression in the human Alzheimer's disease medial temporal lobe	
P13 - Karen Lin	Supervisor: Dr Elizabeth Broadbent
Understanding Embodied Effects of Posture: A Qualitative Study	
P14 - WITHDRAWN	
P15 - Kreesan Reddy	Supervisor: Dr Birger Victor Dieriks
Identifying novel therapeutic targets through the lens of distinct alpha-Synuclein strains	
P16 - Pang Yuk Cheung	Supervisor: Professor Alan Davidson
Effects of oral cysteamine treatment on Ctns knockout rats	
P17 - Pearl Beesley	Supervisor: Dr Veronika Sander
Using human kidney organoids to model cisplatin-induced acute kidney injury	
P18 - Ruby Wangford	Supervisor: Dr Veronika Sander
Investigating Polycystic Kidney Disease in kidney organoids	
P19 - Shelly Scheepers	Supervisor: Dr Andrea Kwakowsky
Nanostring nCounter analysis of the neuroinflammatory pathways in the Midcingulate Cortex in Huntington's Disease	
P20 - Sophie Piesse	Supervisor: Associate Professor Carolyn Barrett
Estrogenic influences on histological changes occurring in heart failure	
P21 - Steven Yoo	Supervisor: Professor Alan Wang
Determination of regions of interests in human brain atlases for upper limb recovery prediction post-stroke	

Poster Session - Grafton Atrium

P22 - Subhasish Das	Supervisor: Distinguished Professor Dame Jane Harding
Can nutrition help moderate-to-late preterm babies thrive: a protocol report	
P23 - Svenja Meissner	Supervisor: Dr Brad Raos
The development of a hydrogel-based ultrasound-triggered delivery system for neurotrophic growth factors	
P24 - Thomas Saju	Supervisor: Dr Petr Tomek
Arresting tryptophan catabolism for cancer immunotherapy	
P25 - Vanshika Chinchalkar	Supervisor: Dr Haruna Suzuki-Kerr
The use of Optical Coherence Tomography to Visualize the Inner Ear	
P26 - Varima Narula	Supervisor: Dr Sue McGlashan
Phenotyping synovial fluid extracellular vesicles from patients with knee osteoarthritis, and with or without obesity	
P27 - Vidit Satokar	Supervisor: Dr Ben Albert
Toxicity of oxidised fish oil in pregnancy - A dose-response study in rats.	
P28 - Yasaman Emad	Supervisor: Professor Keith Petrie
Why do gout patients not take their allopurinol?	
P29 - Juma Rahman	Supervisor: Dr Bapon Fakhruddin
How Frequently Do We Touch Facial T-Zone: A Systematic Review	

3-Minute Elevator Pitch Competition - AMRF Lecture Theatre (505-011)

EP1 - Catriona Miller	Supervisor: Professor Justin O'Sullivan
Untangling the spectrum - using genetics to identify autism and co-occurring traits	
EP2 - Anna Behling	Supervisor: Professor Justin O'Sullivan
Understanding the movement of genes within healthy gut microbiomes	
EP3 - Cherry Sun	Supervisor: Associate Professor Jo James
Term side-population trophoblasts can be maintained in culture and differentiated to mature trophoblast populations	
EP4 - WITHDRAWN	
EP5 - Alina Pavlova	Supervisor: Professor Nathan Consedine
Developing multi-level interventions to facilitate compassion in Aotearoa hospital-based care teams.	
EP6 - Jozie Sharpe	Supervisor: Dr Nike Franke
Risk of neonatal hypoglycaemia, stability of childhood behaviour, and academic outcomes. Is there a connection?	
EP7 - Arpita Dutta	Supervisor: Dr Hayley Reynolds
Radiomics-based Prostate Cancer classification using Machine Learning and multi-parametric MRI	
EP8 - Dian Zhuang	Supervisor: Professor Jennifer Craig
Targeting the inflammatory marker in dry eye disease	
EP9 - Mohammad Shahbaz	Supervisor: Distinguished Professor Dame Jane Harding
Comparison of outcomes assessed by study questionnaire and by data linkage	
EP10 - Jaymie Rogers	Supervisor: Associate Professor Jaqueline Ramke
Addressing access to eyecare in Aotearoa: A qualitative approach	
EP11 - Grace Wei	Supervisor: Associate Professor Christopher McKinlay
A new approach to assessing neurodevelopment and health at early-school-age	
EP12 - Michael Brown	Supervisor: Dr Moana Tercel
What Makes a Good Sulfatase Substrate? Application in the Design of Antibody-Drug Conjugates.	
EP13 - Sophie Cook	Supervisor: Associate Professor Jo Perry
Identifying novel antibody inhibitors targeting mouse growth hormone receptor signalling in cancer cells	

Followed by the Prize-Giving Ceremony - AMRF Lecture Theatre (505-011)
Networking Session - Grafton Atrium



Auckland Medical
Research Foundation
est. 1955



The Auckland Medical Research Foundation congratulates all of the HealthEx 2022 participants. Winners will receive the following prizes:

- | | | |
|---|----------------|---|
| ❖ AMRF Outstanding Emerging Researcher | \$3,000 | ❖ |
| ❖ AMRF Doctoral Oral Presentation Runner Up | \$2,000 | ❖ |
| ❖ AMRF Best Poster Presentation | \$2,000 | ❖ |

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."



Scott Bolam, 2020 HealthEx winner says:



"I am incredibly grateful to AMRF for sponsoring this award and helping me to share my research with the global orthopaedic community. I will use this award to attend international courses and conferences relate to tendon healing research. The global Covid-19 pandemic may mean that I attend these conferences virtually, but they will still bring together scientists and clinicians with extensive knowledge in my area of research and allow me to connect with top researchers."

AMRF's vision

To improve the health and quality of life for all New Zealanders

You can make a difference by supporting medical research.

Please contact us to learn how.

Phone 09 923 1701

Email amrf@medicalresearch.org.nz

www.medicalresearch.org.nz



MAURICE & PHYLLIS PAYKEL TRUST

The Maurice and Phyllis Paykel Trust was established in 1973 by the late Maurice Paykel, philanthropist and co-founder of the Fisher and Paykel group of companies.

It is a charitable trust dedicated to the improvement of health through the support of research and sponsorship of research trainees in any of the health-related sciences.

Competitive grants are offered to support established scientists in a wide range of fields, and grants awarded are in the three main categories of project and equipment grants, travel grants, and conference support grants.

The conference support grants are for use within New Zealand to provide opportunities for NZ scientists to present their findings to a critical audience and for eminent international scientists to visit and share their knowledge. Conferences that provide presentation opportunities to those training to become established scientists are viewed favourably by the Trust and HealthX is an excellent example of this category.

E-mail: info@paykeltrust.co.nz | www.paykeltrust.co.nz

The FMHS and HealthX greatly appreciate the assistance of the Liggins Institute, FMHS Postdoctoral Society, FMHS Postgraduate Student Association, as well as Abacus dx, and New England BioLabs in the funding and staging of HealthX 2022.



F M H S
POSTDOCTORAL
S O C I E T Y



Acknowledgements

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The logo features a stylized human figure in blue, with arms and legs raised in a 'V' shape, positioned to the left of the text.

Healthex 2022

Celebrating Student Research

FRIDAY, 2ND SEPTEMBER
ABSTRACTS

Oral Presentation Room A - 503-024

A1

Pappa2 and igf signalling regulates lymphatic vessel growth

Chen W¹, Misa P¹, Astin J¹

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Background: The lymphatic vasculature is essential for tissue fluid homeostasis. Damaged or underdeveloped lymphatic vessels can cause pathological accumulation of tissue fluid called lymphoedema. Uncovering how lymphatic vessels develop is the key to finding a cure for lymphoedema. The ability to perform in vivo analysis of lymphatic growth in zebrafish makes them an important model in this field. We previously identified craniofacial cartilage as a pre-existing structure required to guide lymphangiogenesis in zebrafish. I found that Pappa2, a cartilage-expressing metalloproteinase regulating Insulin-like Growth Factor (IGF) signalling, is downregulated in a craniofacial mutant lacking lymphatic growth. This data indicates that Pappa2 and igf signalling could be novel regulators of lymphatic guidance. **Objectives:** To characterise the role of Pappa2 and igf signalling in lymphatic vessel development. **Methods:** Igf-signalling was blocked by administering an igf-signalling inhibitor. Knockout of Pappa2 was performed by CRISPR-Cas9 gene editing and subsequently validated by Sanger sequencing. Overexpression of IGF was carried out by cloning the igf2b cassette into a gene expression construct. Lymphatic and cartilage phenotypes were visualised by confocal imaging. **Results:** Inhibition of igf-signalling in zebrafish prevents lymphangiogenesis. Sanger sequencing identified zebrafish carrying pappa2 mutations, indicating successful gene editing. Preliminary analysis of a Pappa2 mutant showed craniofacial cartilage defects and a lack of lymphatic growth. Igf-overexpressing transgenic zebrafish lines were successfully generated. **Discussion:** I have confirmed the knockout of Pappa2 in zebrafish and revealed a potential role of Pappa2 and Igf-signalling in regulating lymphangiogenesis. Future work will focus on confirming the pappa2 downregulation in the craniofacial mutant.

Primary Supervisor: Dr Jonathan Astin

A2

Associations of Imaging Biomarkers in the Progression of Pancreatitis, and the Role of Gut Hormones

Al-Ani Z¹, Ko J¹, Petrov M¹

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Background: Pancreatitis is increasingly viewed as a progressive disorder. Advanced magnetic resonance (MR) techniques have demonstrated precision in measuring ectopic fat phenotypes in the abdomen, which can be effective as biomarkers in pancreatitis progression. Gut hormones may also provide mechanistic insights into the pathogenesis of these phenotypes. **Objectives:** To investigate the association between ectopic fat phenotypes (intra-pancreatic, intra-hepatic, and skeletal) and acute pancreatitis individuals (AP), chronic pancreatitis individuals (CP), and health; and to investigate the role of gut hormones in both fasted and post-prandial states with each ectopic fat phenotype. **Methods:** MR was used to determine intra-pancreatic fat deposition (IPFD), intra-hepatic fat deposition (IHFD) and skeletal muscle fat deposition (SMFD) in 201 study participants. Gut hormones (oxyntomodulin, ghrelin, glucagon-like peptide 1 (GLP-1), gastric inhibitory peptide (GIP), and peptide YY (PYY)) were measured through blood sampling. **Results:** There was a statistically significant association found with IPFD in both the AP group and CP group relative to healthy individuals with p-for-trend analysis being statistically significant across all models ($p < 0.001$, $p < 0.001$, $p = 0.013$, and $p = 0.027$). In the fasted state, ghrelin showed a significant association with IPFD in the AP group across all models ($p = 0.017$, $p = 0.003$, $p = 0.025$, and $p = 0.019$). In the post-prandial state, there were no significant associations found. **Discussion:** These results demonstrate intrapancreatic fat deposition to be an effective biomarker in pancreatitis progression. Ghrelin may play a role in the pathogenesis driving IPFD. The involvement of IPFD with inflammatory and fibrotic changes in pancreatitis have been discovered in regards to disease progression.

Primary Supervisor: Professor Maxim Petrov



A3

Brain temperature as a measure of neuroinflammation: assessment using whole-brain magnetic resonance spectroscopy

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Background: Studies suggest a pathogenic role of neuroinflammation in psychiatric disorders; however, there are no accepted methods that can reliably measure these inflammatory processes in patients. Magnetic resonance spectroscopic imaging (MRSI) is a non-invasive technique that demonstrates sensitivity to neuroinflammation. **Objectives:** Using MRSI in conjunction with echo-planar spectroscopic imaging (EPSI), we aimed to measure brain metabolites to derive estimations of whole-brain and regional brain temperature, which may increase during neuroinflammation. **Methods:** Typhoid vaccine, a safe experimental model of human neuroinflammation, was administered to twenty healthy volunteers in a double-blind, placebo-controlled crossover study including MRSI/EPSI scans before and after treatment administration. Mood, assessed using the Profile of Mood States, was measured hourly up to four hours post-treatment administration. A mixed model analysis of variance tested for treatment effects. **Results:** A significant proportion of brain regions (44/47) increased in temperature post-vaccine compared to post-placebo ($p < 0.0001$). For temperature change in the brain as a whole, no significant treatment effect was observed. Significant correlations were observed between mood scores and post-treatment whole brain and regional temperatures. **Discussion:** Results indicate that regional, rather than whole, brain temperature may be a more sensitive measure of neuroinflammation. Future application of these neuroimaging techniques to patient populations would be of clinical interest.

Primary Supervisor: Dr Joanne Lin

A4

WITHDRAWN



A5

The effects of kawakawa (*Piper Excelsum*) consumption on markers of inflammation.

Tautuiaki S¹, Gojer J¹, Jayaprakash R¹, Pook C¹, Mithen R¹, Ramzan F¹, Foster M²

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Background: Kawakawa (*Piper excelsum*) is a shrub that is endemic to New Zealand, with huge spiritual and medicinal value to Māori. In traditional medicine, kawakawa is used to treat several diseases and infections such as diabetes, genitourinary tract infections and dermatological disorders. Research in animal and cell models have indicated the presence of various bioactive chemicals in kawakawa, that can modulate inflammation and related pathways. Despite the widespread use of kawakawa in traditional Māori medicine, there remains a lack of evidence demonstrating its inflammatory effects in human participants. **Objectives:** The aim of this project is to investigate whether the consumption of kawakawa as a tea has an effect on various inflammatory markers. **Methods:** Changes in the expression of inflammatory markers in healthy human volunteers will be investigated using banked peripheral blood mononuclear cells (PBMCs) samples from a previously performed two-arm randomized crossover study to assess the impact of acute kawakawa tea ingestion on postprandial glucose metabolism in healthy human volunteers (ACTRN12621000311853). Quantitative Polymerase Chain Reaction (PCR) will be conducted to analyse the expression of seven inflammatory genes including IL-6, IL-8, TNF- α , IL-8, CRP, FAS and CD36. **Results:** The results from this project have not been gathered as of yet, however it is hypothesized that due to kawakawa consumption, the expression of pro-inflammatory markers will be reduced, suggesting a possible anti-inflammatory role of kawakawa. **Discussion:** Study findings may provide evidence for the anti-inflammatory role of kawakawa within a healthy population.

Primary Supervisor: Dr Farha Ramzan

A6

Development of an iPSC-derived model of brain pericytes to investigate their role in neuroinflammation

McCullough S¹, O'Carroll S¹, Albers E¹, Connor B², Graham S³

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Background: Brain pericytes are cells found within the vascular basement membrane and have been shown to play a unique role in the mediation of neuroinflammation. Adult human brain pericytes are difficult to obtain and there is a limit to the quantity of these cells available upon culture, making them challenging to study. Differentiating brain pericytes from induced pluripotent stem cells (iPSCs) offers an alternative method to acquire these cells. **Objectives:** To generate human iPSC-derived brain pericytes and determine their potential to study neuroinflammation. **Methods:** Human iPSCs were primed towards a neural crest stem cell (NCSC) lineage. NCSCs were isolated at day 15 and differentiated into pericyte-like cells by day 42. We characterised these cells by investigating gene and protein expression of iPSC and pericyte markers using immunocytochemistry (ICC) and quantitative reverse transcription polymerase chain reaction. We also investigated their ability to respond to the inflammatory cytokines interleukin-1 β (IL-1 β) and tumour necrosis factor (TNF) using ICC to demonstrate nuclear translocation of transcription factors relevant to inflammatory pathways. **Results:** Gene expression of iPSC markers reduced throughout differentiation, while gene and protein expression of pericyte markers was observed in differentiated cells. Both primary and iPSC-derived pericytes responded to IL-1 β and TNF in a concentration-dependent manner. **Discussion:** The results of this study demonstrate the generation of a human iPSC-derived brain pericyte model, which has potential to study neuroinflammation. Future studies will use this model to investigate the effect of secreted factors from various brain cancers where the vasculature is known to be adversely altered.

Primary Supervisor: Dr Scott Graham



A7

See-through the ailment: chronic imaging to study nerve cell activity following spinal cord injury

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Background: Spinal cord injury (SCI) is a life-impairing condition significantly affecting individuals in many ways, e.g., personal, social, and economic. Decades of study have allowed a better understanding of the injury. However, despite this knowledge and the multiple attempts to regrow spinal cord cells, there is no cure. This suggests that our understanding of the injury is still lacking. Therefore, having insights on the injury response in-real time is key to understanding the disease better. **Objectives:** In the current project, we investigate neuronal cell activity within the central nervous system (CNS) before and after the injury. The latter will allow us to comprehend how the injury reshapes the CNS communication. Thus, it will enable us to understand how treatments can correct this activity and promote recovery. **Methods:** We monitor neuronal activity in living animals' CNS using miniaturized or benchtop microscopes. This is achieved through calcium imaging, using genetically encoded calcium indicators (GCAMP), which act as neuronal activity indicators. To optimize GCAMP expression in the rat cortex, we adopted a novel injection method, transverse sinus injection. **Results:** Transverse sinus injection successfully allows a widespread expression of GCAMP throughout the CNS. We found that this injection method allows in vivo imaging of neurons within the brain and spinal cord of restrained and unrestrained rats. **Discussion:** This project offers a novel way to study SCI by investigating the CNS plasticity before and after the injury. This will allow a better understanding of the pathology and assess the means to modulate it with treatments.

Primary Supervisor: Dr Simon J O'Carroll

A8

Regional differences in striatal dopamine transmission between DAT-KO and wildtype rats

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Background: The caudolateral (tail) striatum (TS) is a region of growing interest and distinct from the dorsolateral striatum (DLS). Whereas dopamine transmission has been well characterised in the DLS, it remains poorly understood in the TS. Our previous study identified that evoked dopamine release was considerably smaller in the TS, compared to the DLS, but surprisingly, was significantly larger in animals lacking the dopamine transporter (DAT-KO). Anatomical differences between the DLS and TS have also been identified: D1 and D2 receptors are distributed evenly across the DLS, whereas they are segregated in the lateral (D1-poor) and medial (D2-poor) TS. **Objectives:** To investigate regional differences in striatal dopamine transmission between DAT-KO and wildtype rats. **Methods:** Dopamine transmission was studied in wildtype and DAT-KO rats using fast-scan cyclic voltammetry to measure electrically evoked dopamine release from coronal brain slices (P28±2; 300 µm) in three TS regions (lateral, medial, dorsal), comparing them to the DLS. **Results:** Evoked dopamine release varied between regions in wildtype animals and, as expected, was greater in amplitude, prolonged and slower to reach peak amplitude in all regions in DAT-KO rats. The difference in amplitude (DAT-KO vs wildtype) was greatest in the dorsal TS (3.1x), but surprisingly the half-life (rate of dopamine clearance) increased most in the medial TS (44.8x). **Discussion:** These results show that DAT activity varies between striatal regions and hints additional dopamine clearance mechanisms are involved. The precise mechanisms underlying these regional differences require further investigation, and may identify novel treatment strategies for Parkinson's disease.

Primary Supervisor: Dr Peter Freestone



A9

Identification of stem cells in the posterior limbus

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Background: Stem cells in the superior corneoscleral limbus have been positively identified while those in the posterior limbus have not been clearly defined. The transition zone (TZ) may be a stem cell source of corneal endothelial cells (CECs). Posterior limbal mesenchymal stem cells (P-LMSCs) are more closely associated anatomically with TZ cells than superior limbal mesenchymal stem cells (S-LMSCs) and may prove essential to TZ cell function. **Objectives:** The aim of this investigation was to identify stem cells in the posterior limbus. **Methods:** Immunostaining of α -SMACreER/Ai14 mouse eyes was conducted to identify α -SMA-positive cells in the posterior limbus. Quantitative analysis was used to compare the expression of α -SMA, vimentin (mesenchymal marker), and CD34 (mesenchymal stem cell marker) between P-LMSCs and S-LMSCs, as well as α -SMA and CD166 (corneal endothelial marker) between TZ cells and CECs. **Results:** Different quadrants of the limbus have shown different intensities of α -SMA. LMSCs contain more α -SMA-positive cells than keratocytes. The α -SMA intensity in the limbus is significantly higher than that in the cornea. Vimentin and CD34 were stained in P-LMSCs and S-LMSCs, and CD166 was stained in TZ cells and CECs. Quantitative analysis of immunostaining showed that the percentage of α -SMA-positive cells was significantly higher in P-LMSCs than S-LMSCs and markedly higher in TZ cells than CECs. **Discussion:** We have identified α -SMA as a marker for P-LMSCs and TZ cells. This study positively identifies stem cells in the posterior limbus, which may contribute to corneal endothelial rejuvenation.

Primary Supervisor: Dr Jie Zhang

A10

Characterising Tau Pathology in the Huntington's Disease human brain

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Background: Huntington's Disease (HD) is a heritable neurodegenerative disease arising from a mutation in the huntingtin (htt) gene, resulting in the pathogenic production of mutant htt protein. Other non-mutant htt pathogenic proteins have been reported in HD, which may contribute to the neuropathology and variable symptomatology between patients. One of these pathogenic proteins is tau, which can present in many forms. However, tau has not been well-characterised in the HD human brain, particularly in the context of clinicopathology. **Objectives:** To characterise tau-associated pathology in the HD human brain. **Methods:** Human brain tissue microarrays comprising of cortical tissue from 28 HD and 27 neurologically normal brains were immunolabeled with antibodies targeting 4R and 3R tau isoforms using 3'3-diaminobenzidine immunohistochemistry. Image acquisition and analysis followed by statistical analysis investigating correlations between tau immunoreactivity and clinicopathological features of HD were conducted. **Results:** Preliminary results demonstrate immunoreactivity of 4R tau in 5/17 of HD cases and 3R tau in 1/17 of HD cases. Further studies will quantify the expression levels for each antibody and correlate this data with clinicopathological features of HD. **Discussion:** These results implicate tau isoforms relevant to the pathogenesis of HD in a subset of HD cases. Further studies are needed to determine if the selective presence of certain tau isoforms are associated with clinicopathological features of HD, including symptomatology, degree of htt protein accumulation, degree of gene expansion and extent of cell loss. These findings suggest the possible potential need for personalised treatments for certain HD patients exhibiting tau pathology.

Primary Supervisor: Dr Malvinder Singh-Bains



A11

Cardiovascular and cerebral perfusion changes during post-asphyxia seizures in preterm fetal sheep

Mills OJ¹, Dhillon SK¹, Gunn E¹, King VJ¹, Beacom M¹, Lear CA¹, Davidson JO¹, Gunn AJ¹, Bennet L¹

¹Department of Physiology, University of Auckland

Background: Seizures in preterm human infants are associated with adverse neurodevelopmental outcomes. The true burden of seizures in preterm infants is unclear as the majority of seizures are subclinical (i.e., they are present on electroencephalographic monitoring, but they don't manifest clinically), therefore they are at risk of under-detection. Further, little is known about how preterm seizures affect cardiovascular parameters and cerebral perfusion and whether these changes could contribute to neural injury. **Objectives:** To examine cardiovascular and cerebrovascular responses during seizures in preterm fetal sheep. **Methods:** Chronically instrumented preterm fetal sheep received sham asphyxia (n=8) or asphyxia induced by complete umbilical cord occlusion for 25 minutes (n=8). Electrocardiogram, blood pressure, electroencephalogram, carotid blood flow and cerebral oxygenation were recorded using near-infrared spectroscopy. Physiological recovery was monitored until 72 hours post-asphyxia. **Results:** Fetuses developed stereotypic evolving seizures on average 10.9h post-asphyxia, with an average seizure count of 39.2, duration 84.7s, amplitude 160.5 μ V and seizure burden of 136.9s/h. During individual seizures, there was an increase in fetal heart rate and blood pressure. There was either no change or a reduction in carotid blood flow associated with increased carotid vascular resistance, but there was no change in cerebral oxygenation. **Discussion:** These findings suggest metabolic demand associated with short-duration seizures in the preterm brain is insufficient to alter cerebral perfusion, suggesting they may not contribute to neural injury. Increase in heart rate and blood pressure during seizures are potentially associated with activation of central autonomic networks and could be a biomarker for detecting preterm seizures.

Primary Supervisor: Professor Laura Bennet

A12

Predicting long-term outcomes after Hypoxia-ischemia in preterm fetal sheep

Lear BA¹, Lear CA¹, Dhillon SK¹, Davidson JO¹, Gunn AJ¹, Bennet L¹

¹Department of Physiology, University of Auckland

Background: Preterm infants are disproportionately affected by hypoxia-ischemia resulting in high rates of adverse neurodevelopmental outcomes. Clinical studies group these infants as suffering from mild-moderate or moderate-severe hypoxia-ischemia. Importantly, there is no distinct threshold between severities. New biomarkers of hypoxia-ischemia should differentiate between these categories to facilitate clinical interventions. **Objectives:** Investigate the differences in pathology between mild, moderate and severe hypoxia-ischemia in preterm fetal sheep. **Methods:** Instrumented preterm fetal sheep received complete umbilical cord occlusion (UCO) to induce hypoxia-ischemia. Fetal sheep randomly received either sham-UCO (n=9), 15 minutes (n=9), 20 minutes (n=9), or 25 minutes-UCO (n=9). Electroencephalogram and blood-gas parameters were recorded for 21 days post-UCO before fetal brains were collected. **Results:** 15, 20 and 25mins-UCO were associated with mild, moderate and severe brain injury, respectively. The 15mins-UCO group showed mild injury with reduced myelin and increased immature oligodendrocytes compared to sham-UCO ($p<0.05$). 20mins-UCO had reduced mature oligodendrocytes and increased inflammatory-associated glial cells ($p<0.05$). 25mins-UCO had macroscopic injury including cystic lesions, reduced myelin and increased inflammation ($p<0.05$). 24-hours post-UCO, 20mins-UCO and 25mins-UCO groups had high partial pressure of oxygen compared to sham-UCO and 15min-UCO but only 25mins-UCO had elevated lactate ($p<0.05$). A significant difference in high-frequency electroencephalogram power was observed between all groups ($p<0.05$). **Discussion:** This study demonstrated that the severity of hypoxia-ischemia was associated with differences in blood gas parameters and electroencephalogram activity within 24-hours post-UCO and correlated with histological outcomes. Based on this, an electroencephalogram-based biomarker is being investigated to predict the long-term outcomes of hypoxic-ischemic preterm infants.

Primary Supervisor: Professor Laura Bennet



A13

Characterising the nature of inflammation-induced cerebellar injury in the preterm-equivalent rat.

Wilson H¹, Prasad J¹, Karunasinghe R¹, Dean J¹

¹Department of Physiology, University of Auckland

Background: Postnatal infection and inflammation is an ongoing issue in neonatal intensive care units, disproportionately affecting premature infants. In particular, very premature babies (born <32 weeks' gestation) are at the highest risk of brain injury and subsequent adverse neurological outcomes. Evidence indicates that these impairments have potential links to abnormal cerebellar development. However, the extent to which cerebellum development is affected by postnatal infection/inflammation is yet to be defined. **Objectives:** To characterise the nature of injury in the cerebellum in response to mild-to-moderate inflammation in the newborn rat. **Methods:** Sprague-Dawley rat pups received a single injection of 0.3 mg/kg of lipopolysaccharide (LPS) or saline (control) on postnatal days (PND) 1-3, and were recovered to PND2-21 for immunohistochemical analysis of white and grey matter regions of the cerebellum. **Results:** Compared with control animals, rats exposed to LPS exhibited dampened growth trajectories from PND2-21 ($p < 0.0001$). Initial pilot studies showed that while LPS exposure at PND2 was not associated with cell death or gliosis in the central white matter, there were trends for increased apoptosis and astrocytic densities in the intragryal white matter. **Discussion:** The results from this study suggest that mild postnatal systemic inflammation may result in increased apoptosis and gliosis in the white matter tracts of the intragryal regions of the cerebellum in PND2 rats. Further studies examining the cellular pathologies and mechanisms related to impaired development are undergoing, and will focus on characterizing cell death and maturation from PND4-21, in both white and grey matter regions.

Primary Supervisor: Associate Professor Justin Dean

A14

Detrimental effects of slow rewarming after therapeutic hypothermia for cerebral ischemia in near-term fetal sheep

McDouall A¹, Davies A¹, Zhou KQ¹, Wassink G¹, Bennet L¹, Gunn AJ¹, Davidson JO¹

¹Department of Physiology, University of Auckland

Background: Therapeutic hypothermia significantly reduces death and disability in infants with neonatal hypoxic-ischemic encephalopathy. After hypothermia current clinical protocols involve rewarming at no more than 0.5°C per hour. However, this was based on a best guess at the time, and there is still little controlled evidence for how quickly infants should be rewarmed after therapeutic hypothermia. **Objectives:** To determine whether slow rewarming improves neurophysiological and histological recovery from cerebral ischemia compared to rapid rewarming. **Methods:** Term-equivalent chronically instrumented fetal sheep were randomised to sham control, ischemia-normothermia, ischemia-hypothermia rapid rewarming and ischemia-hypothermia slow rewarming. Cerebral ischemia was induced by 30 minutes of bilateral carotid artery occlusion followed by normothermia or hypothermia from 3-72 h. In the rapid-rewarming group, fetuses were allowed to spontaneously rewarm over <1 h, while in the slow-rewarming group, fetuses were rewarmed at 0.5°C per hour over 10 h. **Results:** There were no significant differences between the hypothermia groups in recovery of EEG power or spectral edge frequency after cerebral ischemia. Both rapid and slow rewarming were associated with significantly greater cortical and hippocampal neuronal survival than normothermia ($P < 0.05$). Interestingly, after rapid rewarming but not slow rewarming, neuronal survival was not significantly different from sham-control values. Moreover, rapid but not slow rewarming was associated with a significant increase in oligodendrocyte survival in the intragryal and periventricular white matter ($P < 0.05$). **Discussion:** These data strongly suggest that rapid-rewarming after therapeutic hypothermia is associated more effective protection of neurons and oligodendrocytes than slow-rewarming.

Primary Supervisor: Associate Professor Joanne Davidson



A15

Embracing the chaos of fetal heart variability: a biomarker for evolving fetal hypoxic-ischaemic brain injury

Beacom MJ¹, King VJ¹, Lear BA¹, Lear CA¹, Dhillon SK¹, Gunn AJ¹, Bennet L¹

¹Department of Physiology, University of Auckland

Background: Hypoxia-ischaemia (HI) during fetal life is a major cause of brain injury leading to life-long neurodevelopmental disability. Detection and treatment during pregnancy would improve neural outcomes. Fetal heart rate variability (FHRV) derived from electrocardiographic (ECG) can be used as a diagnostic biomarker. However, current methods do not account for the non-linear nature of the physiological signals. **Objectives:** To evaluate the diagnostic potential of linear and non-linear FHRV measures after hypoxia-ischemia. **Methods:** Preterm fetal sheep were surgically instrumented for continuous measurement of ECG activity. 5-days post-surgery, fetuses underwent sham-HI (n=8) or HI (n=8; 25min of umbilical cord occlusion and were recovered in-utero for 21d post-insult. Evolving injury was classified into phases: recovery (latent; 0-6h), secondary loss of oxidative metabolism (secondary; 6h-4d), and tertiary (mixed cell repair and death 4d onwards). **Results:** The latent phase was best delineated by frequency and Distribution-entropy. All measures marked the start and general duration of the secondary phase, but detrended-fluctuation analysis (DFA) provided temporal precision. Circadian rhythmicity was lost in both phases and progressively returned by 7d. The mean (mesor) was lower for most measures, but day/night, peak/nadir oscillatory swings were 30-50% greater than controls, most prominently seen in time-domain, frequency, and entropy measures. A greater morning nadir ~10am was the most significant oscillatory change consistently observed. **Discussion:** These findings suggest that the combination of linear and non-linear FHRV measures are useful biomarkers to delineate phases and demonstrates that diurnal oscillations in FHRV may be a key biomarker for the tertiary phase evolution of HI.

Primary Supervisor: Professor Laura Bennet

A16

To vape or not to vape that's the question: A state of the artery investigation.

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Background: Electronic cigarettes (also known as e-cigarettes and vapes) are marketed as alternatives to tobacco smoking and have rapidly gained popularity, particularly among young people. Cigarette smoke is known to negatively affect the cardiovascular system including increasing large artery stiffness, an independent risk factor for the development of hypertension and cardiovascular disease. Tobacco smoking also affects the regulation of breathing by increasing peripheral chemoreflex sensitivity, which is associated with poor outcomes. **Objectives:** Herein, the effects of e-cigarettes / vaping on arterial stiffness and peripheral chemoreflex sensitivity will be described in young people for the first time. **Methods:** Two groups will be recruited; healthy young participants who currently vape and have done so for ≥ 1 year (n=15) and age- and sex-matched participants who have never vaped (n=15). Central and peripheral arterial stiffness will be assessed using applanation tonometry (Sphygmocor) to non-invasively determine carotid-femoral and carotid-radial artery pulse wave velocity, respectively. Peripheral chemoreflex sensitivity will be assessed from the minute ventilation (spirometry) responses to breathing 100% oxygen (hyperoxia; 2 min) to deactivate the peripheral chemoreflex and breathing 10% oxygen (hypoxia; 5 min) to activate the peripheral chemoreflex. **Results:** It is anticipated that regular vapers will have increased arterial stiffness (i.e., increased central and peripheral pulse wave velocity) and augmented ventilatory responses to peripheral chemoreflex modulation with hyperoxia and hypoxia compared to non-vapers. **Discussion:** The anticipated findings will provide important insights into the impact of e-cigarettes/vape use on physiological markers of cardiovascular risk.

Primary Supervisor: Associate Professor James P. Fisher



Oral Presentation Room B - 503-024

B1

Persistent opioid use after hospital admissions for surgery and trauma in New Zealand

Gong J¹, Sheridan J¹, Tomlin A¹, Chan AHY¹, Merry A², Jones P³, Beyene K⁴, Campbell D¹, McCall J⁵, Frampton C⁶

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Background: Hospital admissions related to surgery and trauma may contribute to opioid-related adverse outcomes, including persistent opioid use. New Zealand (NZ) has a paucity of data on persistent opioid use after surgery or trauma.

Objectives: We aimed to determine the rate of persistent opioid use in NZ following discharge from the hospital after surgery or trauma. **Methods:** This was a retrospective cohort study using linked data from national health databases from 1st January 2007 to 31st December 2019. Patients admitted for surgery or trauma, who were dispensed opioids on discharge and survived 365 days were included. Those with prior and recurrent surgery or trauma, opioid use or diagnosis of opioid misuse were excluded. Persistent opioid use was defined as any opioid dispensing between 91-365 days. The predictors of outcome were assessed using a multivariable regression adjusted for socio-demographic, clinical, comorbidity, routine medications, and discharge prescription variables. **Results:** 260,726 surgery and 205,201 trauma cases were dispensed opioids on discharge and included for analysis; the rate of persistent opioid use was 9.1% for surgery and 16.9% for trauma. Significant modifiable predictors ($p < 0.001$) for both cohorts included: receiving multiple opioids, high initial opioid load, and subsequent switching of opioids during follow-up. **Discussion:** In NZ, approximately one in ten patients who received opioids upon discharge following surgery or trauma between 1st January 2007 to 31st December 2019 became persistent opioid users. Our findings suggest using a single clinically appropriate opioid on and after discharge may reduce the likelihood of developing persistent opioid use.

Primary Supervisor: Dr Amy Chan

B2

Psychedelic Microdosing in Reality: exploring what people who microdose are consuming and effects experienced

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¹School of Pharmacy

Background: The practice of "microdosing" with psychedelic drugs has recently gained popularity. Microdosing involves taking minute amounts of psychedelic compounds on a routine schedule. There are myriad anecdotal reports and observational studies evidencing that microdosing may improve a number of facets in adults, such as mental wellbeing. No studies have analysed microdose samples that adults are consuming, therefore the drug identity and doses of substances consumed remain unknown. **Objectives:** To investigate psychological and physiological health of adults in New Zealand who are currently microdosing with psychedelics relative to controls. This work will also investigate drug sample content. **Methods:** Microdosers and controls will complete a range of measures over three time points. An online study run over three months will collect data using psychological questionnaires. Afterwards, an in-person study will collect further psychological data as well as microdose samples over two in-person visits. Measures include mental health, creativity, personality, cognition, heart health, and CYPDD6 genotype. Drug samples will be analysed using HPLC for drug type and dose. **Results:** Results are hypothetical at this stage. We hypothesise that given the illegal and unregulated nature of drugs used for microdosing, what people are taking is either not the expected drug and/or the "microdose" contains a different dose to that expected. We also hypothesise that microdose consumers will generally report positive psychological measure outcomes relative to controls. **Discussion:** This work will contribute novel outcomes for both the scientific field of psychedelic research and the field of harm reduction, promoting safer use of illicit drugs.

Primary Supervisor: Dr Rhys Ponton



B3

Changing medication mindsets: A brief intervention to improve patients' experience of methotrexate

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Background: Patient expectations about medication can influence side-effects and adherence. Many medications produce uncomfortable symptoms, fostering poor persistence and diminished treatment outcomes. Interventions encouraging adaptive mindsets about medication symptoms may reduce concern about side-effects and improve outcomes. **Objectives:** To determine the feasibility and impact of a brief mindset intervention encouraging patients to see non-severe side-effects of methotrexate as positive signals of medication efficacy. **Methods:** Two studies recruited patients prescribed methotrexate to treat autoimmune-based inflammatory arthritis. Patients were randomised to watch a mindset intervention video, or a standard side-effects information video. Study one was a cross-sectional evaluation, utilising patients with experience taking methotrexate (n=30). Measures included opinion of study videos, emotional response, symptom expectations, and methotrexate anxiety. Study two was a pilot randomised clinical trial (RCT) with 4-week follow-up, with patients starting methotrexate (n=18). Measures included emotional response, methotrexate anxiety symptom burden, and adherence. **Results:** In study one the intervention video was rated more understandable and convincing than the standard-information video. Intervention participants reported lower anxiety, expectation of side-effects and severe reactions than standard-information participants. In study two the intervention increased motivation to take methotrexate, belief of medication effectiveness and belief in side-effects as positive signals, as well as lowering symptom burden and expectation of severe reactions compared to the standard-information group. **Discussion:** These are the first studies testing a 'symptoms as positive signals' mindset intervention in an adult clinical population. The findings illustrate the potential of brief medication-mindset interventions and support testing with a fully-powered RCT and diverse clinical populations.

Primary Supervisor: Professor Keith Petrie

B4

Developing an evidence-based model of meaningful mobility in the context of positive ageing

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Background: Mobility, defined as meaningful movement within/across an environment, underpins many features of positive ageing for community-living older adults, including activities of daily living and community engagement. A comprehensive approach to understanding mobility, including older adults' perspectives, is needed. **Objectives:** We triangulate data sources and older adults' perspectives to address the following question: What role does mobility play in positive ageing? **Methods:** First, we developed an evidence-based model of meaningful mobility for older adults by consolidating four conceptual frameworks and supplementary literature. Second, we applied the model to our published scoping review on 'understanding positive ageing'. Through a thematic synthesis of 21 articles, we explored the nuances of mobility in the context of positive ageing. Finally, we demonstrated the utility of our meaningful mobility model using real-world data. Drawing from a larger project, four older adults (76-84 years; two male, two female) engaged in an online group discussion and shared their perspectives on mobility. **Results:** Our evidence-based model of meaningful mobility incorporated six elements: physiological, subjective, contextual, environment, temporal, and political. Through thematic synthesis, we highlighted the nuance, interconnectedness, and complexity within and between each element. Participants' descriptions further captured nuance and dynamic interconnections between the elements and enabled us to reflect critically on the utility of our model, and potential future adaptations and applications. **Discussion:** Our evidence-based model demonstrates utility across empirical literature and real-world contexts. By triangulating data and perspectives, we have developed an inclusive and meaningful understanding of older adults' mobility in the context of positive ageing.

Primary Supervisor: Professor Melody Smith



B5

Scopolamine's effect on heart rate variability and electroencephalography measures in participants with and without depression

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Background: Depression is typically treated with antidepressants which have been shown to decrease electroencephalography (EEG) alpha power along with modulate heart rate variability (HRV). Scopolamine has recently been investigated for its EEG effects in healthy individuals and antidepressant effects in individuals with depression, but not its HRV effects in depression. **Objectives:** This trial investigates scopolamine's antidepressant, EEG, and HRV effects in individuals with and without depression. **Methods:** Forty individuals with depression were administered 15-minute infusions of scopolamine or glycopyrronium. Glycopyrronium was chosen as the active placebo due to its similar antimuscarinic properties to scopolamine, but its inability to cross the blood-brain barrier. Mood outcomes via the Montgomery-Åsberg Depression Rating Scale (MADRS) were assessed pre-infusion to 6-weeks post-infusion. Furthermore, 12 healthy individuals were administered scopolamine. All 52 individuals underwent EEG and electrocardiography recordings from pre-infusion to 4-hours post-infusion. **Results:** Scopolamine improved MADRS scores in a similar magnitude to glycopyrronium yielding a non-significant antidepressant effect size ($d=0.17$) at day 3 in depressed individuals. When including the healthy individuals, significant group*time effects were observed in HRV ($F(32,309)=193, p<2e-16$), global EEG delta ($F(32,422) = 80.3, p=5e-6$) and alpha ($F(32,293) = 48.1, p=0.03$). Post-hoc analyses indicated that scopolamine increases HRV, delta, and alpha the most in healthy individuals compared to both individuals with depression given scopolamine and glycopyrronium. **Discussion:** The mood results raise questions about the magnitude of the placebo response. Furthermore, the different effects of scopolamine on healthy individuals and individuals with depression suggest both a central and peripheral antimuscarinic contribution to depression.

Primary Supervisor: Dr Suresh Muthukumaraswamy

B6

Seeking genetic modifiers to the drug trastuzumab emtansine (T-DM1) to advance HER2-targeted therapy

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Background: Trastuzumab emtansine (T-DM1) is an antibody-drug conjugate consisting of the human epidermal growth factor receptor-2 (HER2)-targeted antibody trastuzumab linked to DM1, a potent tubulin inhibitor. T-DM1 shows clinical activity in HER2-positive breast cancer, however, resistance remains a major challenge. Greater understanding of the resistance mechanisms could identify predictive biomarkers for T-DM1 therapy, leading to improved responses in stratified patients or provide a therapeutic target for combination therapy. **Objectives:** Validate candidate genes identified in clustered regularly interspaced short palindromic repeats (CRISPR) screens for genetic determinants of T-DM1 sensitivity in HER2-positive breast cancer cell lines. **Methods:** This study utilised MDA-MB-361 NUMA1, SLC46A1, MIEN1 and IRF2BP2 knockout clonal cell lines. MIEN1 silencing was achieved in MDA-MB-361 and HCC1954 cell lines. Sensitivity of the cell lines to T-DM1, DM1 and neratinib was measured by growth inhibition sulforhodamine B assay. An in vivo T-DM1 CRISPR knockout screen using MDA-MB-361 cells was carried out in NOD scid gamma mice. Bioinformatic analysis determined gene knockouts enriched or depleted in response to T-DM1. **Results:** NUMA1 knockout may promote resistance to T-DM1, while SLC46A1 knockout did not appear to influence T-DM1 response. Validation of CRISPR-mediated MIEN1 knockout revealed off-target unintended excision of nearby genes. Investigation into IRF2BP2 was halted due to reduced HER2 expression. Gene silencing suggests MIEN1 knockdown may promote sensitivity to T-DM1. The in vivo T-DM1 CRISPR screen identified potential candidate genes involved in T-DM1 sensitivity. **Discussion:** These candidate genes provide foundations that further biomarker discovery can build upon for T-DM1 therapy in HER2-positive breast cancer.

Primary Supervisor: Dr Barbara Lipert



B7

Investigating ligand and adjuvant combinations for development of a polyvalent *Staphylococcus aureus* vaccine

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Background: *Staphylococcus aureus* is an opportunistic human pathogen that can cause a wide range of infections that vary in severity. It is a major cause of nosocomial infection and in recent years, the emergence of multi-drug resistant strains has prompted the need to investigate other avenues for protection, such as vaccines. One possible avenue for at-risk patients would be a prophylactic vaccine that reduces *S. aureus* disease burden or colonisation. Our group is developing a polyvalent vaccine comprised of three different highly conserved proteins. Prior studies using mouse vaccination challenge models are promising, and I investigated further optimisation of the vaccine using the addition of ligands. These ligands are pattern recognition receptor agonists, and their addition has been shown to enhance protection and immunogenicity in other vaccine models. **Objectives:** Investigate the effect of ligand addition to the vaccine formulation in a murine model of infection. **Methods:** A mouse vaccine challenge study was performed, and bacterial burden was measured in tissues. Total specific antibody response to the vaccine components were measured via endpoint titre enzyme-linked immunosorbent assays. Functional assays to determine the ability of generated antibodies to neutralise these targets were also measured. **Results:** It was found that the addition of some ligands significantly reduced *S. aureus* burden in tissues ($p < 0.05$), as well as improved animal welfare during infection compared to their counterparts without ligand. Vaccine receiving groups generated specific antibodies, and some showed neutralising activity. **Discussion:** Additional studies will investigate the cellular response that is prompting this enhanced protection.

Primary Supervisor: Dr Fiona Radcliff

B8

The Development and Testing of a Novel Solute for Nasal Irrigation in CRS

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Background: Chronic rhinosinusitis (CRS) is a common multifactorial condition that presents with long-term inflammation of the sinonasal cavity. As a condition which produces significant economic burden, novel therapies are needed to reduce symptom severity, limit proliferation of bacterial biofilms, and assist with post-surgical recovery. Nasal irrigation is a safe, well-established management with a positive effect on symptom reduction at all stages of CRS. Despite new evidence suggesting that complex ion solutions and additives such as xylitol significantly improve symptom relief and have antimicrobial effects, saline nasal irrigation is still predominantly prescribed. **Objectives:** To design an evidence-based novel solute for nasal irrigation that is safe and optimised for CRS. **Methods:** pH and osmolarity of existing commercial solutes were investigated to establish standards for development. The in vitro effect of a novel solute at differing antimicrobial doses on bacterial biofilms was evaluated using the MBEC Assay system, before testing adherence and tolerability compared to commercially available rinses using the Meltzer Clinical Trial Patient Preference Questionnaire in a cohort of healthy participants. **Results:** The physical characteristics of commercial sinus rinse solutions suggested tolerability between significant pH and osmolarity ranges. Preliminary results will be presented investigating the in vitro antibiofilm effect of the solutions on preformed *S. aureus* and *P. aeruginosa* biofilms, as well as the tolerability based on healthy volunteer trials. **Discussion:** Through these methods we aim to produce a novel solute that is optimised for long-term symptom control, post-operative recovery, and recalcitrant disease in CRS.

Primary Supervisor: Professor Richard Douglas



B9

Delivery of bovine lactoferrin to osteoblasts in vitro using niosomes

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Background: Bovine lactoferrin (bLF) stimulates osteoblast proliferation and has antimicrobial and antibiofilm activity. Therefore, it may be used to complement therapy for bone and prosthetic joint infections. However, bLF degrades rapidly in the gastrointestinal tract and in blood plasma. Packaging it within a nanocarrier will protect it from degradation and prolong its effect. Niosomes are nanocarriers that can enhance drug stability and permeability. Compared to liposomes, they are cheaper to fabricate. Niosomes are also biodegradable and biocompatible with human cells. **Objectives:** To encapsulate bLF into niosomes and investigate how this affects bLF activity on primary rat osteoblast cell cultures in vitro. **Methods:** Niosomal bLF will be fabricated by thin film hydration using span 60, cholesterol and dicetyl phosphate in a certain molar ratio and characterized by measuring zeta potential, particle size, entrapment efficiency (EE) and in vitro release profile. Niosomal bLF will then be co-cultured with osteoblast cells. Osteoblast cell counts, cell proliferation (measured by thymidine incorporation) and cell viability (measured by AlamarBlue) will be quantified. **Results:** The average EE for our bLF-loaded niosomal formulation was 99.7%. This is higher than that for other formulations of bLF reported in the literature. The osteoblast cell culture study is ongoing. **Discussion:** A high EE means most of the drug added during niosomal fabrication has been incorporated into niosomes, reducing the amount of encapsulating material used, increasing cost-effectiveness of the formulation and reducing potential toxicity from excipients. Now, the release of bLF from niosomes to osteoblasts needs to be measured.

Primary Supervisor: Professor Jillian Cornish

B10

Regulation of Estrogen Receptors by DNA Methylation and Hydroxymethylation in Human Endometrium

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Background: Steroid hormones, receptors, and epigenetic mechanisms work together to control the dynamic endometrium. Abnormal gene expression is associated with compromised steroid hormone action. While the role of Ten Eleven Translocation (TET) in the endometrium remains relatively unexplored, growing evidence suggests its involvement in mediating DNA hydroxymethylation and regulating gene expression. **Objectives:** To explore the involvement of steroid hormones in transcriptional and translational regulation of TETs and estrogen receptor alpha (ER α) in the human endometrium. **Methods:** Endometrial stromal cell lines (HESCs) were treated with control, 24hrs estrogen, or 24, 48, and 72hrs combined estrogen/progesterone. TETs and ER α gene expression was examined using RT-PCR. DNA from HESCs, and proliferative and secretory phase normal endometrium were extracted, bisulfite-oxidised bisulfite converted, and sequenced to assess methylation and hydroxymethylation. **Results:** In HESCs, TET1 transcription increased after 48hrs combined estrogen/progesterone, while TET3 decreased following 72hrs combined treatment. No significant changes were observed in TET2 expression. 24 and 48hrs combined estrogen/progesterone treatment upregulated ER α . Methylation analysis revealed site-specific differential methylation in response to hormones in HESCs. No methylation changes in examined CpG sites were observed between proliferative and secretory endometrial tissue samples. **Discussion:** Results imply co-regulated steroid hormone receptors and TET expression. Promoter methylation analysis of specific CpG sites suggest not all sites are controlled by steroid hormones or involved in ER α transcriptional activation. Improved understanding of complex co-regulatory relationships between epigenetic mechanisms and steroid hormone throughout the menstrual cycle may indicate how alterations contribute to abnormal hormone signalling in conditions such as endometriosis.

Primary Supervisor: Dr Anna Ponnampalam



B11

Small and squishy: growth restriction in the chronically instrumented fetal sheep

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Background: Fetal growth restriction (FGR) is a leading cause of adverse outcomes in pregnancy. Most cases occur later in gestation, with moderate, asymmetrical (brain-sparing) growth restriction. As we lack biomarkers, ~50% are undetected until acute demise or birth. **Objectives:** To develop a FGR animal model with long-term, comprehensive fetal monitoring to identify biomarkers. **Methods:** 0.7 gestation fetal sheep (~27-30 weeks human brain development) were instrumented with catheters for blood sampling and electrodes for electroencephalogram and electrocardiogram recording. A silicone occluder was placed around one umbilical artery (UA). A maternal artery was catheterised. 5 days post-surgery the UA occluder was gradually inflated to reduce blood flow to the placenta. **Results:** UA occlusion induced moderate FGR (2.92kg vs 3.39kg, $p < 0.05$), brain-sparing (brain: bodyweight ratio 15.71 vs 11.93, $p < 0.05$), and global placental inflammation. Fetal oxygen saturation was reduced during the first week (50.9% vs. 64.4%, $p < 0.05$). By experiment end, electroencephalogram amplitude was increased (116% of controls, $p < 0.05$). There was an earlier, greater fall in electroencephalogram frequency (88% of controls, $p < 0.05$). Fetal and maternal heart rate circadian rhythmicity (nadir/peak cycling) was reduced ~40% during the first week and then resolved. This rhythmicity reduction was seen again in fetuses who became hypoxic and/or died later in gestation. **Discussion:** These data demonstrate the utility of gradual UA occlusion in producing moderate, late-onset asymmetrical FGR. EEG data are consistent with brain sparing, reduced connectivity and altered sleep state development as seen in human FGR cases. Changes in fetal and maternal heart rate may be a biomarker for progressive fetal deterioration.

Primary Supervisor: Professor Laura Bennet

B12

Proliferation and invasion-associated miRNAs in first-trimester and term placental extracellular vesicles: inspirations for cancer-regulation

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Background: The human placenta and tumor are both invasive structures. However, placental invasion and proliferation are tightly regulated and reduced as the pregnancy ends. Micro and nano Placental extracellular vesicles (pEVs) are different-sized lipid-enclosed packages secreted by placentae. They carry DNA, RNA, proteins and lipids derived from placentae, which are thought to contribute to the regulation of placental invasion and proliferation. **Objectives:** To identify the differences in the miRNA profiles in first-trimester and term pEVs, and to identify miRNAs that might help regulate placental and tumorous invasion and proliferation. **Methods:** pEVs from the first-trimester and term placentae were collected, followed by small RNA sequences. MicroRNAs with differential abundance between the two groups were identified. Literature searches combined with the target genes enrichment analysis identified differentially abundant miRNAs associated with proliferation and invasion pathways. **Results:** 300 (in micro-pEVs) or 208 (in nano-pEVs) miRNAs were differentially abundant between term and first-trimester pEVs. Gene enrichment analysis showed that some of those differently abundant miRNAs in pEVs participate in pathways associated with growth and invasion control. Oncogenic miRNAs including miR-455 and miR-9, which promote the proliferation and invasion of tumors, were significantly less abundant in term pEVs; while anti-oncogenic miRNAs including miR-100-5p and miR-125a, which inhibit the proliferation and invasion of tumors, were significantly more abundant in term pEVs. **Discussion:** Significant differences in the abundance of miRNAs in pEVs could be a mechanism for controlling invasion and proliferation in placental development. This may also explain some of the differences between the placenta and tumor.

Primary Supervisor: Professor Larry Chamley



B13

Proteomic analysis of placental extracellular vesicles on inhibiting the growth of ovarian cancer

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Background: Placental extracellular vesicles (EVs) are lipid-enclosed packages of cellular contents that are used for targeted intracellular communication. We have previously shown that treatment with placental EVs, but not monocyte-derived EVs significantly inhibited the growth of ovarian cancer cells. However, the mechanism underlying this inhibitory effect has not been fully investigated. In this study, we compared the proteomes of placental and monocyte-derived EVs. **Objectives:** To identify specific targetable, regulatory molecules in placental EVs that confer protection against ovarian cancer growth. **Methods:** Placental EVs and monocyte-derived EVs were collected from cultures by ultracentrifugation. Label-free proteomic sequencing and quantification was conducted. In addition, human ovarian tumour tissues were collected and were then cultured with placental EVs. The expressions of proteins associated with cell death were performed by western blotting. **Results:** By comparison of the protein profiles between placental EVs and monocyte-derived EVs, we found that many proteins associated with promoting cell death, such as programmed cell death 1 ligand 1, are only present in placental EVs, but not detected monocyte-derived EVs. The cell death-associated proteins were significantly upregulated ($p < 0.01$, fold change > 2) in ovarian tumour tissues following treatment with placental EVs. **Discussion:** Our data suggested that one mechanism underlying the inhibitory effect of placental EVs on ovarian cancer cell growth is upregulation of cell death signals in the cancer cells by placental EVs.

Primary Supervisor: Professor Larry Chamley

B14

Characterising haematopoietic progenitors within the placental villous core

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Background: In early pregnancy, placental macrophages (Hofbauer cells) and red blood cells (RBCs) are thought to arise de novo from specialised villous core progenitors, but little is understood about this process. Our prior work has identified two populations (CD31+/CD34+ placental endothelial progenitors and CD73+/CD90+ placental mesenchymal cells) that preliminary data suggest may be capable of generating macrophages or RBCs respectively. **Objectives:** This work aimed to better characterise placental villous core progenitors and identify potential sub-populations with phenotypic potential to give rise to haematopoietic lineages. **Methods:** First-trimester placentae (7-9 weeks of gestation) were denuded of trophoblast and enzymatically digested. The resulting villous core cells were analysed using a 19-colour flow cytometry panel to characterise both potential progenitor and mature haematopoietic populations. **Results:** Within CD73+/CD90+ mesenchymal cells, large variations in the amount of CD271+ cells ($53.03\% \pm 37.29$ $n=2$) was seen between samples. As CD271+ cells are thought to have superior differentiation and colony forming capacity in MSCs, we hypothesise CD271+/CD73+/CD90+ mesenchymal cells improve RBC differentiation in culture. Within CD31+/CD34+ placental endothelial cells a subpopulation of CD144- cells was identified ($44.16\% \pm 2.52$, $n=2$). We suggest loss of CD144 expression, an endothelial junctional marker, may mark a transition from endothelial to haematopoietic potential within CD31+/CD34+ cells promoting macrophage differentiation in culture. **Discussion:** The sub-populations identified in this work are of interest for their potential ability to differentiate into haematopoietic lineages, and their potential to do this will be assessed in vitro in future functional differentiation experiments.

Primary Supervisor: Associate Professor Joanna James



B15

Predictors of injury among young children in New Zealand: a longitudinal trajectory approach

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Background: In New Zealand (NZ), unintentional injuries pose a major public health threat to children and are one of the leading causes of hospitalisation and death among children. Falls, struck by/against, burn, and foreign body ingestion are leading injury mechanisms among infants because of their limited coordination and exploratory nature with an inability to predict danger. In NZ, there is limited information about the trajectories of risk factors for unintentional childhood injury. **Objectives:** To explore the longitudinal relationship between a wide range of child, family and environmental factors and the risk of injury among preschool children. **Methods:** Secondary data analysis was conducted using the Growing up in NZ cohort linked to routinely gathered injury claims. Distribution and predictors of injury were identified using the theoretical life-course framework of child injury prevention domains: individual, maternal, social and environmental factors fitting a multivariable robust Poisson regression model for the longitudinal analyses. **Results:** Up to age five, 74% (of N=5,637) of children experienced at least one injury. Among these children, most injuries (75%) occurred at home. Individual factors (male sex, poor child health, developmental concern and behaviour difficulty), maternal and social factors (maternal depressive symptoms, single-parent homes, and living in public housing) were identified as predictors of higher injury risk. **Discussion:** The findings of this research have helped to provide the evidence needed to mitigate the risk associated with injuries and to inform targeted and effective policies and interventions to reduce the incidence of preschool child injury morbidity and mortality in NZ.

Primary Supervisor: Professor Bridget Kool



Oral Presentation Room C - 503-028

C1

The Epidemiology of Eye Melanoma in New Zealand - A 20-year Study

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Background: Despite being a rare cancer, eye melanoma is the most common primary cancer in the adult eye and the second most common site of melanoma following the skin. The annual incidence and mortality in New Zealand (NZ) are unknown. **Objectives:** To investigate the incidence and survival of eye melanoma in NZ. **Methods:** Epidemiological data on histologically confirmed eye melanoma between 01/01/2000 to 31/12/2020 were extracted retrospectively from the NZ cancer registry. The main outcome measures were patient demographics, crude and age-adjusted incidence, trends and survival. **Results:** A total of 771 eye melanoma cases (1.6%) were identified from 47,997 cases of all melanomas. Most cases (94.9%) were of European ethnicity, with only 3.6% Māori, 0.9% Asian and 0.5% Pacific Peoples. Half (50.8%) were female. The mean follow-up time was 6.7 ± 5.2 years. The mean age at diagnosis was 63.89 ± 14.57 years, and the mean age at diagnosis in Māori was on average 7.5 (95%CI: 2.1-13.0, $p=0.007$) years lower than in Europeans. The age-standardised incidence was 6.97 ± 1.10 per million population per year, and no significant trend was observed over 21 years. The 1-, 5- and 10-year overall survival probabilities were 94.5%, 67.7% and 51.0%. **Discussion:** Consistent with international studies, eye melanoma in NZ predominantly occurs in patients with fair skin and light irises. The stable incidence and favourable survival (compared to previous global studies) should be interpreted in the context of advancing technology, which may have facilitated earlier detection, and therefore, treatment of smaller sized tumours that did not require tumour renewal.

Primary Supervisor: Professor Charles McGhee

C2

Predicting ophthalmic clinic non-attendance using machine learning

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Background: Clinic non-attendance in New Zealand is associated with poorer health outcomes and costs \$29m per annum. Initiatives to improve attendance typically involve expensive and ineffective brute-force strategies. **Objectives:** To develop a predictive model for ophthalmic-clinic attendance. **Methods:** Nationwide ophthalmology clinic data were aggregated for analysis. Variables included patient age, ethnicity, sex, deprivation quintile, weather and several clinic related factors. Feature engineering included binary encoding of predictive categorical variables. Machine learning models were evaluated using the area under the receiver operating characteristic curve (AUROC), sensitivity, specificity and precision. Model weighting was adjusted to account for the highly imbalanced dataset. 10-fold cross validation was used. **Results:** Data included 3.3 million clinic appointments with 5.9% non-attendance rate. Raw data were divided for model training, validation and testing to enable a robust validation framework. A nationwide model achieved sensitivity of 73%, specificity of 69%, AUROC of 0.76 and precision of 12.8%. Predictive performance increased when models were constrained to DHBs with modest increases in non-attendance rates. Using a comprehensive dataset from Waikato Hospital, a marginally improved AUROC of 0.8 was achieved. **Discussion:** It is possible to use machine learning algorithms to predict clinic non-attendance. The AUROC confirms this model enables clinically useful predictions of clinic attendance. The model AUROC in the current study is competitive with previously published predictive models of attendance in the literature. This level of discrimination is high enough to be used in advanced scheduling methods and targeted public health interventions.

Primary Supervisor: Dr James McKelvie



C3

Crystallin Clear: Improving Bioengineered Corneal Stromal Materials

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Background: The cornea is the outermost structure of the eye. An estimated 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 the chronic shortage of cadaveric donor corneal tissue, only 1 in 70 people worldwide who require a corneal transplant will receive one. **Objectives:** To develop and characterise corneal stromal equivalents to supplement the insufficient supply of cadaveric corneal tissue required for sight-restoring corneal transplant surgery. **Methods:** A small animal study was conducted to test the biocompatibility of lens crystallin protein films developed for ocular therapeutics. Corneal health was scored according to a modified McDonald-Shadduck Scoring System, using indirect ophthalmoscopy and slit-lamp biomicroscopy. Lens crystallin proteins will be combined with type I collagen to produce electro-compacted stromal equivalents. Physiological-pressure inflation testing with ellipsoid modelling and compression testing will assess mechanical properties against human and porcine corneal tissue. Stromal cell proliferation and gene expression profiles will be used to evaluate biocompatibility. **Results:** Animal study results show crystallin proteins are well tolerated in biological systems and resistant to degradation on the ocular surface. The inflation testing rig has been constructed and allows for accurate pressure monitoring and image capture of corneas for analysis. 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 Laura Domigan

C4

Comprehensive grading system for experimental autoimmune uveitis in mice

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Background: Experimental autoimmune uveitis (EAU) is the most commonly used animal model for studying the progression of chronic uveitis as well as test novel therapies. However, to accurately evaluate the effectiveness of such treatments, it is important to have a grading system that combines latest imaging techniques with quantitative grading thresholds. **Objectives:** This study aimed to develop a comprehensive grading system that objectively evaluates EAU progression in C57black6 mice. **Methods:** EAU was induced in mice following immunisation with IRBP1-20 (inter-retinoid binding protein) and pertussis toxin. Weekly fundus and ocular coherence tomography (OCT) images were acquired over 12 weeks using Micron IV imaging system. Each mouse eye was graded (0-4) based on changes seen in both fundus (optic disc, retinal blood vessels and retinal tissue) and OCT (vitreous and retinal layers) images. A total EAU response was calculated for each EAU mouse based on the sum of individual grades. **Results:** Analysis of clinical scores depicted a gradual increase (p-value <0.05) in inflammatory signs, starting at week 2-3 and peaking at week 9-11 post immunisation, including optic disc and vascular swelling, vitreous leukocyte infiltration, retinal lesions and formation of granulomas and hyper-reflective foci in retinal layers. Optic disc atrophy, structural damage to the retina and sub-retinal oedemas were noted in 80-90% of mice. **Discussion:** In contrast to previous grading systems, our system allowed us to quantitatively track the progression of multiple inflammatory signs not only in fundus but also in OCT images providing a complete picture of inflammation occurring in EAU mice.

Primary Supervisor: Assoc. Professor Ilva Rupenthal



C5

Optimising Umbilical Cord Mesenchymal Stem Cells for the Treatment of Keratoconus

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Background: Keratocytes in the corneal stroma help maintain corneal transparency. In Keratoconus, these cells are progressively lost, leading to vision loss. In serious instances, corneal transplants are performed; however there is a global lack of donor tissue. The umbilical cord (UC) is an abundant source of mesenchymal stem cells (MSCs), which can differentiate into keratocytes and be used for cellular therapy. Yet, isolation and differentiation success rates vary. **Objectives:** Optimise the isolation of MSCs by exploring the characteristics and distribution of MSCs in the UC. Establish the location with the most MSCs. **Methods:** UC structural and cellular anatomy were explored by H&E and immunohistochemistry (IHC). MSCs were identified in situ by IHC triple labelling. Antibody validation was performed by Western Blot. MSC marker expression was measured using droplet digital polymerase chain reaction. Cellular distribution was quantified by DAPI staining. **Results:** The UC stained positive for vimentin, laminin, α SMA and cytokeratin. All umbilical stromal cells expressed positive MSC markers CD105, CD90, and CD73. CD34 and CD73, negative MSC markers, were also expressed. Cells furthest from the placenta insertional region of the cord showed significantly decreased CD105 and CD34 expression, and increased CD90 expression. More cells were found surrounding the vasculature and at either ends of the umbilical cord than the centre. **Discussion:** There is variability in MSC stemness along the UC. Research into the functionality of MSC markers and the UC region with the highest MSC potencies is warranted to optimise cellular therapy for Keratoconus treatment.

Primary Supervisor: Professor Trevor Sherwin

C6

Are we Compromising the Dabigatran Product Stability by Using Adherence Packaging?

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Background: Dabigatran (Pradaxa™, Boehringer Ingelheim) is an anticoagulant used for the prevention of thromboembolic events. Ageing populations and polypharmacy led to use of dose administration aids (DAA) to improve adherence. However, the moisture sensitivity of dabigatran capsules outside of the manufacturer's packaging prevents use of dabigatran in DAAs and its stability data in DAAs as per the New Zealand climatic conditions is lacking. **Objectives:** To assess the stability of Pradaxa capsules over 16 weeks in DAA (Medico Pak, unit-dose sachet) and compare with the original packaging when stored in different conditions. **Methods:** High-performance liquid chromatography (HPLC) assay was developed and validated to quantify dabigatran. Pradaxa 110mg capsules repacked in Medico Pak and unit-dose sachets were stored at room temperature, bedroom, fridge and extreme conditions (40°C, 75% relative humidity) over 16 weeks. At predetermined days, capsules were analysed for drug content using HPLC assay. Dissolution testing was also conducted to assess the effect of storage conditions on the drug release profile. **Results:** The content assay from day 7 samples is complete and the percentages recovered were within limits, $100 \pm 2\%$ (Pharmeuropa 3303 E) for all the tested storage conditions. Analysis of samples from other time points and dissolution study are in progress. **Discussion:** The manufacturer's requirement to keep the capsule in the original packaging compromises patient adherence. The results from this study will directly impact pharmacy practice and will guide the Pradaxa dispensing practices in New Zealand community pharmacies.

Primary Supervisor: Dr Manisha Sharma



C7

Intra-subject and inter-subject accuracy in predicting gait parameters using wearable sensors and Random Forest

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Background: Gait analysis outside the laboratory has been possible by recent advancements in wearable sensors like inertial measurement units (IMUs). To date, a few studies have used IMUs and machine learning to predict a few joint angles and moments. **Objectives:** The aim of this study was to develop models to estimate lower-limb joint kinematics and kinetics from IMUs. **Methods:** Seventeen healthy volunteers (9F, 28±5 yrs) were asked to walk over-ground for 16 trials. For each trial, marker trajectories and three force-plates data were recorded to calculate the targets (pelvis, hip, knee, and ankle kinematics and kinetics). IMUs data were recorded and used as input to a Random Forest (RF) model for targets' prediction. The intra-subject model was trained on 11 trials and tested on five trials for the same participant. A leave-one-out analysis was also used to quantify inter-subject accuracy and predict targets for an unseen participant. Data analysis consisted of Root Mean Square Error (RMSE) calculation. **Results:** Intra-subject model outperformed inter-subject model, as it has been tested for participants that were used in training. The best and worst kinematics predictions were related to pelvis obliquity and ankle inversion/eversion angles, respectively. While in kinetics predictions, the lowest and highest errors came from hip rotation and pelvis tilt moments, respectively, for both models. **Discussion:** This study suggests that combining IMU with an RF model has a high potential to predict gait parameters. The performance of the inter-subject model can be improved by increasing the sample size in a future study.

Primary Supervisor: Dr Julie Choisine

C8

Developing a bioinformatics tool to identify stable isotope incorporated compounds in imaging mass spectrometry data

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Background: Metabolomics research with Imaging Mass Spectrometry (IMS) is powerful. Distributions of hundreds of small molecules are detected simultaneously from thin tissue sections and displayed in two-dimensional images. To focus on specific metabolic pathways, a stable isotope labelling (SIL) approach is introduced to replace endogenous compounds. However, identification of more obscure SIL compounds is challenging. Therefore, developing a bioinformatics tool for uniformly-labelled SIL metabolites is necessary. **Objectives:** To develop a novel workflow of automated SIL metabolite annotation and use our bioinformatics tool to interpret glucose-related metabolism in bovine lens. **Methods:** IMS data on bovine lens is obtained from a previous glucose uptake study in bovine lens. Statistical analysis is used for metabolite selection including test of significant and correlation analysis to reduce the compounds that are not related to glucose metabolism. An existing annotation algorithm used for endogenous compounds has been modified to expand its application to uniformly-labelled SIL metabolites by constructing a library of SIL (Carbon-13) metabolites. **Results:** The developed Carbon-13 library increases the coverage of total and significant metabolite hits on the predefined pathways, offering an overview of glucose metabolism in bovine lens. Specifically, 67 SIL compounds are annotated in up to 41 possible metabolic pathways. **Discussion:** Our proposed pipeline can give annotations to SIL metabolites and profile the metabolic pathways that are present in different regions of the lens. We initially use it to map the glucose metabolism in bovine lens, but this approach has a wide biomedical application where SIL IMS is used.

Primary Supervisor: Dr George Guo



WITHDRAWN

C10

Go big: the power of the mesoscope

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Background: Widefield calcium imaging is a popular method to study populations of cellular activity over large areas of the brain. Conventional widefield microscopes tend to have small field of view (FOV), limiting images to be taken regionally, whereas the large FOV of the mesoscope allows imaging over the whole mouse cortex. **Objectives:** To compare widefield microscopes with different FOVs for in vivo calcium imaging neuronal activity in the cortex. **Methods:** The genetically encoded calcium indicator, GCaMP7 was injected into the transverse sinus of mouse pups at postnatal day 1. Brain activity in the form of change in fluorescence were recorded in neonatal and adult mouse under either a conventional upright fluorescence microscope or a custom-built mesoscope. **Results:** The 1.5x objective of the conventional microscope gave a FOV of 5mm x 5mm, which was not large enough to capture the whole brain, even for a pup at 8-10 days old. Furthermore, hardware limitation meant low expression of the calcium indicator led to a "bright spot" artefact. The FOV of the mesoscope at 10.5mm x 13mm was able to image the whole cortex of the adult mouse with good signal-to-noise ratio. **Discussion:** The smaller FOV from conventional fluorescence microscope enables activity to be imaged from one specific region of the brain. In contrast, the large FOV of the mesoscope allows imaging of cortex-wide activity in mouse with the good signal-to-noise ratio. The mesoscope provides a good approach to study processes that span throughout the cortex, such as sensory processing and cognition.

Primary Supervisor: Dr Juliette Cheyne



C11

When Death becomes Life: determinants of deceased organ donation consent

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Background: Deceased organ and tissue donation (DOD) saves lives. DOD in New Zealand operates under an opt-in system, which requires consent from families of patients diagnosed with brain death (BD) or circulatory death (CD) while in the Intensive Care Unit (ICU). The donation demand and supply mismatch cannot be ignored. **Objectives:** To understand staff and families' perspectives on determinants to DOD decision making in ICU settings. **Methods:** An integrative review involving systematic searching of CINAHL Plus, SCOPUS, Proquest and Medline Ovid databases and manual ancestry searches. Data were systematically extracted and coded onto Excel spreadsheets and analysed using an inductive, thematic approach. **Results:** 21 studies (12 qualitative, seven quantitative, two mixed methods) were included. Publication dates ranged from 1993 to 2021, studies were from multiple countries (18 opt-in, three opt-out systems). Four overarching themes were generated: important knowledge, challenging communication, internal and external determinants. Families experienced knowledge deficits of BD concepts, purpose of ventilation, DOD procedures and patients' wishes. These factors, compounded by dissonant grief, conflicting values, lack of comfort/closure, miscommunications with staff and interrupted continuity of care dissuaded families from consenting. For staff, lack of DOD training, challenges managing extensive multidisciplinary collaboration, organisational constraints, personal attitudes and balancing duty to potential donors and transplant recipients hindered their ability to meet families' needs. **Discussion:** Factors underpinning DOD are multifaceted and complex. Staff actions and families' decisions were inextricably intertwined. Research in New Zealand exploring DOD experiences of staff/families and evaluating current performance could benchmark practice and identify opportunities for improvement.

Primary Supervisor: Associate Professor Rachael Parke

C12

Functional dyspepsia association with retrograde slow waves detected by a body surface gastric mapping device

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Background: Functional dyspepsia (FD) is a prevalent gastroduodenal disorder. The pathogenesis is undefined, limiting therapeutic progress. Gastric dysmotility and electrophysiological disturbances have been proposed, but reliable clinical methods to evaluate these abnormalities have been lacking. A new medical device for non-invasively evaluating gastric dysfunction called body surface gastric mapping (BSGM), which measures novel biomarkers including wave propagation analysis, was applied to assess FD. **Objectives:** To define gastric electrophysiological abnormalities and their symptom correlation in patients with FD compared to healthy matched controls. **Methods:** 25 patients with FD as defined by Rome IV criteria were matched by age, sex and BMI to 25 healthy controls. BSGM was performed using Gastric Alimetry (New Zealand), employing a high-resolution electrode array, wearable Reader, and simultaneous symptom logging on a validated App. Participants underwent a 30-min baseline recording, followed by standardised meal (482kCal) and 4-hr postprandial recording. Data was analysed using the Gastric Alimetry processing pipeline. **Results:** Patients with FD showed a substantially higher percentage of retrograde propagating gastric waves in the post-prandial period (median 16.70% (IQR 3.30 to 26.70) vs 30.00% (IQR 20.00 to 43.30) $p < 0.001$). Additionally, retrograde slow wave propagation correlated with symptoms of excessive fullness, early satiety, bloating, heartburn, and pain, as well as the total Gastroparesis Cardinal Symptom Index (all $r > 0.4$; $p < 0.05$). Other BSGM biomarkers showed no difference. **Discussion:** BSGM allows detection of new biomarkers of gastric function including gastric wave propagation direction. Additional studies are in progress to further define this new finding and its pathophysiological role in FD.

Primary Supervisor: Professor Greg O'Grady

C13

An evaluation of digital humans in delivering relaxation for wound healing and stress reduction

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Background: Virtual humans are a form of artificial agent that shows promise for delivering e-health interventions, but research designs have been preliminary to date. Therefore, more randomised controlled trials (RCTs) are needed to evaluate their effectiveness in delivering interventions and improving health outcomes. **Objectives:** To evaluate the effectiveness of a brief relaxation intervention delivered by a virtual human on wound healing and stress, compared with a real human audiotope condition, and a control condition. **Methods:** An RCT with a mixed factorial design was conducted. 159 participants underwent a non-invasive tape-stripping procedure to disrupt the skin barrier, followed by 20 minutes of relaxation (randomly allocated to either the virtual human, audiotope or reading magazines). Psychological (stress, relaxation, anxiety, and pain), and physiological (heart rate and electrodermal activity) measures and stress hormones (salivary cortisol and alpha-amylase) were collected at three time points. **Results:** Results indicated no significant differences between the delivery methods in skin barrier recovery, psychological or physiological stress measures. However, the digital human and audiotope groups had significantly greater relaxation levels than the control group. In the audio-tape group, anxiety reduced significantly more, and satisfaction and engagement levels were greater than the other groups. Hormone results are pending. **Discussion:** The findings demonstrate that a virtual human can relax people, similar to traditional audiotapes. The null effects on other outcomes may be due to insufficiently high levels of stress at baseline, and recommendations for future research are discussed.

Primary Supervisor: Dr Elizabeth Broadbent

C14

Investigations of post-operative gastric dysfunction using novel technologies

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Background: Gastric surgeries are performed for a variety of conditions including obesity and cancer. These alter the native human anatomy and patients can develop chronic symptoms post-operatively including nausea, pain and bloating. A novel non-invasive Body Surface Gastric Mapping (BSGM) device was recently developed at the University of Auckland, allowing researchers to define gastric electrical abnormalities in symptomatic patients. **Objectives:** To assess feasibility of the novel BSGM device in non-invasively diagnosing gastric electrical disorders after surgery. **Methods:** BSGM (64 electrodes) was performed on patients within 5 years of surgery, including 20 patients after sleeve gastrectomy, 5 after esophago-gastrectomy, with comparison to 100 controls. Recordings comprised of 30 minutes of baseline, followed by 4 hours following a standardised meal. Symptom tracking was performed using a validated App. Gastric frequency, amplitude, and propagation patterns were recorded. **Results:** BSGM was successfully completed in all patients. Gastric frequency was found to be lower in patients following surgery- 2.48 cycles per minute (cpm) for sleeve gastrectomy and 2.68cpm for esophagectomy ($p < 0.05$). Amplitude was unchanged in the sleeve gastrectomy group (32.9 vs 32.8 μV) and the esophagectomy group (24.44 vs 32.8 μV) ($p > 0.05$). Gastric propagation was consistently antegrade demonstrating successful pacemaker remodelling. Subgroups of patients demonstrated rhythm abnormalities. **Discussion:** BSGM is a feasible method for non-invasively evaluating gastric function following surgery. Surgery is found to impact the gastric conduction system with lower frequency post-operatively, due to conduction system remodelling, however some patients develop long-term gastric rhythm abnormalities.

Primary Supervisor: Professor Greg O'Grady



Using Days Alive and Out of Hospital to measure inequities after cardiovascular surgery

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Background: In Aoteroa New Zealand (NZ), being of Māori ethnicity is often associated with poorer health outcomes, including following cardiovascular surgery. Days Alive and Out of Hospital (DAOH) is an emerging surgical outcome metric which may be useful in identifying inequities and is a composite measure of outcomes. **Objectives:** To validate DAOH as an appropriate outcome measure following cardiac surgery and investigate inequities after cardiovascular surgery. **Methods:** We have conducted a secondary data analysis using data from the National Minimum Data Set. We have calculated unadjusted and risk-adjusted DAOH values between Māori and non-Māori using direct risk standardisation. We report DAOH values across three time periods and 9 deciles of the DAOH distribution. **Results:** The level of inequity between Māori and non-Māori depends on the quantiles reported. At the median, there is an unadjusted 2-day difference in DAOH, however at the 0.1 quantile there is an 8-day difference and at the 0.25 quantile there is a 4-day difference. There is no difference at the 0.8 quantile. After risk-adjustment for a range of factors, the level of inequity decreased but did not disappear. **Discussion:** Health inequities exist between Māori and non-Māori after cardiovascular care. Through measuring DAOH scores after risk adjustment we have quantified inequities which are present. The level of inequity differs across quantiles, illustrating that when things go well, there is little difference in outcomes. However, when things go poorly, outcomes for Māori become worse faster. The highest level of inequity is between the highest risk patients.

Primary Supervisor: Professor Thomas Lumley



Oral Presentation Room D - 501-010

D1

Two in One: Killing Leukaemia Stem Cells while Supporting Normal Haematopoietic Stem Cells

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Background: Acute leukaemia is a devastating disease with poor prognosis. Leukaemia stem cells (LSCs) sustain the disease, are able to survive treatment and drive relapse. This highlights the importance of identifying and characterizing LSCs. Targeting a signaling pathway that is common to LSCs could be a novel, promising treatment strategy. The aryl hydrocarbon receptor (AHR) pathway was shown to be critical for the self-renewal properties of normal hematopoietic stem cells (HSCs). **Objectives:** To study the effect of manipulation of the AHR pathway on LSCs and HSCs in vivo in a pre-clinical models and on transcriptome. **Methods:** Modulation of AHR signaling using AHR agonist ITE and antagonist CH-223191 in 1) LSCs in a murine bone marrow transplantation leukaemia model and 2) normal HSCs in a competitive repopulation assay. RNA-sequencing with the DESeq2 analysis after 0, 2 and 12 hours following AHR modulation. **Results:** AHR modulation depleted LSC (with ITE; LCS frequency of 1:163 versus 1:44 in a vehicle control) or eliminated them (CH-223191). That is despite testing on a very aggressive AML model (LSC frequency of 1:4). We detected differential expression of genes involved in apoptosis and proliferation in leukaemia cells treated with CH-223191. We observed an enhancing effect of CH-223191 on wild type HSCs (a steady increase in the percent of engraftment is observed over 47 weeks post transplantation compared with that of controls). **Discussion:** It is important and promising for potential treatment strategies to observe that CH-223191 is able to inhibit LSCs properties, whereas it enhances performance of HSCs.

Primary Supervisor: Professor Stefan Bohlander

D2

WITHDRAWN



D3

Understanding Transforming Growth Factor Beta signalling family's relationship with endometrial cancer through novel mutations.

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Background: The Transforming growth factor β (TGF- β) signalling family is a highly conserved pathway whose dysregulation is known to promote endometrial tumorigenesis in murine models. It's effect in humans is unknown. ACVR1 and BMPR1A are two receptors in the TGF- β family previously linked to human disease – fibrodysplasia ossificans progressiva and familial adenomatous polyposis respectively. Mutations in these receptors are also seen in endometrial cancer samples but the functions of these mutations are uncharacterised. I hypothesize that these novel TGF- β family mutations will deregulate TGF- β signalling which will affect endometrial tissue homeostasis. **Objectives:** Catalogued all known ACVR1 and BMPR1A mutations present in endometrial cancer via public databases. Curated mutations are introduced into receptors. Mutated receptor activity assessed in C2C12 and HEK293T cell lines. Finally, the response of multiple human endometrial cancer (hEC) cell lines to TGF- β family ligands will be observed. **Methods:** Engineered curated mutations into expression plasmids via overlap extension polymerase chain reaction (PCR) based site-directed mutagenesis. Luciferase assay and western blotting performed on C2C12 and HEK293T, respectively, to assess mutated receptor activity. Quantitative PCR of multiple hEC cell lines for baseline responses. **Results:** Mutation curation from public databases reveals 52 ACVR1 and 46 BMPR1A mutations in endometrial cancer. Of these, 15 ACVR1 and 6 BMPR1A mutations were selected. Currently 13/15 ACVR1 mutations have been cloned. **Discussion:** Successfully engineered mutations will be assessed for receptor activity. The response of hEC cell lines to TGF- β family ligands will be determined for baseline response of hEC cells to TGF- β family ligands.

Primary Supervisor: Dr Anassuya Ramachandran

D4

Identification of genes involved in lymphatic vessel development through forward genetic screening

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Background: Lymphoedema is characterised by the painful buildup of lymph caused by lymphatic dysfunction. Primary lymphoedema is caused by mutations in genes required for lymphatic development; highlighting the importance of identifying genes involved in lymphatic development to understand these lymphatic disorders. The molecular basis of Hennekam's syndrome, a primary lymphoedema syndrome caused by mutations in CCBE1, was discovered through a forward genetic screen using zebrafish. Zebrafish are a commonly used model to study lymphatic development and have been instrumental in showing that the Ccbe1/Vegfc/Vegfr3 pathway is required for lymphatic development. This study aims to identify the causative mutations of two potentially novel zebrafish lymphatic mutants called D502 and B537. **Objectives:** To phenotypically characterise and identify the causative mutation(s) of B537 and D502. **Methods:** Phenotypic analysis was performed by confocal imaging of the lymphatic-marking lyve1:DsRed zebrafish line. Complementation test was performed by screening for mutant phenotypes in the progeny of outcrossed zebrafish lines of interest. **Results:** The B537 and D502 mutants have lost over 90% of their thoracic duct with a 46% and 82% reduction in facial lymphatic vessels. They appear to have lymphatic sprouting defects. The mutants B537 and D502 failed to complement. Due to similar lymphatic phenotypes, a complementation test was performed by outcrossing carriers of D502 and ccbe1nz186. This also failed to complement. **Discussion:** The complementation tests show that D502 and B537 likely contain mutations in the ccbe1/vegfc/vegfr3 pathway. Future work will focus on further characterising the phenotype and identifying the mutations present in these mutant lines.

Primary Supervisor: Dr Jonathan Astin



D5

Understanding the role of IL-6 -174 G/C (rs1800795) promoter variant in metabolic responses to exercise

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Background: Interleukin-6 (IL-6) is a pleiotropic cytokine that is secreted from skeletal muscle during exercise. Recent evidence shows that this acute increase in IL-6 signalling is essential for coordinating metabolic benefits from exercise training. In contrast, chronic elevations in IL-6 signalling is associated with metabolic dysfunctions. A common genetic variant in the IL-6 promoter region, rs1800795 (IL-6 -174 G>C) is associated with elevated circulating levels of IL-6, obesity and insulin resistance. **Objectives:** To investigate the role of rs1800795 in metabolic responses to exercise. **Methods:** Mice were generated with a GG (wild-type) or CC (variant) genotype for rs1800795. IL-6 levels in blood and muscle were measured following 60 minutes of high-intensity exercise in GG and CC mice. GG and CC mice were fed chow (CD) or high-fat diet (HFD) for 10 weeks with and without access to running wheels and metabolically phenotyped. **Results:** Acute exercise induced a ~2-fold greater IL-6 response in increase in skeletal muscle and blood of CC mice with wild-type GG mice. While CC and GG mice had similar body composition, energy expenditure, glucose homeostasis and exercise performance under chow conditions, when fed HFD, CC male showed greater exercise (running wheel) induced benefits in reduction in body weight and improvements in glucose homeostasis. **Discussion:** We hypothesize that the C-allele associated increase in exercise induced IL-6 during exercise may underpin greater improvements in metabolic health in response to exercise. Further experiments are underway examining the effect of rs1800795 in the molecular mechanisms underpinning these observations.

Primary Supervisor: Associate Professor Troy Merry

D6

Comorbidity genetic risk and pathways impact SARS-CoV-2 infection outcomes

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Background: Understanding the genetic risk and biological mechanisms through which severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection outcomes and comorbidities interact to impact acute and long-term sequelae is essential if we are to reduce the ongoing health burdens of the COVID-19 pandemic. **Objectives:** To identify the genetic variants, genes and biological pathways within lung, blood, coronary artery, and brain tissue that underlie the associations between SARS-CoV-2 and comorbidities. **Methods:** Here we use publicly available data and a de novo computational analysis that integrates protein interaction networks with tissue-specific gene regulatory networks, to identify putative mechanisms for associations between SARS-CoV-2 infection outcomes and comorbidities. **Results:** We identified genetic variants, genes and biological pathways that link inherited risk factors for SARS-CoV-2 infection with over 200 co-occurring traits. Complex networks of genes and pathways that connect SARS-CoV-2 infection outcomes, coronary artery disease (CAD) and Parkinson's disease are identified for the first time. For example, 30 variants and 18 genes (i.e. ERBB4, NOTCH4) that encode proteins which interact within 8 protein clusters are implicated in linking CAD with SARS-CoV-2 infection. **Discussion:** Collectively our results support the potential for a much greater post-acute SARS-CoV-2 burden if these genetic predispositions are realised. The gene products and their interacting partners we identified as underlying the associations between SARS-CoV-2 infection and comorbidities (e.g. CAD) are potentially high-value therapeutic targets for alleviating the impacts of acute and post-acute COVID.

Primary Supervisor: Professor Justin O'Sullivan



WITHDRAWN

De novo identification of asthma multimorbidities

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Background: Detangling the relationships between complex phenotypes is challenging due to the molecular mechanisms that influence their presentation through interactions that occur across multiple levels of biological information. As such, biological network analysis represents a powerful approach for untangling disease-disease relationships. **Objectives:** To identify diseases multimorbid with asthma and elucidate the mechanisms that mediate their interaction. **Methods:** We integrated information on physical contacts between common single nucleotide polymorphisms (SNPs) and expressed genes with expression quantitative trait loci (eQTL) data to construct a lung and blood-specific spatial gene regulatory network (GRN). Using this GRN, we located the genes that are functionally affected by asthma-associated SNPs to identify the asthma-specific network. We then expanded outwards to identify curated protein-protein interactions occurring up to 4 edges away from the asthma network. The eQTLs spatially regulating the identified genes were used to interrogate the genome-wide association study (GWAS) Catalog to identify enriched traits (hypergeometric test) within each of the expanded levels. **Results:** This approach led to de novo identification of traits both previously reported (e.g., lung cancer) and unreported (e.g., disc-degeneration) to be multimorbid with asthma and pinpoints the variants and genes bridging asthma to the multimorbidities. **Discussion:** Our discovery approach identifies significantly enriched traits in the regulatory space proximal to a disease of interest, in the tissue of interest, without a priori selection of the interacting diseases. The predictions it makes expand our understanding of possible shared therapeutic targets, especially for diseases such as asthma, where no cure is currently available.

Primary Supervisor: Professor Justin O'Sullivan



Oral Presentation Room E - 505-011

E1

Investigating cardiac sympathetic transduction and its effects on vascular function

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Background: Sympathetic transduction is the study of how impulses of sympathetic nerve activity (SNA) affect an end-organ and its function. SNA controls vascular tone through bursts of activity, variable in size, that contract vascular smooth muscle and in the case of the heart, can also alter heart rate (HR). Current literature focuses on reflex-mediated or externally induced SNA and how it alters vascular function. How resting SNA can dynamically influence vascular function has been explored in peripheral muscle, but not in the heart. **Objectives:** Investigate how cardiac SNA regulates HR, blood pressure (BP), and coronary blood flow (CoBF) dynamically during resting conditions. **Methods:** Instrumentation was undertaken to record cardiac SNA and relevant vascular variables in conscious animals. These recordings were made at least 3 days post-surgery in conscious, unstressed animals. The transduction of cardiac SNA on these vascular variables were analysed. **Results:** Results suggest that after every cardiac SNA burst, there is an increase in HR (n=5, nadir Δ : +2.45 bpm), CoBF (n=5, nadir Δ : +0.72 mL/min), and vascular conductance (n=4, nadir Δ : +0.004 mL/min/mmHg). We also showed that the rate of change in left ventricular volume decreases following a cardiac SNA burst. **Discussion:** This study is the first to explore resting sympathetic transduction in the heart. We show that cardiac SNA bursts can dynamically change HR and CoBF. We are currently investigating the role of β -receptors in cardiac sympathetic transduction through β -adrenergic blockade. Future steps may be to investigate how cardiac sympathetic transduction is altered in ageing and disease.

Primary Supervisor: Dr Rohit Ramchandra

E2

Cardiovascular medication drop-in during 12-year follow-up and insights for risk prediction equations

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Background: Current cardiovascular disease (CVD) risk prediction equations do not consider medication initiation during follow-up (treatment drop-in), and its influence on equation performance remains unclear. Previous studies have investigated treatment drop-in over 5-year follow-up, but reports on longer follow-up period are scarce. **Objectives:** We aim to quantify the extent of CVD treatment drop-in during a 12-year follow-up period and to provide recommendations for addressing this issue in future risk prediction studies. **Methods:** Anonymised Individual-level linkage of New Zealand administrative health datasets identified 1,746,695 participants without CVD and heart failure, aged 30-74 years in 2006. We examined individuals who were dispensed blood pressure lowering (BPL) and lipid lowering (LL) medications at baseline (2006) and during follow up (1st January 2007 - 31st December 2018). The proportions of person-years of follow-up during which drop-in CVD medications were dispensed among those not treated at baseline were calculated. **Results:** Of 1,399,348 individuals not taking CVD medications at baseline, proportions of follow-up time for BPL and/or LL was 14.2%, and this increased with age (4.2% in 30-34y group and 31.8% in 70-74y group) and baseline 5-year CVD risk (12.4% in <5% group and 34.2% in \geq 15% group). **Discussion:** Treatment drop-in needs to be addressed in the development of CVD risk prediction equations, especially in studies including the elderly and high-risk groups. Pooling of short-term observations could be one approach, and more studies using different analytical approaches are warranted to explore ways to reduce the impact of treatment drop-in in prediction equations.

Primary Supervisor: Professor Rod Jackson



E3

Addition of Biochemical Markers to Population-Level Cardiovascular Disease Risk Prediction Equations

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Background: Cardiovascular disease (CVD) is a leading cause of morbidity and premature mortality in New Zealand. Risk prediction equations are an established tool to inform clinical decisions regarding CVD prevention. Certain equations can also predict CVD cases across entire populations, thus informing population-based CVD prevention efforts. These population-level equations can only utilize routinely collected predictor information, limiting their performance. Recent data-sharing efforts mean all laboratory test results in Auckland and Northland have become available to create better-performing risk prediction equations. **Objectives:** Determine the added predictive value of routinely collected laboratory tests (estimated glomerular filtration rate, haemoglobin A1C, total cholesterol: high density lipoprotein ratio) to population-level risk prediction equations. **Methods:** Laboratory results were extracted for all individuals aged 30-75 years in Auckland and Northland (23,467,297 tests across 819,281 people). Results were processed and individually linked to previous routinely collected CVD risk predictor data and demographic information. Preliminary sex-stratified Cox-proportional hazards equations were developed to estimate 5-year CVD risk. Equations were internally validated in the whole population and relevant subpopulations using statistical measures of model calibration and discrimination. **Results:** Models incorporating laboratory results outperformed standard models across all measures of calibration and discrimination. Subpopulation analysis showed slightly improved calibration in ethnic and age-based subpopulations. **Discussion:** These results show that the incorporation of laboratory tests improves the performance of population-level equations, notably for ethnic subpopulations in which previous models underperformed. This research further supports the efficacy of population-level risk prediction as an equity-enhancing public health tool to accurately predict CVD cases.

Primary Supervisor: Professor Rod Jackson

E4

Components underlying synaptic plasticity in the carotid body

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Background: Glutamate and Gamma-aminobutyric acid (GABA) are major modulators of excitatory and inhibitory signals in the adult mammalian brain. Glutamate transmission is critical for neural plasticity, learning and memory, whereas GABA plays a fundamental role in controlling excitability and in the generation of neuronal oscillations. In the carotid body, evidence suggests glutamatergic and GABAergic signalling is involved in its sensitisation upon repeated stimulation. We hypothesize that glutamate and GABA systems may underpin enhanced chemoreflex responses in disease states. **Objectives:** To investigate the full scope of glutamatergic and GABAergic signalling components in the carotid body in a model of experimental hypertension. **Methods:** We used RNA-sequencing (RNAseq), in two independent laboratories, to identify transcriptomic differences in the carotid body between 12-16-week-old normotensive Wistar and Spontaneously Hypertensive Rat (SHR). Digital droplet polymerase chain reaction (ddPCR) was performed to validate the expression of glutamatergic and GABAergic target genes identified in the RNAseq screen. **Results:** In carotid body extracts, RNAseq data revealed the presence of novel glutamatergic and GABAergic signalling components and their respective ion-gated and metabotropic receptors, not previously described. ddPCR analysis revealed GABA and glutamate signalling to be altered in the carotid body of SHRs. **Discussion:** Whether or not these changes underpin the dysregulation of synaptic sensitivity associated with hypertension remains to be established functionally. Nonetheless, this dataset identifies rudimentary components for synaptic plasticity, learning and memory and synaptic inhibition. We are now determining whether hypertension is linked to deviations in these processes in the carotid body.

Primary Supervisor: Dr Audrys Pauza



E5

Fish oil supplementation in pregnant mothers with overweight/obesity to improve infant body composition and metabolism.

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Background: Maternal obesity during pregnancy is associated with adverse metabolic changes in the offspring, which increase their risk of obesity and metabolic disease. This may be mediated by exaggeration of maternal insulin resistance, and hypertriglyceridemia. Supplementation with fish oil (FO), which is insulin sensitizing, during pregnancy in women with overweight and obesity may prevent this risk. **Objectives:** To determine the effects of FO supplement taken throughout the second half of pregnancy and lactation by women with overweight or obesity on infant body composition and metabolism. **Methods:** A double-blind randomized controlled trial of FO (3g/day n-3 polyunsaturated fatty acids) versus olive oil (control) taken from 12-20weeks gestation until 3-months postpartum. Eligible women had singleton pregnancy and BMI ≥ 25 kg/m². The primary outcome was between-group difference in infant body fat% at 2-weeks of age. Secondary outcomes included maternal metabolic indices, and infant anthropometric and metabolic measures at 2-weeks or 3-months of age. **Results:** 129 women were randomized. There were no between-group differences in infant body composition or anthropometric measures. FO supplementation led to 16% lower maternal triglycerides at 30-weeks of pregnancy ($p=0.0001$), a lower rate of emergency caesarean section (RR=0.37 (0.13, 0.78), $p=0.006$) and 25% lower triglycerides in the 3-month-old infants ($p=0.021$). FO did not affect maternal homeostatic model for assessment of insulin resistance. **Discussion:** Maternal FO supplementation did not impact body composition in infancy. However, maternal triglycerides were suppressed during pregnancy, and infant triglycerides were lower at 3 months of age. This may represent a long-term beneficial change in infant metabolism.

Primary Supervisor: Dr Ben Albert

E6

Cardiac fructose inhibition is a promising therapeutic target for treating diastolic dysfunction in diabetes.

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Background: Diastolic dysfunction is characterised as a primary manifestation of diabetic cardiomyopathy, linked with metabolic disturbance. Reports indicate that diabetic patients display both elevated circulating and cardiac fructose levels, that may be linked to the development of diabetic cardiomyopathy. **Objectives:** The aim of this study was to evaluate the therapeutic potential of inhibiting fructose metabolism to treat diastolic dysfunction in diabetes. **Methods:** Left ventricular cardiac function was assessed using echocardiography in type 2 diabetic (T2D) mice (high fat high sugar (HFSD) dietary intervention). Cardiac fructose metabolism was inhibited in T2D mice using a short hairpin adeno-associated virus (AAV)-9 virus to induce knockdown of Fructokinase-A (single jugular vein injection). Cardiac fructose levels were assessed using gas chromatography-mass spectroscopy. **Results:** After 11 weeks of HFSD, type 2 diabetic mice exhibited significantly impaired diastolic function (increased E/e' doppler (1.2-fold, $p=0.0001$) and reduced longitudinal peak diastolic strain rate (0.8-fold, $p=0.005$)), elevated body weight (1.3-fold, $p<0.0001$), increased fasting blood glucose (1.5-fold, $p=0.001$) and impaired glucose tolerance. Systolic function was unchanged (ejection fraction). Following 8 weeks of AAV9-induced fructose inhibition, diastolic function (E/e' doppler and longitudinal peak diastolic strain rate) was significantly rescued in T2D mice. Cardiac fructokinase-A knockdown did not further increase cardiac fructose accumulation nor alter systolic function and systemic phenotype. **Discussion:** This study demonstrates for the first time that inhibiting cardiac fructose metabolism has therapeutic potential for treating diastolic dysfunction in type 2 diabetes. Further investigation into the role of cardiac fructose in the development of diastolic dysfunction is warranted.

Primary Supervisor: Dr Kim Mellor



E7

Impact of kawakawa on the postprandial levels of circulating microRNA's related to insulin sensitivity

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Background: Kawakawa, an indigenous plant used in traditional Māori medicine is reported to have health benefits as its leaves contain bioactive compounds which have shown to improve insulin sensitivity in animals. However, the mechanism behind it is unknown, with limited research in humans. One mechanism could involve alteration of the circulatory microRNAs which are small, single stranded RNA molecules that function as regulators of post-transcriptional gene expression. Active dietary compounds from foods can influence microRNA levels. Therefore, this study focuses on exploring the functional effects of kawakawa on the postprandial circulatory microRNAs involved in the insulin signalling pathway. **Objectives:** To examine changes in the postprandial circulatory microRNA levels in response to acute kawakawa tea consumption in healthy human participants. **Methods:** This project will utilize plasma samples banked from a previously conducted randomized, two-arm, crossover study. Thirty self-reported healthy participants (Age 18-45 yrs., BMI=18-25 kg/m²) were asked to consume kawakawa infused tea and water followed by a high glycemic breakfast on two subsequent visits (with 48-hour washout period). Blood samples collected at 0min, 60min and 120min will be used for miRNA quantification using quantitative polymerase chain reaction (qPCR) technology. **Results:** This study hypothesizes that upon intake of 4g of kawakawa there will be changes in the levels of circulatory microRNA at different time points compared to water. **Discussion:** A postprandial modification of circulating microRNA after intake of 4g of kawakawa will suggest that kawakawa has a positive impact on insulin sensitivity by regulating microRNA levels involved in insulin signaling pathway.

Primary Supervisor: Dr Farha Ramzan

E8

Fish oil supplementation increases omega-3 content of human milk, in women with overweight and obesity.

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Background: Maternal overweight or obesity is the strongest predictor of childhood obesity. This may in part be mediated by differences in human milk (HM) composition, including greater lipid and leptin concentration, and omega-6:omega-3 fatty acid ratio, in the HM of women with overweight/obesity. As fish oil (FO) supplementation improves metabolism, it may improve HM composition in this group. **Objectives:** To determine the effects of maternal FO supplementation on HM composition of women with overweight/obesity. **Methods:** Women with a body mass index (BMI) ≥ 25 were randomised to consume FO or olive oil (OO) control supplements during pregnancy and lactation. HM samples were collected at 2 weeks (n=66) and 3 months (n=62) postpartum. HM was analysed for macronutrients (direct detect), adipokines (ELISA), glucocorticoids (LC-MS/MS) and fatty acid content (GC-MS). **Results:** FO supplementation led to greater omega-3 concentration (2 weeks: FO 2.6 \pm 0.1%, OO 1.7 \pm 0.1% P<0.001, 3 months: FO 2.4 \pm 0.1%, OO 1.7 \pm 0.1% P<0.001) and lower omega-6:omega-3 ratio (2 weeks: FO 4.5 \pm 0.5%, OO 7.6 \pm 0.4% P<0.001, 3 months: FO 5.4 \pm 0.6%, OO 7.5 \pm 0.6% P=0.02) in HM. At 2 weeks, FO supplementation led to lower HM adiponectin (P=0.047), with an interaction with infant sex (P=0.01). Amongst mothers with a female infant, FO supplementation led to lower HM adiponectin at 2 weeks (P=0.02). There were no differences in HM protein, lipid, leptin or glucocorticoids between groups. **Discussion:** FO supplementation raised omega-3 and lowered omega-6:omega-3 in HM of women with overweight/obesity, ameliorating the known effect of raised BMI on the fatty acid profile of HM.

Primary Supervisor: Dr Ben Albert



Potential Impact of fast-food sodium reduction targets on the consumption of sodium in New Zealanders.

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Background: Excess sodium consumption is associated with increased risk of stroke, heart disease, and gastric cancer. The mean consumption of sodium for adults in Aotearoa (NZ) is 3,373mg/day, greater than the World Health Organization (WHO) upper limit of 2000mg. Most excess dietary sodium comes from packaged and processed foods, and recently new sodium reduction targets were developed for NZ fast-foods. **Objectives:** To estimate the effect the proposed sodium reduction targets would have on sodium consumption from fast food in NZ. **Methods:** A literature review was conducted to examine the amount and types of fast-food most commonly consumed in NZ. A database of the largest NZ fast food chains and their products (Nutritrack) was used to apply the proposed fast food targets to individual items and combo meals. The estimated sodium reduction was calculated and weighted by popularity of fast food chain. **Results:** Limited data were available on the amount and types of fast food commonly consumed in NZ. The mean weighted sodium reduction was 196 mg (SD= 87) (15%) for single items and 863mg (SD=203) (40%) for combo meals. For each combo meal consumed per week, the targets would bring an adult New Zealander 9% closer to the WHO recommendation. **Discussion:** The limited data on fast-food consumption available in NZ made estimating the impact of the sodium reduction targets challenging. Although a small reduction it would not require change in consumer behaviours and would have larger impact for young adults, men, Māori whānau and Pacifica communities, who have greater exposure.

Primary Supervisor: Dr Helen Eyles



3-Minute Elevator Pitch - 505-011

EP1

Untangling the spectrum - using genetics to identify autism and co-occurring traits

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Background: Autism represents a complex group of neurodevelopmental states. Whilst genetic variants linked to autism have been identified, little is known about how the genes these variants control interact with genes impacted by co-occurring traits. **Objectives:** To identify traits that co-occur with autism by analysing the interaction between genes controlled by autism-associated genetic variants and genes which play a role in the co-occurring traits. **Methods:** Genetic variants (single nucleotide polymorphisms [SNPs]) associated with autism were downloaded from the GWAS (genome-wide association studies) Catalogue. Potential co-occurring conditions were identified using the Multimorbid3D pipeline on adult and fetal cortical tissue separately. A protein-protein interaction network (PPIN) was developed to identify the proteins, and their genes, that interact with the proteins encoded by autism-associated expression quantitative trait loci (eQTLs). This network was expanded to four levels. At each level, traits associated with the proteins were identified using a modified phenome-wide association study (PheWAS) analysis. **Results:** Mood disorders, fatty acid levels, neurological conditions, and lung-related traits were identified as co-occurring with autism. There were developmental stage-specific differences in the co-occurring traits and genes that were identified between the adult and fetal cortical tissue. **Discussion:** This study has identified traits that have a genetic risk of co-occurring with autism. Differences in genes identified in adult and fetal tissue offer insight into the development of different forms of autism. The identification of groups of co-occurring conditions linked by common genetic variants paves the way for future work improving understanding and diagnosis of autism and co-occurring traits.

Primary Supervisor: Professor Justin O'Sullivan

EP2

Understanding the movement of genes within healthy gut microbiomes

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Background: Antibiotic resistance is a consequence of bacterial evolution that affords bacteria protection against antibiotics that previously could kill them. It poses a number of serious public health risks, including severe and prolonged illness, increased hospital admissions and complications, and higher mortality rates. Genes encoding resistance traits can spread rapidly throughout bacterial populations via horizontal gene transfer (HGT), which enables the exchange of genetic material outside of clonal lineages. **Objectives:** To identify signatures of HGT in the gut microbiomes of healthy faecal microbiota transplantation (FMT) donors who participated in the Gut Bugs Trial. **Methods:** Metagenomic contigs from the Gut Bugs Trial were analysed to identify putative HGT events using the bioinformatics tool WAAFLE. Results were compared with the microbial community profiles to identify any overrepresented taxa among those contributing to HGT. **Results:** Overall, contigs with putative HGT events represented less than 1% of classified contigs (those containing genes). The frequency of HGT was donor-specific, and largely constant throughout the sampling period. Firmicutes was the primary phylum contributing to HGT, mirroring its predominance in the community profiles. Alpha diversity measures were typically higher for the background community phyla than those contributing to HGT. **Discussion:** We observed a largely unchanging frequency of genes obtained through HGT over time, suggesting that either HGT did not occur during the sampling period, or that it occurred at a constant rate in an open system. Notwithstanding, we anticipate that the rate of HGT among FMT recipients will differ before and after FMT.

Primary Supervisor: Professor Justin O'Sullivan



EP3

Term side-population trophoblasts can be maintained in culture and differentiated to mature trophoblast populations

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Background: Isolation of trophoblast stem cells (TSC) from term human placentae is pivotal to better understand placental function, but to date has proved challenging. We previously utilised the side-population technique to isolate TSC from first-trimester placentae that differentiate into mature trophoblast lineages (syncytiotrophoblast (STB) and extravillous trophoblast (EVT)). Application of this technique to term placentae will aid understanding of TSC dysregulation in pregnancy disorders. **Objectives:** To optimise culture conditions for term side-population trophoblasts and demonstrate their differentiation capacity into mature trophoblasts. **Methods:** The side-population technique was used to isolate trophoblasts from normal term placentae. The effect of matrices (5 µg/mL Collagen-IV, 10 µg/mL Laminin-521), or cytokine supplementation (25ng/mL decorin and/or 50ng/mL IL-8) on colony formation was assessed over 14 days. Differentiation to STB/EVT was undertaken by modifying prior TSC differentiation protocols. Data are mean±SEM. **Results:** Laminin-521 increased attachment of term side-population trophoblasts 3.8-fold (n=3, p=0.026) over Collagen-IV. Colony size was significantly increased by addition of Decorin/IL-8. Combined supplementation enabled culture for ≥30 days. Term side-population trophoblasts could be differentiated into syncytin-1 (66.09%±9.428 in STB-Medium; 23.37%±2.307 in undifferentiated controls, p<0.05) and hCG (human chorionic gonadotropin) expressing STB (25.28%±11.09 in STB-Medium, no expression in undifferentiated controls, p=0.0848, n=3), or HLA (Human leukocyte antigen)-G expressing EVT (29.05%±11.42 in EVT-Medium; no expression in undifferentiated controls, p=0.0637, n=3). **Discussion:** These data indicate term side-population trophoblasts can be propagated, and similar to first-trimester side-population trophoblasts exhibit the differentiation potential of a TSC population. Culture of TSCs from term placentae enables future functional studies of normal and pathological placentae.

Primary Supervisor: Associate Professor Jo James

EP4

WITHDRAWN



EP5

Developing multi-level interventions to facilitate compassion in Aotearoa hospital-based care teams

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Background: Compassionate care is expected by patients, stipulated by ethical codes, and morally mandated. Compassion predicts better patient outcomes and greater practitioner wellbeing. Unfortunately, exacerbated by systemic pressures, compassion in medicine is at risk of becoming the exception rather than the rule. **Objectives:** The two main aims of this thesis are to (1) assess how organisational contexts affect the ability to show compassion, and (2) develop multi-level interventions to facilitate compassion in Aotearoa hospital-based care teams. **Methods:** Conducted two large scale systematic reviews identifying predictors of compassion in healthcare samples, run a national clinicians' institutional barriers to care survey (N=1032), and run a series of co-design workshops to come up with multi-level interventions suited to Aotearoa. **Results:** Systematic reviews suggested that organisational contexts, notably cultures and values, predict compassion (or the lack thereof). Observational data showed clinicians perceived that their organisations valued enjoyment, holistic care, and humanity *less* and money, authority, and control *more* than clinicians personally. Regressions confirmed that working in value-discrepant environments reduced clinicians' ability to care. In co-design, clinicians noted that compassion was valued but often forgotten due to organisational pressures. The needs for compassion within teams to create safer environments of practice as well as the role of leadership in providing good role modelling and necessary resources were emphasized. **Discussion:** Improving compassion is a systemic problem requiring system thinking and solutions. Unlike compassion interventions focusing on the individual, this research suggests compassion is a "collective endeavour" with organisational and cultural contexts being paramount to improving care.

Primary Supervisor: Professor Nathan Consedine

EP6

Risk of neonatal hypoglycaemia, stability of childhood behaviour, and academic outcomes. Is there a connection?

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Background: The Children with Hypoglycaemia and their Later Development (CHYLD) study has shown high rates of academic underachievement at 9-10 years for children born at risk of neonatal hypoglycaemia. Understanding behaviour trajectories for this cohort and the relationship between the stability of behaviour and academic outcomes is important for identifying children that may benefit from early intervention. **Objectives:** To investigate the stability of behaviour from early to mid-childhood and to determine how behaviour stability relates to academic outcomes at age 9-10 years. **Methods:** Behaviour data was collected by parent and teacher measures at 2, 4.5, and 9-10 years from 614 children in the CHYLD study. Behaviour data was also collected for this cohort from the national school readiness screening programme at 4 years. Academic achievement data for reading comprehension, writing, and mathematics was collected at 9-10 years using a standardised assessment tool. Data will be analysed using regression models to investigate the relationships between different types of behaviour concerns and academic achievement. **Results:** The preliminary results will show the changes in behavioural concerns from early to mid-childhood, the variation in types of behavioural concerns at 2, 4, 4.5, and 9-10 years, and their relationship to academic underachievement at 9-10 years. **Discussion:** Behaviour concerns are associated with poor academic outcomes. Findings from this study will help identify children at risk of persistent problem behaviour before school entry. This will allow intervention to occur prior to formal learning helping to improve school readiness and increase the likelihood of experiencing academic success.

Primary Supervisor: Dr Nike Franke



EP7

Radiomics-based Prostate Cancer classification using Machine Learning and multi-parametric MRI

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Background: Prostate cancer is the most common cancer in New Zealand men. Prostate Specific Antigen (PSA) blood tests are currently used to assess the effectiveness of radiation therapy, a common form of treatment, although it lacks specificity and cannot provide information about individual tumours. In contrast, multi-parametric MRI (mpMRI) can quantitatively characterise tumour phenotype and 3D spatial heterogeneity and are expected to provide better assessment of the changes in tumours following treatment. **Objectives:** To identify mpMRI-based quantitative imaging biomarkers for prostate cancer classification, which may be used for treatment response assessment. **Methods:** In-vivo mpMRI were co-registered with ground truth histological data, from 60 patients with localised prostate cancer (training set: 48; test set: 12). Voxel-based radiomics features were extracted from the MR images, including handcrafted features (i.e., texture features and first-order statistics) and deep-learning derived features. Machine learning techniques were applied to select relevant features for building a tumour classification model and to determine which features were the most discriminative. **Results:** Logistic regression (LR) performed best for tumour classification, and a deep-learning features based model (area-under-curve (AUC): 0.92) outperformed handcrafted feature-based model (AUC: 0.77). The most discriminating features were texture features from perfusion and diffusion MRI, which represented biological and spatial heterogeneity within tumours. **Discussion:** mpMRI-based radiomics features can classify tumour voxels in in-vivo prostate MR images and capture spatial heterogeneity within the prostate and tumour volume. The most discriminating radiomics features will be tested for their ability to assess tumour response after radiation therapy through a prospective clinical trial.

Primary Supervisor: Dr Hayley Reynolds

EP8

Targeting the inflammatory marker in dry eye disease

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Background: With inflammation a recognized pathophysiological feature of dry eye disease, the quantification of inflammatory marker levels may provide insight into disease severity and help guide individualized treatment. However, various tear sampling methods are reported in the literature and further investigation is warranted into the impact of different collection techniques on inflammatory marker quantification. **Objectives:** This study evaluated two commonly reported clinical sample collection methods; the Schirmer strip test and the 'Flush' method. **Methods:** Tears of 9 dry eye and non-dry eye participants were collected under 5 experimental conditions. Inflammatory markers interleukin (IL)-1 β , IL-6, IL-8, IL-10, IL-18, interferon (IFN)- γ and matrix metalloproteinases (MMP)-9 were quantified by Luminex High Performance Multiplex Assay (R&D Systems, USA). Biomarker profiles across the different test methods were then compared using one way-ANOVA and Turkey post-hoc for statistical analysis. **Results:** The single eye Flush 60 μ L method yielded the highest levels of IL-8 (165.15 ± 67.92 pg/mL) and MMP-9 (1937.71 ± 796.95 pg/mL) from the five test methods, significantly higher than the Schirmer methods ($p < 0.05$). Conversely, the single eye Schirmer method produced higher levels of IL-18 (3.27 ± 1.38 pg/mL) than the Flush methods ($p < 0.05$). No further statistically significant differences were identified. **Discussion:** Further research with a larger sample size and assessing more severe disease is warranted. Nevertheless, current results demonstrated that outcomes from different methods cannot not be considered interchangeable. Use of a consistent sampling technique is critical to reliably demonstrate relative change between disease groups and over time.

Primary Supervisor: Professor Jennifer Craig



EP9

Comparison of outcomes assessed by study questionnaire and by data linkage

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Background: The best way to assess participants in long term follow-up studies is to involve them actively in the follow-up. However, this method is time-consuming and resource demanding. These obstacles can have negative impacts on follow-up studies. However, determining the outcomes from administrative datasets is potentially cost-efficient, and bias-free. **Objectives:** To compare outcomes assessed by questionnaire and by data linkage to explore the usefulness and validity of each of six data sources alone and in combination to determine participant outcomes. We will define a hierarchy of data sources and determine the data sources that can provide maximum information for each outcome of interest. **Methods:** A total of 424 surviving adult children of mothers recruited to the Auckland Steroid Trial (1969-1974) were asked to provide consent to various record linkages and complete a questionnaire. We assessed the agreement between TestSafe dispensary data and questionnaire data for the outcomes: diabetes, hypertension, hyperlipidaemia, and asthma in adulthood. **Results:** The agreement between the questionnaire and TestSafe data was higher for diabetes than for hypertension, hyperlipidaemia, and asthma (Kappa coefficient 0.65, 0.45, 0.30, 0.54 respectively). Adding TestSafe data to questionnaire data increased the proportion of participants with diabetes (11.6 to 12.0%), hypertension (29.8 to 34.2%), hyperlipidaemia (32.5 to 35.1%), and asthma (29.6 to 36.6%). **Discussion:** Data linkage in addition to questionnaire data might be a practical tool for follow-up of trial cohorts.

Primary Supervisor: Distinguished Professor Dame Jane Harding

EP10

Addressing access to eyecare in Aotearoa: A qualitative approach

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Background: New Zealand has limited evidence on the prevalence of vision impairment. Over a range of health conditions Māori and Pacific People have worse health outcomes compared to New Zealand Europeans. Inequities in health are largely driven by disparities in access to health care. **Objectives:** To qualitatively explore barriers and enablers to accessing eye health services among adults with vision impairment in Tāmaki Makaurau. **Methods:** Participants with vision impairment were identified from a community-based research project and invited to take part in a telephone based semi-structured interview about accessing eye health services. The interviews were audio recorded, transcribed, and coded using thematic analysis. **Results:** We interviewed 25 participants aged 47 to 71 years (52% female, 52% Pacific People 24% Māori, 16% New Zealand European). A total of 405 comments were coded. Thematic analysis revealed five themes relating to factors affecting access to eyecare: 1) Financial capacity to use services, 2) People can identify services and value the importance of good eye health, 3) The role of location and transport in reaching care, 4) Appropriately addressing eye health needs, and 5) Vital role of whānau in seeking eye health services. **Discussion:** The identified themes align with the five dimensions of patient-centred access to health care conceptualised by Levesque et al 2013, which suggests we have captured important factors affecting access to eyecare. The findings of this study enhanced our understanding of access to eyecare and can assist decision-makers to plan equitable eye health services in Aotearoa.

Primary Supervisor: Associate Professor Jaqueline Ramke



EP11

A new approach to assessing neurodevelopment and health at early-school-age

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Background: Long-term follow-up is essential to understand the impact of perinatal interventions, such as the prophylaxis of dextrose gel for neonatal hypoglycaemia (pre-hPOD Study). Early-school-age is an optimal time for assessment as neurodevelopmental and physiological trajectories become more stable, but there is time to intervene if problems are detected. **Objectives:** To test the feasibility of a brief, standardised, portable battery, used by a single non-specialist assessor, measuring neurodevelopment and cardiometabolic health of pre-hPOD participants at early-school-age. **Methods:** A test battery was established by a broad group of experts to provide standardised measures of cognitive/executive/language function (NIH ToolBox), numeracy (Checkout Game), coordination and balance (NIH ToolBox), visual perception (Motion Coherence), body composition (skinfold, bioimpedance, muscle strength), and vascular function (Brachial/central BP). Assessors included students, research assistants, and health professionals. Assessments took place at school, or at home if preferred, from June 2020-June 2022. **Results:** Of 416 children, 393 were eligible for early school-age follow-up, of whom 309(79%) consented to in-person assessment at a mean(SD) age 6.8(0.3) years. Testing was completed within 2 hours, 85% were seen at school and 15% at home. Measured/assigned results were obtained for $\geq 95\%$ of children for all tests except for central BP (no reading 10%) and standing balance (no result 11%). There were no floor or ceiling effects, except for motion coherence (expected biological lower limit) and Checkout Game (expected threshold test). **Discussion:** A brief, portable, comprehensive, school-based assessment of neurodevelopment and cardiometabolic health by a single non-specialist assessor is feasible at early-school-age.

Primary Supervisor: Associate Professor Christopher McKinlay

EP12

What Makes a Good Sulfatase Substrate? Application in the Design of Antibody-Drug Conjugates.

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Background: Antibody-drug conjugates are an emerging class of targeted cancer therapy comprised of a monoclonal antibody, a linker, and a cytotoxic "payload". The linker must be stable in circulation yet labile within target cells. Enzyme-cleavable linkers have emerged as an effective strategy, utilising intracellular enzymes to trigger payload release. Recently, sulfatase-cleavable linkers have been reported. Sulfatases are selective for their natural substrates however also hydrolyse small synthetic arylsulfates. How sulfatases bind substrates is poorly defined; thus, improved understanding of substrate recognition is needed to design optimal sulfatase-cleavable linkers. **Objectives:** Synthesise a library of model sulfatase-cleavable linkers and apply them to an enzyme-activity assay. To generate an empirical structure-activity-relationship of sulfate hydrolysis and payload release. **Methods:** We have developed a synthetic methodology suitable for preparation of an array of model sulfatase-cleavable linkers carrying fluorescent payloads. Payload fluorescence is quenched until release. An enzyme-activity assay will screen model-linkers against human arylsulfatase A (hARSA) measuring sulfate cleavage and payload release across 24-hours by HPLC-UV spectroscopy and fluorometry. **Results:** Nine linkers are in the synthetic pipeline, three have been completed and screened against hARSA. A further four analogues have bound their payload through a carbamate linker and await the final synthetic step. Differences in the rate of sulfatase cleavage have been observed between the analogues so far. **Discussion:** Formation of the carbamate linkers proved less facile than anticipated. A model study was conducted to optimise reaction conditions which were successfully applied to target substrates. Differences in substrate structure influence the rate of sulfatase activity.

Primary Supervisor: Dr Moana Tercel



Identifying novel antibody inhibitors targeting mouse growth hormone receptor signalling in cancer cells

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Background: Increased expression of growth hormone (GH) and its receptor have been identified in a range of cancers and are implicated in tumour growth, metastasis, resistance to radiation therapy and reduced survival. In addition, GHR deficiencies have been linked to a reduced risk of cancer. Mouse and human GH have limited amino acid sequence similarity and therefore a mouse-specific inhibitor is required for use in mouse models of cancer. **Objectives:** The aim of this project was to develop an inhibitory monoclonal antibody targeting mouse GH for use in preclinical cancer research. **Methods:** In earlier studies a panel of parental hybridoma cell lines secreting antibodies specific for mouse GH was generated and screened for inhibitory activity. Monoclonal cell lines were then generated by subcloning using limiting dilution, and hybridoma supernatants were screened for the presence of anti-mouse GH antibodies by ELISA. Antibodies were purified and tested for GH inhibition using a cell viability assay. **Results:** A panel of hybridoma cell lines was established and found to recognise mouse GH by ELISA. Cell viability assays demonstrated that antibodies from one cell line significantly inhibited GH activity. This cell line underwent three rounds of subcloning and antibodies from two subclones were purified for further testing. **Discussion:** A novel anti-GH monoclonal antibody was developed and found to effectively recognise and inhibit mouse GH in vitro. This antibody therefore has potential utility as a mouse GH inhibitor in preclinical cancer research. Further characterisation of this antibody in cancer cell biology assays will establish its efficacy.

Primary Supervisor: Associate Professor Jo Perry



Poster Presentations - Grafton Atrium

P1

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

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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 (UC) 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 optimise the isolation of HUVECs and investigate their potential for corneal endothelial repair. **Methods:** A successful HUVEC isolation protocol was developed. Isolated HUVECs (n=4) were characterised, by polymerase chain reaction (PCR) and immunocytochemistry (ICC). HUVECs were differentiated into CECs (n=2) by using differentiation protocols: (1) a ROCK inhibitor and a TGF-beta inhibitor, (2) a CEC-conditioned medium, and (3) seeding cells onto Descemet's membrane. Differentiation was measured by changes in morphology, ICC, and PCR analysis. Cryopreservation techniques were optimised to allow for long-term storage and application of these cells. **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. HUVECs also showed viability and growth on corneal tissue. **Discussion:** These results show that HUVECs can be isolated and differentiated into CEC-like cells. Differentiated CECs show a hexagonal morphology and an upregulation of CEC markers. As such, UC stem cells may represent a novel and innovative treatment for endothelial dystrophies.

Primary Supervisor: Professor Trevor Sherwin

P2

Ex vivo T cell re-stimulation protocol for adoptive cell therapy

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Background: Immunotherapy harnesses a patient's own immune system to target tumours and has become a central pillar of cancer treatment. Most immunotherapy modalities rely on a pre-existing immune response towards tumour cells, and therefore fail in patients who lack this response. Activating the immune response is a key focus of immunology research, which may make therapy effective for a wider range of patients. **Objectives:** Adoptive cell therapy involves the *in vitro* culturing and activation of autologous T cells towards patient tumour antigens. The T cell product administered back to the patient will contain clinically relevant numbers of activated CD8+ cells, highly specific for the patient's tumour. The host lab is optimising this protocol, and my particular focus is the *ex vivo* stimulation of T cells by antigen presenting cells (APC). **Methods:** We tested the efficacy of peptide-pulsed APCs to elicit an antigen-specific T cell response in a mixed cell context. We used flow cytometry to determine the quality and quantity of these responses as well as track APC fate. **Results:** We found that the maturation status and timing of APC additions impacted the ability to generate a reliable antigen-specific T cell response. We also discovered a combination of markers that reliably allow tracking of monocytes and monocyte-derived dendritic cells in a heterogeneous culture situation. **Discussion:** Our findings will effectively guide the manufacture of a product that can elicit significant and ongoing anti-tumour effects. Thus, it offers exciting potential as a personalised treatment for patients not responding to other therapy.

Primary Supervisor: Professor Rod Dunbar



P3

Development of eHealth-Based Behavior Change Support for Young Adults Using the Nine Principles Framework

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Background: Multiple frameworks based on behavioural models exist to guide researchers on the development of interventions (e.g. the Nine Principles framework). Utilising these has the potential to enhance adherence, improving research validity and decreasing resource waste. Further integrated theory and practice research is needed to demonstrate how to effectively incorporate behaviour change strategies, including mode of delivery via eHealth, into nutrition related randomised controlled trials (RCTs). **Objectives:** Describe the development of a user-centred, theory-based eHealth behaviour change support (BCS) programme to enhance young adults' adherence (20-35 years) to the behaviours of (i) eating healthily and (ii) recording dietary intake on a smartphone app, when participating in a RCT. **Methods:** The Nine Principles framework integrated literature review findings, qualitative focus group data, and the Theory of Planned Behaviour. The resultant BCS, delivered via text and Facebook, was piloted in a 10-week RCT (n=20). Pilot mixed methods outcomes include diet and recording adherence scores, social media engagement and process evaluation. **Results:** The BCS appeared to support optimal dietary recording (mean recording score: 86/100±17), which can be a burdensome behaviour for participants, and helped participants maintain current dietary behaviours. Forty-one percent of Participants reported engaging with the Facebook page once a week or more. Process evaluation identified that participants preferred mode of delivery was via Facebook Messenger. **Discussion:** Using a framework underpinned by theory and user-centred design to develop BCS is a promising avenue to enhance adherence in RCTs. Further practical support is needed to guide researchers through this development process.

Primary Supervisor: Dr Andrea Braakhuis

P4

Uncovering neural activity in the spinal cord recorded by a novel bioelectronic implant

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Background: Spinal cord injury is a devastating medical event, introducing many neurological problems. There is a lack of understanding of changes in electrical activity in the spinal cord as a result of injury and throughout recovery. We have developed a bioelectronic implant to record spinal electrical activity, where we aim to identify electrical biomarkers related to injury. **Objectives:** To determine whether recordings taken from a subdural spinal implant represent neural activity. **Methods:** Electrical activity was recorded from the dorsal surface of the spinal cord in freely moving rats. Recordings were filtered with a 300-1200Hz band pass filter, which uncovered spike-like activity. We hypothesised that these spikes were compound action potentials (CAP's) in the fibre tracts and validated this by investigating the propagation speed of these waveforms between electrodes, comparing these to those of spinal neurons recorded in literature. Spikes were extracted using template-based detection, with templates based on the triphasic nature of CAP's. These spikes were assessed for similarity between channels and timing delays were determined using correlation analysis. **Results:** We demonstrate a detectable delay in spike propagation. Propagation was detectable in both directions, suggesting afferent and efferent activity. Spikes were determined to have velocities in the range -100 to 100ms⁻¹, with a cluster at 30-40ms⁻¹, falling in the expected velocity range reported in literature. **Discussion:** These results suggest that our bioelectronic implant is recording electrical signals of neural origin. This finding paves the way for investigation into how the properties of these spikes may change with an injury.

Primary Supervisor: Associate Professor Darren Svirskis



P5 Investigating White Matter Hyperintensities in the Context of Cognitive Decline and Alzheimer's Disease

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Background: White matter hyperintensities (WMHs) are ischaemic expressions of cerebrovascular pathology that are identified on Magnetic Resonance Imaging (MRI). They may contribute to cognitive decline in Alzheimer's disease (AD) but findings to date are mixed. **Objectives:** Assess WMH volume and its relationship with clinical classification (ranging from cognitively normal to AD) and cognition in participants recruited from the Dementia Prevention Research Clinics. **Methods:** Participants were classified into five groups ranging from cognitively normal to AD dementia by a multidisciplinary team after clinical, neuropsychological and neuroimaging assessments. Total WMH volumes were automatically extracted from T2-weighted MRI images for 220 participants and were subdivided into periventricular WMHs (pWMHs) or deep WMHs (dWMHs). Additionally, total WMH volumes were subdivided by lobe. **Results:** Total WMH, pWMH, frontal WMH, and parietal WMH volumes were significantly different across and between groups ($p < .05$). For participants with neuropsychological data ($n = 158$), total WMH, pWMH, and dWMH volumes correlated with poorer executive functioning, whilst total WMH and pWMH volumes were correlated with poorer episodic memory and lower global composite scores (an average of executive functioning, processing speed, and episodic memory scores). Frontal, parietal, and occipital WMH volumes correlated with poorer executive functioning. Frontal and parietal WMH volumes also correlated with poorer episodic memory and lower global composite scores. **Discussion:** Our findings indicate that WMHs are associated with increased levels of AD-related clinical impairment and with deficits in multiple aspects of cognition. These findings support the relevance of WMHs to cognitive decline and thus encourage further study.

Primary Supervisor: Professor Lynette Tippett

P6 Phosphorylated tau and α -synuclein presentation in the human olfactory epithelium

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Background: Olfactory dysfunction and pathological protein aggregations occur in the olfactory bulb (OB) six to ten years before clinical symptoms of dementia, Alzheimer's, or Parkinson's disease are evident. Additionally, glomeruli, the functional units of olfaction, are reduced in volume in the OB of Parkinson's disease patients. To reach the OB, olfactory sensory neurons (OSNs) send signals through axons that project from the olfactory epithelium (OE) in the nasal cavity into the OB where they coalesce to form glomeruli. OSNs are the only neurons in direct contact with the external environment putting them at risk of exposure to toxins, viruses, and bacteria. However, there is limited research into the human OE and its role in the progression of dementia. **Objectives:** We investigated the presence of phosphorylated tau and α -synuclein in the human OE and its association with OSNs and dementia. **Methods:** Sections from 7 cases containing both OE and the OB were stained for mature OSNs, immature OSNs, and phosphorylated tau or phosphorylated α -synuclein and imaged using a VSlide scanner. Staining densities of OSNs, phosphorylated tau, and α -synuclein were measured using an analysis method that preserved their anatomical distribution in the OE. **Results:** Pathological aggregations were present in every case, and furthermore, there was no single location of elevated accumulation of pathology. Instead, pathology is heterogeneously distributed throughout the mucosa, varying in each case. **Discussion:** Even though there are analysis and experimental limitations, understanding patterns of pathological aggregations in the OE might help with early diagnosis and even early treatment delivery.

Primary Supervisor: Professor Maurice A. Curtis



P7

Regional variation of dopamine transmission in the caudolateral (tail) striatum

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Background: The caudolateral (tail) striatum is a poorly studied region of the basal ganglia circuit. Our previous work has suggested that dopamine transmission in this region is different in amplitude and kinetics, compared to the much better studied dorsolateral striatum (DLS). Moreover, recent studies show the tail striatum having discrete regions of dopamine receptor D1- and D2-poor zones located ventral-laterally (VLT) and ventral-medially (VMT), respectively. **Objectives:** Our aim was to examine dopamine transmission in these tail striatum regions (VLT, VMT, dorsal), and compare them to the DLS. **Methods:** Fast-scan cyclic voltammetry was used to measure electrically evoked dopamine release from DLS and tail striatum regions in coronal rat brain slices (Wistar; P28±2; 300 µm). **Results:** Evoked dopamine release in the DLS (596±73 nM) was almost double that of any tail striatum region (VMT: 322±85nM; VLT: 275±49 nM). Blocking the dopamine transporter (DAT), with the DAT inhibitor 3 µM GBR12909, increased the evoked dopamine release in all regions as well as the full-width half-max- a measure of dopamine clearance - confirming the central role of DAT in clearing dopamine from these regions. **Discussion:** These are the first detailed measurements of dopamine transmission in the regions within the tail striatum. Further study will determine the mechanisms underlying these differences, in particular, how dopamine receptors D1 and D2 modulate dopamine release.

Primary Supervisor: Dr Peter Freestone

P8

Presbyopia and Water Regulation in the Human Lens: The Relationship Between Syneresis and Protein Structure

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Background: With age, the eye lens stiffens and loses the ability to focus on nearby objects (presbyopia). This is thought to be due to accumulating damage to lens proteins, causing modifications in protein structure and inhibiting their ability to bind water. Lens stiffening may be a precursive stage to age-related nuclear cataract formation. Whether water in the lens is "bound" to proteins or "free" can be measured using Raman Confocal Microscopy (RCM). **Objectives:** Develop a model to induce ageing in bovine lenses. Measure bound and free water in young, fresh lenses, and lenses aged by the model using RCM. **Methods:** For the ageing model, lenses are treated with hyperbaric oxygen (HBO) to deplete lens antioxidants and ultraviolet radiation (UVR) to induce oxidative stress. The physical appearance of both fresh lenses, and those aged through the model are assessed through dark and light field microscopy. For RCM, young, fresh lenses and treated lenses are sectioned onto microscope slides. **Results:** Microscopy shows that the HBO-UVR treatment produces opacification of the outer layers of lens tissue. Preliminary RCM results show differences in free and bound water between fresh and HBO-UVR treated lenses. **Discussion:** The RCM measurements of fresh lenses can be compared to lenses aged through the newly developed model. This will show how ageing effects the lens protein's ability to bind water, in addition to future mass spectrometry-based experiments to show protein structural changes. Understanding structural changes in proteins gives better understanding of the underlying mechanism of lens stiffening in ageing lenses.

Primary Supervisor: Dr Gus Grey



WITHDRAWN

P10

The potential involvement of Benzalkonium Chloride in inflammasome activation

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Background: The majority of funded topical antiglaucoma drugs contain the preservative Benzalkonium Chloride (BAK). It is well-recognised that the efficacy of glaucoma topical eye drops is lost over time and may induce subclinical inflammation. The aim of this study is to investigate whether BAK is involved in the mechanism of subclinical inflammation and its potential role in activating the inflammasome. **Objectives:** To investigate whether BAK treatment induces inflammasome complex upregulation in an ATP-dependent manner in an in vitro model, initially using primary human corneal epithelial cells (HCEC), and human trabecular meshwork cells in future experiments. **Methods:** ATP assay studies were conducted on HCEC to investigate the sustained release of ATP following BAK treatment. This treatment group was compared to a challenge group which received interleukin (IL)- 1beta and tumour necrosis factor (TNF)-alpha which are both known to sustain ATP release in vitro and activate the inflammasome. **Results:** Preliminary results suggest that BAK induces cell death in a dose-dependent manner, however, BAK concentrations of 0.00005% (a concentration believed to be comparable to the penetrated dose of BAK in the anterior segment) induced sustained ATP release comparable to the challenge group and statistically highly significant compared to the basal group ($p < 0.001$). **Discussion:** These findings suggest that BAK at sub-clinical concentrations of 0.00005% may be involved in inducing the sustained release of ATP in human corneal epithelial cells. Future experiments will assess this BAK concentration in glaucoma relevant in vitro models and investigate, using immunohistochemistry, whether inflammasome markers are also upregulated.

Primary Supervisor: Dr Lola Mugisho



P11

Optimisation of Corneal Tissue Engineering

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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. Central corneal wound healing occurs primarily through migration of basal epithelial cells, derived from limbal stem cells. Corneal epithelial cells have been shown to elongate and align along surface topographical features. **Objectives:** Functional synthetic engineered corneas have been successfully implanted in clinical trials. However, postoperative corneal haze has been observed in implanted corneas, attributed to incomplete epithelial monolayers. The objective is to optimise (reduce) the healing time required to achieve complete coverage of the stroma with an epithelial monolayer. **Methods:** An in silico cell automata random-walk model was developed to study the influence of surface topography and chemotaxis on the time for complete monolayer coverage of a two-dimensional wound. **Results:** The average healing time was significantly longer than previously reported. However, the addition of surface topography decreased healing time by approximately 14%. Increasing mitotic rate decreased healing time by a further 46%. In vitro measurement of cell migration speed, with no surface topography and chemotaxis, was lower than published in vivo recordings. **Discussion:** The developed model provides a successful framework for analysis of the influence of various factors on cell behaviour. The healing time is unlikely to be representative of in vivo corneal wound healing due to several identified omitted factors. These include non-stochastic representation of cell parameters, mechanical interactions, and accurate representation of topography. Successful clinical translation requires development in model complexity for more accurate in vivo representation.

Primary Supervisor: Dr Laura Domigan, Associate Professor Richard Clarke

P12

K⁺-Cl⁻ – co-transporter 2 (KCC2) expression in the human Alzheimer's disease medial temporal lobe

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Background: Alzheimer's disease (AD) is a neurodegenerative disorder that currently has no cure. Hallmarks of the disease include declining cognitive function and neuronal death in the hippocampus and cerebral cortex. The co-transporters K⁺-Cl⁻ – co-transporter 2 (KCC2) and Na-K-Cl (NKCC1) regulate intracellular chloride levels. Mouse models of AD and other neurological disorders have demonstrated altered neuronal KCC2 and NKCC1 expression that makes GABA, the primary inhibitory neurotransmitter, switch to excitatory resulting in cognitive impairment. The excitatory/inhibitory equilibrium is a delicate feature of the brain that needs to be maintained to avoid pathological consequences. **Objectives:** To investigate our hypothesis that altered expression of KCC2 in the AD human medial temporal lobe might be a contributing factor to the excitatory/inhibitory balance disruption and cognitive deficit observed in the hippocampus. **Methods:** We quantified KCC2 density in the hippocampus, subiculum, entorhinal cortex, and superior temporal gyrus (STG) of healthy and AD post-mortem human brains by using free-floating fluorescent immunohistochemistry and confocal laser-scanning microscopy. **Results:** We detected significant downregulation of KCC2 levels in the STG when comparing control healthy cases to AD cases, suggesting a disturbed excitatory/inhibitory balance in this brain region. Other brain regions examined showed no altered KCC2 expression. **Discussion:** We detected significant downregulation of KCC2 in the STG when comparing healthy control cases to AD affected cases, suggesting that in AD less KCC2 is seen in the STG. AD has a large impact on affected individuals and their families, highlighting the need to investigate the pathology of the disease. This study could provide a possible novel avenue of treatment for neurodegenerative diseases.

Primary Supervisor: Dr Andrea Kwakowsky



P13

Understanding Embodied Effects of Posture: A Qualitative Study

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Background: Psychological theory and contemporary experimental research support the idea of a bi-directional relationship between physical posture and psychological states. Previous studies have evaluated a set of dominant and submissive postures, and assessed outcomes using pre-defined quantitative scales. However, it is possible that each individual posture within the set has different effects, and that some effects have not been captured. A qualitative approach to examine the effects of posture may reveal insights into these aspects. **Objectives:** This study aimed to investigate how people felt while adopting different postures, using qualitative methods. **Methods:** Participants completed a demographic questionnaire and then were asked to sit or stand in eight different postures while reporting on how they felt in each posture. Interview sessions were audio recorded and data were transcribed. Inductive thematic analysis was used to identify patterns in the data. **Results:** Three themes were identified which described how participants perceived and experienced different postures: 1) a power differential, 2) the appropriateness of a posture, and 3) the specific emotions elicited. Cognitive interpretations of contextual information, including cultural appropriateness and functional meaning of a posture, shaped emotional states. For some postures, observations of the meaning of a body position differed from the actual experience of it. **Discussion:** This research found that each posture created different feelings and were bound by cultural interpretations of appropriateness. This may have implications for the choice of postures in future research on embodiment. Further research into cultural views of posture is needed. **Primary Supervisor: Dr Elizabeth Broadbent**

P14

WITHDRAWN



P15

Identifying novel therapeutic targets through the lens of distinct alpha-Synuclein strains

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Background: Parkinson's Disease (PD), Dementia with Lewy body disease and Multiple system atrophy are defined by aggregated alpha-Synuclein (α -Syn). Recent evidence suggests α -Syn forms conformationally distinct polymorphs which may be disease-specific. **Objectives:** In this study, we treated human brain-derived pericytes with distinct α -Syn polymorphs. Subsequent RNAseq analysis revealed polymorph-specific changes in gene expression. Here we validated some of the changes identified at the gene transcript level using fluorescent immunolabelling. **Methods:** We optimised and validated 39 antibodies specific for 29 proteins, a subset of the differentially expressed transcripts, on middle temporal gyrus tissue from normal and PD brains. Middle temporal gyrus tissue microarrays were then used to determine the differential expression of proteins in normal and PD cases. In addition, we detected proteins in normal and PD human-derived pericytes treated with distinct α -Syn polymorphs. **Results:** Ten proteins were successfully detected through immunolabeling human brain, while eight were detected in cultured human brain-derived pericytes. One protein was differentially expressed in human brain and pericytes. SAT1 displayed decreased nuclear ($p=0.0101$) and vascular ($p=0.0093$) protein expression in PD tissue. Whereas GMNN expression was upregulated ($p=0.039$) in treated normal vs PD pericytes but downregulated in PD brain tissue ($p=0.0424$). **Discussion:** Our results align with the literature indicating that SAT1 expression is decreased in PD post-mortem brainstems. Furthermore, SAT1 activity enhances α -Syn toxicity in yeast models highlighting its potential role in PD pathogenesis. Links between GMNN and PD are yet to be established. Further investigation will unravel their therapeutic potential and relationships with α -Syn polymorphs.

Primary Supervisor: Dr Birger Victor Dieriks

P16

Effects of oral cysteamine treatment on Ctns knockout 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 without treatment results in renal failure in early life. We have shown previously that a combination treatment of cystine-depleting drug, cysteamine and the mTOR inhibitor, everolimus, can rescue the cystinotic phenotype in induced pluripotent stem cells. To evaluate the therapeutic potential of this therapy in vivo, we will perform pre-clinical testing in our rodent model of cystinosis which faithfully recapitulates the human disease. **Objectives:** To determine any synergistic effect of everolimus we will first identify the optimal dose of cysteamine that results in a 50% reduction of cystine levels in Ctns knockout (KO) rats. **Methods:** Ctns KO rats were fed with cysteamine jelly pills twice daily starting from 6 weeks of age to 6 months. Plasma and urine were collected each month while body weights were measured weekly. Following treatment, tissues were harvested for cystine measurements. **Results:** Treated animals showed decreased cystine levels, weight gain and reduced polydipsia and polyuria. Urine analysis revealed less protein and glucose were excreted at 6-months in treated animals while urea and creatinine were significantly increased. **Discussion:** Cysteamine-treated animals displayed improved kidney function but were not rescued to wild-type levels suggesting that long-term treatment of cysteamine in cystinotic rats can delay the onset of renal failure but not prevent it.

Primary Supervisor: Professor Alan Davidson



P17

Using human kidney organoids to model cisplatin-induced acute kidney injury

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Background: Acute kidney injury (AKI) denotes the sudden loss of kidney function. AKI manifests as a side effect from common clinical drugs, such as the chemotherapeutic agent cisplatin. In vivo, cisplatin-induced AKI preferentially targets the renal tubules. AKI can progress to Chronic Kidney Disease and subsequent renal failure, yet no effective treatment is available. **Objectives:** To determine whether the pathological effects of cisplatin can be modelled on human induced pluripotent stem cell-derived kidney organoids. **Methods:** Kidney organoids were treated with cisplatin and monitored by brightfield microscopy for gross morphological changes. Injury analysis on the cellular and molecular level was performed by quantitative PCR and immunohistochemistry. Epithelial cells were isolated from the organoids using Magnetic Activated Cell Sorting to measure the effects of cisplatin specifically on the kidney tubules. **Results:** We observed that cisplatin-treated organoids were smaller compared to untreated controls, indicative of increased cell death. This was further confirmed by immunolabelling on organoid sections, which revealed severe cell damage and loss of nuclei in the tubules. Additionally, gene expression of kidney injury and inflammation markers was strongly and specifically upregulated in the organoid tubules after cisplatin (p value of <0.0001), mimicking injury seen in AKI patients. **Discussion:** Our work revealed that cisplatin treatment on kidney organoids leads to tubular damage and cell death, reminiscent of the in vivo pathology of AKI. The ability to recapitulate the injurious effects of cisplatin in a human in vitro model provides a platform for drug development, aiming to reduce the burden of AKI.

Primary Supervisor: Dr Veronika Sander

P18

Investigating Polycystic Kidney Disease in kidney organoids

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Background: Polycystic kidney disease (PKD) is a common genetic disorder characterised by the formation of numerous cysts in the kidney tubules and gross enlargement of the kidney, which ultimately lead to kidney failure. PKD is caused by mutations in the PKD genes. Despite extensive investigations, the processes underlying cystogenesis remain poorly understood, and no cure for PKD exists. **Objectives:** To recapitulate PKD in human kidney organoids and screen a drug library for new treatment options. **Methods:** Kidney organoids were generated from induced pluripotent stem cells (iPSCs). A PKD2 knockout mutation was introduced into iPSCs using CRISPR/Cas9 to create cystic organoids. Cyst formation was monitored in PKD2-mutant and control organoids using brightfield microscopy. Quantitative (q) PCR and immunolabeling were performed to characterise gene/protein expression in organoids and establish a panel of disease markers for the drug screen. **Results:** We found that cyst formation in PKD2-mutant organoids started from day 7. By day 15, 85% of the PKD2-mutant organoids contained multiple cysts, compared to 2% in controls. qPCR and immunostainings revealed that known PKD markers, including CTGF, SERPINE1 and COL12A1, were upregulated in PKD2-mutant organoids (with P-values of 0.0003, 0.002 and 0.0001 respectively), and organoid cysts displayed PKD-like cellular characteristics. In preparation for the drug screen, we developed a method to immobilise cystic organoids in a hydrogel matrix. **Discussion:** Our organoids recapitulate human PKD cystogenesis and present a promising model for the drug screening approach, aiming to find new PKD therapies that slow or stop cyst growth.

Primary Supervisor: Dr Veronika Sander



P19

Nanostring nCounter analysis of the neuroinflammatory pathways in the Midcingulate Cortex in Huntington's Disease

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Background: Huntington's Disease (HD) is a genetic neurodegenerative disorder. Cell loss is putatively associated with chronic neuroinflammation. HD symptom profiles include mood, motor, and cognitive changes. Cell loss and inflammation in the anterior cingulate cortex are associated with mood symptomology. **Objectives:** To validate post-mortem human HD-related expression changes found in a previous mRNA sequencing (RNAseq) study on inflammatory mRNA transcripts in the midcingulate cortex (MCC). **Methods:** Nanostring nCounter analysis was conducted on 50 inflammatory-related mRNA transcripts, of which 46 were previously found to have differential expression in the MCC of 14 HD and 9 control cases. **Results:** 36 differentially expressed transcripts were significantly altered. 34 were consistent with the RNAseq changes seen between HD and control or HD symptom cases, validating 22 upregulated and 12 downregulated inflammatory-related markers. Expression changes in controls compared to mood, motor, and mixed symptom HD profiles showed 17 symptom-specific transcript changes, with six genes validating the RNAseq symptom changes. These included leukocyte, chemokine, and proinflammatory astrocytic cytokine-related transcripts such as aquaporin (AQP4); upregulated in motor cases. Some of the most significant HD vs control expression changes included the upregulation of S100 calcium binding protein A9 (S100A9) and the downregulation of G protein-coupled receptor 85 (GPR85); which correlated with mixed and motor symptoms. **Discussion:** Differential inflammation-related expression in the MCC appears to be associated with motor and mixed symptomology. This study highlights the importance of validating RNAseq data and further corroborates the complex mRNA expression changes found in the inflammatory pathway that contribute to HD pathology.

Primary Supervisor: Dr Andrea Kwakowsky

P20

Estrogenic influences on histological changes occurring in heart failure

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Background: Globally, 1-2% of people are affected by heart failure (HF), with men and women at equal risk of developing the disease. Aetiology, clinical presentation and outcome of HF are sexually dimorphic. Rate of HF development in women accelerates after menopause, suggesting an association between sex hormones and development of HF in women. **Objectives:** To compare cardiac remodelling following myocardial infarction (MI) between pre- and post-menopausal states, alongside age-matched males. **Methods:** Ovariectomized female Wistar rats modelled the post-menopausal state. MIs were modelled by ligation of the left anterior descending coronary artery. Six groups were studied: sham ovariectomy + sham MI (n=8), sham ovariectomy + MI (n=8), ovariectomy + sham MI (n=7), ovariectomy + MI (n=4), male + sham MI (n=6) and male + MI (n=3). At eight weeks post MI, hearts were fixed and embedded in paraffin, sectioned, and stained. Heart dimensions, infarct size and presence of fibrosis were quantified using Masson's trichrome. Myocyte diameter, circumference and area were quantified after fluorescent staining with phalloidin and wheat germ agglutinin. **Results:** Trends indicate OVX females had smaller ejection fraction (P=0.805), increased collagen deposition (P=0.5965), and longer cardiomyocytes (P=0.299) compared with ovary intact females following MI. Sex related differences were negligible. **Discussion:** The cessation of ovarian estrogen production may have a negative impact on myocardial remodelling in female Wistar rats. Larger sample sizes would allow a complete understanding of estrogenic influence. Understanding these relationships could lead to changes in clinical management of women to improve health outcomes for women with HF.

Primary Supervisor: Associate Professor Carolyn Barrett



P21

Determination of regions of interests in human brain atlases for upper limb recovery prediction post-stroke

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Background: Neuroimaging features have the potential to aid motor recovery prognostication after stroke but are seldom utilised in prediction model development. An important part of neuroimaging feature development is the selection of suitable atlases. However, the abundance of human brain atlases and the discrepancies between them make it difficult to elucidate which atlas or atlases are most useful for motor recovery prediction. **Objectives:** To determine regions of interest (ROIs) within commonly used human brain atlases for motor recovery prediction. To develop a novel, easily accessible upper limb recovery atlas for use in motor recovery prediction. **Methods:** ROIs were delineated from existing anatomical atlases according to current literature on motor function and recovery. Then, data from 104 stroke patients were included in a Classification and Regression Tree (CART) analysis to identify the most important features from the ROIs. Six commonly used atlases were analysed in the 2006 MNI space. **Results:** Precentral gyrus, postcentral gyrus, paracentral lobule, supplementary motor area, basal ganglia structures and the corticospinal tract were identified as regions important in motor recovery from literature. CART analysis was used to identify which atlas features or set of features were the most important for model development. **Discussion:** This study reduced several common human brain atlases into key ROIs important for upper limb recovery and further identified the most prominent features for model development from across the atlases. While limited to a specific lesion quantification method, the identified regions can be used to build more accurate multimodal stroke recovery prediction models.

Primary Supervisor: Professor Alan Wang

P22

Can nutrition help moderate-to-late preterm babies thrive: a protocol report

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Background: Children born between 32 to <37 completed weeks of gestation are known as moderate-to-late preterm (MLPT). Of all preterm children, approximately 80% are born MLPT. MLPT children have higher chances of suffering from neuro-developmental impairments than their term-born counterparts. Additionally, they have increased risk of growth failure, mortality, and morbidities during infancy and beyond than term-born children. They also have higher chance of developing metabolic syndrome, obesity, and hypertension during adulthood. However, scientific evidence to support optimal nutrition for children born MLPT is very limited and variable. **Objectives:** To assess the role of parenteral nutrition, milk supplementation and taste/smell of breast milk on neurodevelopment, growth, and body composition at 2 years' corrected age. **Methods:** A total of 532 infants born MLPT and receiving intravenous fluids were recruited to a multi-centre, factorial, randomised clinical trial. At least 240 children per intervention arm were randomly allocated to receive a combination of intravenous amino acid solution vs. intravenous dextrose solution, milk supplement vs. exclusive breastmilk, and taste/smell given or not given before gastric tube feeds. Neurodevelopment (cognitive, motor, and language), growth (linear, ponderal and circumferential) and body composition (lean- and fat mass accumulation) at 2 years' corrected age are the outcome variables to be studied. **Results:** Trial recruitment finished in March 2022. To date 76% of eligible children (241/316) reaching minimum assessment age have been assessed at 2 years. **Discussion:** Data from this study will help to develop evidence-based nutrition guidelines for children born MLPT to optimise their later growth and development.

Primary Supervisor: Distinguished Professor Dame Jane Harding



P23

The development of a hydrogel-based ultrasound-triggered delivery system for neurotrophic growth factors

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Background: Growth factors have recently been explored as therapeutic agents for tissue engineering. Neurotrophic growth factors (NF), specifically, have been shown to support and direct the regrowth of nerve cells. NFs have potential for the treatment of a range of disease states and injuries, including spinal cord injuries. However, key challenges in using NFs include their short half-life in vivo and their potential for off-target effects. These challenges could be overcome by encapsulation in hydrogels, and spatial and temporal targeting of NF delivery. **Objectives:** The objectives of this research are to i) create a delivery system where release of an active model drug can be triggered by ultrasound and ii) investigate the optimal ultrasonic parameters to trigger release. **Methods:** A small, positively-charged model drug (ibuprofen) was loaded into alginate and poloxamer hydrogel drug delivery systems, and different ultrasonic parameters were explored. The release of ibuprofen was compared at low-frequency (24 kHz), high-frequency (1 MHz), and no ultrasound stimulation. **Results:** The results show that ultrasound stimulation increased ibuprofen release and low-frequency stimulation was the most efficient at triggering release from both hydrogels. Alginate hydrogel was more responsive to ultrasound stimulation than poloxamer hydrogel. **Discussion:** These results suggest that low-frequency ultrasound stimulation and alginate hydrogel are suitable to achieve spatial and temporal targeted delivery of NF. In the future, our lab will load hydrogel-based ultrasound-triggered delivery systems with NFs, and NFs will be released controllably to support the regrowth of nerve cells.

Primary Supervisor: Dr Brad Raos

P24

Arresting tryptophan catabolism for cancer immunotherapy

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Background: Cancers fend off cancer-killing immune cells by producing an immunosuppressive tryptophan metabolite called kynurenine, generated by hemoproteins, IDO1 and TDO (Indoleamine 2,3-dioxygenase and tryptophan dioxygenase). Inactivating IDO1/TDO has enormous potential for sensitising patients to immunotherapy but no IDO1/TDO inhibitors have reached the market yet. That is likely due to poor efficacy and tendency to cause toxicities by inhibition of other haemoproteins such as haemoglobin. To overcome these limitations, we aim to develop drugs that exclusively inactivate the immature haem-free form of IDO1 and TDO, that is hypothesised to be the dominant intracellular species. **Objectives:** To develop tools for determining haem occupancy of intracellular IDO1/TDO. **Methods:** Haem was detected by the horseradish peroxidase (HRP)-tetramethylbenzidine colorimetric assay based on reactivation of the inactive haem-free HRP with exogenous haem. Immunoprecipitation and immunoblotting enabled the extraction and detection of IDO1 from SKOV3, an ovarian cancer cell line. Absorption spectroscopy was applied to determine HRP purity and haem occupancy. **Results:** This study optimised a technique for stripping haem from HRP (140 ppm residual haem). The haem-free HRP quantified exogenous haem with sensitivity of 0.011 ± 0.03 absorbance units per pM of haem and a limit of detection of 10 ± 2 pM. IDO1 was purified from SKOV3 at quantities likely detectable by the HRP assay. **Discussion:** The HRP assay optimised here provides a simple and sensitive way for quantifying minute haem levels, immeasurable using conventional techniques. This high-throughput technique enables studying haemoprotein regulation and investigating the feasibility of targeting haem free IDO1/TDO for cancer therapy.

Primary Supervisor: Dr Petr Tomek



P25

The use of Optical Coherence Tomography to Visualize the Inner Ear

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Background: Hearing loss is a prevalent condition affecting over 1.5 billion people globally, a number suggested to rise to 2.45 billion by 2050. Current diagnosis of hearing loss relies on physiological techniques which provide very limited information about the pathologies within the inner ear (cochlea). Optical Coherence Tomography (OCT) is proposed as an imaging method to provide information of the cochlear microanatomy, helping further diagnose hearing disorders.

Objectives: Determine the feasibility of the use of OCT on the round window (RW) as a tool to visualize the cochlea in-vivo. **Methods:** Cochleae from sheep and human are fixed in formalin-based fixative and dissected to expose the RW. Some key OCT parameters include imaging samples by different OCT systems of varying wavelengths (800nm, 950nm and 1300nm). The resolution and depth penetration from the different OCT systems will be compared. From this, the accuracy of the visualization of cochlear anatomy will be compared against other imaging modalities such as microscopy and micro computed tomography. **Results:** The RWM is visible through the different OCT systems- using a longer wavelength of 1300nm allowed a larger penetration into the cochlea, whereas the 800nm system provided images of a higher resolution. This led to the crude visualization of internal structures. **Discussion:** Our approach to utilizing OCT on the RW is promising. OCT could benefit in-vivo visualization of the cochlear microstructure of patients through the round window membrane (RWM) and determine whether it can aid in refining a drug delivery system, targeting the inner ear.

Primary Supervisor: Dr Haruna Suzuki-Kerr

P26

Phenotyping synovial fluid extracellular vesicles from patients with knee osteoarthritis, and with or without obesity

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Background: Obesity is a major risk factor for osteoarthritis (OA) due to extra joint loading and systemic inflammation. Synovial fluid (SF) bathes the joint and plays an important role in joints health. This study hypothesises that extracellular vesicles (EVs) present in SF mediate inflammatory inter-cellular communication in OA joints that is exacerbated in patients with obesity. **Objectives:** Phenotype biochemical and proteomic content of SF EVs from OA patients, with or without obesity. **Methods:** SF was obtained with consent from adult patients undergoing joint replacement. Four different enzymatic treatments of SF were tested for greatest EV yield. EVs were isolated using the size exclusion chromatography. EVs were phenotyped for obese (BMI>35;n=11) and non-obese (BMI<30;n=11) for particle content by Nanosight300, biochemical content by Surface-enhanced Raman Spectroscopy (SERS) and protein content by mass spectrometry. Bioinformatics was used to identify the differentially expressed proteins and Gene Ontology to classify related cellular components, biological processes, and molecular functions. **Results:** Biochemical fingerprinting identified differences in the protein content between obese and non-obese SF EV populations. Proteomics identified fourteen differentially expressed proteins. Gene ontology showed associations of up-regulated proteins in obese group with innate and adaptive immune response, complement activation, and defense response. Down-regulated proteins showed a negative regulation of inflammatory processes. **Discussion:** This study is the the first known study to successfully perform SERS on SF EVs. The biochemical and proteomic analyses support our hypothesis that the SF EVs may play a role in mediating inflammation in the OA joints that may be exacerbated with obesity.

Primary Supervisor: Dr Sue McGlashan



P27

Toxicity of oxidised fish oil in pregnancy - A dose-response study in rats.

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Background: Fish oil (FO) supplements are consumed during pregnancy as a source of omega-3 fatty acids. However, FO products are frequently oxidised past recommended limits. In rats, a large dose of a highly oxidised FO caused substantial newborn mortality but the effects at human-relevant doses are unknown. **Objectives:** To conduct a dose-response study at human-relevant doses of oxidised FO in rats to estimate the safe levels of oxidation during pregnancy. **Methods:** 100 rat dams were time-mated and provided with a gel treatment on each day of pregnancy. Treatment groups differed only in the FO content of the gel; control (no oil), PV5, PV10, and PV40 (0.05ml of FO oxidized to a peroxide value (PV) of 5, 10, or 40meq/kg), or PV40(1ml) (1ml of PV40). A subset of dams and their fetuses were sampled on Gestational Day 20. The primary outcome was newborn mortality by day 2. **Results:** There were no signs of unwellness or differences in plasma biochemical markers in dams during pregnancy. However, there was markedly increased neonatal mortality by day 2 of life affecting the PV40(1ml) (12.8%) and PV40 (6.3%) groups, but not the control, PV5 or PV10 groups (1-1.4%). Dietary oxidised FO led to altered expression of placental genes involved in antioxidant pathways, and production of free radicals. **Discussion:** Highly oxidised FO was toxic in rat pregnancy even at human relevant dose leading to greater mortality. No toxic effects were observed in FO oxidised to a $PV \leq 10$ meq/kg, suggesting this is an appropriate maximum limit for consumer products.

Primary Supervisor: Dr Ben Albert

P28

Why do gout patients not take their allopurinol?

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Background: Gout is one of the most prevalent inflammatory diseases. However, continuation rates for allopurinol as the most effective agent for controlling this progressive disease are very low. **Objectives:** The objectives of this study were to examine the reasons patients given for nonadherence to allopurinol and to examine differences in intentional nonadherence for patients with and without serum urate (SU) at treatment target. **Methods:** Sixty-nine men with gout attending rheumatology clinics, all prescribed allopurinol for ≥ 6 months, completed the Intentional Non-Adherence Scale (INAS). Differences in the types of intentional nonadherence were analyzed between those with and without SU at treatment target (< 0.36 mmol/L, 6 mg/dL). **Results:** The most frequently endorsed reasons for not taking their allopurinol were because participants wanted to lead a normal life (23%) or think of themselves as a healthy person again (20%). Patients also reported not taking allopurinol as a way of testing if they really needed it (22%). Participants with SU above target endorsed significantly had more medicine-related concerns, and were more likely to give testing treatment as a reason for nonadherence. Participants who were younger, single, and non-New Zealand European also endorsed more reasons for not taking their allopurinol. **Discussion:** The major reasons behind the patient's decision not to take allopurinol relate to the desire to lead a normal life and the strategy of testing the treatment to see if they could reduce the dose without getting symptoms. These results provide some potentially modifiable targets for adherence interventions.

Primary Supervisor: Professor Keith Petrie



How Frequently Do We Touch Facial T-Zone: A Systematic Review

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Background: Coronavirus (CoV) enters and replicates in mucous membranes of the upper respiratory tract. Hence not touching the T-zone is predicted to be one of the life-saving behaviours without any cost associated. **Objectives:** To appraise the frequency of T-zone (eyes, nose, mouth, chin) touching in humans to comprehend the challenge of its restriction. **Methods:** Data were collected by keyword searching, and the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist, PECO (Patient, Intervention, Comparison, Outcome) protocol and STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines were followed in this review. Raw data were processed into useful standard meta-data. All outcomes were transformed to “face touch per hour” in the review. Pooled data from the included studies were analysed using R version 4. A Gaussian distribution was applied to calculate the scores, which lie over a certain interval with high confidence based on other research. Principal Component Analysis (PCA) was used to emphasise variation, and Chi-square analyses did hypothesis testing. **Results:** A total of 10 single-arms observational studies were included. The pooled average (SD) facial self-touch per hour was 50.06 (± 47) times, and a specific touch of T-zone was 68.7 (± 27). T-zone self-touch within the total facial self-touch was found higher $R = 0.680$, with 95% CI 0.14, 0.91, $P = 0.02$ and $X^2 = 167.63$, $P < 0.0001$. **Discussion:** The review found that the frequency of T-zone touching is the highest within the total facial self-touch. Face-touch is a type of consistent regulatory movement in humans.

Primary Supervisor: Dr Bapon Fakhruddin



