PREP Professional & Research Education Program

Graduate Student Research Day

May 31, 2022
CHEB - 170

DALHOUSIE UNIVERSITY FACULTY OF MEDICINE

dalhousie medical research foundation

FMGSS DALHOUSIE UNIVERSITY

DALHOUSIE UNIVERSITY FACULTY OF HEALTH

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DALHOUSIE UNIVERSITY
Faculty of Graduate Studies

COVID SAFETY PROTOCOL

1

Masks are required in indoor public places, if up from your seat

2

Physical distancing is not required, but encouraged

3

Stay home if you are unwell

For updates and more information, please visit the following links:

Dalhousie University - COVID Health & Safety Resources
https://www.dal.ca/covid-19-information-and-updates/covid-19-resources.html

Nova Scotia Government - Phase 5 Info
https://novascotia.ca/reopening-plan/phase-five/

Nova Scotia Government - Mask Requirements
https://novascotia.ca/coronavirus/masks/#When

Welcome to PREP Graduate Student Research Day

Graduate Student Research Day has been an annual event since 2005, when it began in the Faculty of Medicine. Now, this event invites participation from graduate students from across the University, who are involved in health research.

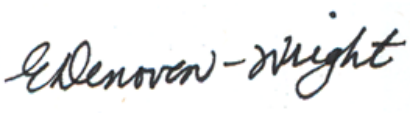
Normally held in May, this event typically receives over 80 abstracts, which are presented during this full-day of platform and poster presentations. Presentations are adjudicated by experienced researchers, in the spirit of helping students further develop their presentation and research skills. All Dalhousie graduate students are welcome to present their health-related research at this event.

In addition to providing an opportunity for students to present their research, this event allows a rare chance for these students to learn about other health research happening in their community and to develop research collaborations with others outside their fields of expertise.

This is one of the largest research showcases on Dalhousie University campus and promotes the importance and presence of the excellent research happening here.
The main objectives of graduate student research day:

- to help students and trainees enhance their awareness of ongoing research and opportunities
- to allow students and trainees an opportunity to critically assess the features of a good research project
- to provide students and trainees an opportunity to consider how research fits with the ongoing process of health education

I hope you can join us in supporting the great work of these students.



Eileen Denovan-Wright, PhD
Associate Dean, Research
Faculty of Medicine

Schedule of Events

May 31, 2022
CHEB - 170
https://www.dal.ca/faculty/prep/programs/gsrd/2022.html

9.00-9:15	**Welcome and Opening Remarks Dean Dr. David Anderson and ADR Dr. Eileen Denovan- Wright**
9:15 – 10:20	**Presentations by the 2022 Faculty of Medicine - Excellence in Research Award winner(s) (MSc, PhD, PDF and RA categories)**
10.20-10:50	**Presentation by the Faculty of Health - Excellence in Research Award winner(s)**
10:50-11:30	**Coffee break and Poster Presentation Viewing and Judging**
11.30–12.30	**Platform Presentations – graduate student nominees from Departments**
12.30-1:00	**Lunch and Poster Presentation Viewing**
1:00 – 2:00	**Keynote Speakers Dr. Susan Howlett and Dr. Ken Rockwood**
2:00- 2:30	**Coffee break and Poster Presentation Viewing and Judging**
2:30-4:00	**Platform Presentations – graduate student nominees from departments**
4:00 -4:30	**Closing Remarks and Prizes by Assistant Dean Dr. Paola Marcato**
4:30 -5:30	**FMGSS Social Mixer (Pizza & Pops)**

Graduate Student Research Day is supported by:

DALHOUSIE UNIVERSITY FACULTY OF MEDICINE

dalhousie medical research foundation

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Keynote Address – Drs. Kenneth Rockwood and Susan Howlett

Dr. Kenneth Rockwood

Kenneth Rockwood is Professor of Medicine (Geriatric Medicine & Neurology) at Dalhousie, an active staff physician at the Queen Elizabeth II Health Sciences Centre, and the Senior Medical Director of Frailty and Elder Care Network for Nova Scotia Health. He serves as the Dalhousie Medical Research Foundation Kathryn Allen Weldon Professor of Alzheimer Research at Dalhousie University. He is Associate Director of the Canadian Collaboration on Neurodegeneration in Aging.

A native of Newfoundland, Ken received his MD from Memorial University, completed internal medicine training at the University of Alberta and Geriatric Medicine at Dalhousie.
A leading authority on frailty, he has more than 500 peer-reviewed publications and nine books to his credit, including the eighth edition of *Brocklehurst's Textbook of Geriatric Medicine & Gerontology*.

Since 2017, facilitating his work with the National Health Service of England and Wales, Ken has held an appointment as Honorary Professor of Population Science and Experimental Medicine, University College London. He is President of Ardea Outcomes, a spin-off company that focuses on individualized outcome measurement in several complex diseases.

Dr. Susan Howlett

Susan Howlett is Professor of Pharmacology and Medicine (Geriatric Medicine) at Dalhousie University, Halifax, Nova Scotia, Canada, where she has taught for more than 30 years. Her laboratory is very well known for work on cardiac function in health and disease in older preclinical models. She has discovered profound differences in the way male and female heart cells function, how this changes with age and how declining sex hormones levels during aging regulate these processes.

Her laboratory has pioneered the measurement of frailty in naturally aging animals with a novel "frailty index" (FI) tool based on deficit accumulation. Her recent work with this tool shows that maladaptive, age-dependent changes in heart structure and function are better graded by the level of frailty than by age itself. Many of these adverse, frailty-associated changes are expressed differently in males and females. Her current work explores fundamental frailty mechanisms as well as novel strategies to treat frailty and thereby attenuate diseases of aging, especially heart disease. She has translated one of the frailty tools she developed for mice to measure frailty based on routine blood work and medical tests in humans (FI-Lab).

As a frequent contributor to prominent journals including JGBS, Nature Ageing, Mech Ageing & Dev, JMCC, J Physiol, and AJP, reviewer, editor and editorialist, Susan has a wide view of basic and translational research. Her personal and collaborative scientific experience allows insight into the needs of researchers across the career span. Her mentorship of now generations of young scientists, the great bulk of whom have pursued academic careers, speaks to her ability to inspire young researchers.

Information Kiosk:

Pulse – Dalhousie's Health Innovation Sandbox

Are you interested in learning more about health innovation? Do you want to explore what health innovation means, and how it can contribute to your future career goals? Come and visit Pulse, Dalhousie's Health Innovation Sandbox to learn about our health innovation programs and events for students!

Faculty of Medicine – CORES RESEARCH FACILITIES

ADVANCE YOUR RESEARCH WITH STATE-OF-THE-ART FACILITIES AND SERVICES
Through its strategic CORES program (Centralized Operations of Research Equipment and Supports), the Faculty of Medicine has developed a range of multi-user research facilities providing access to sophisticated equipment and services supported by trained experts. The CORES facilities welcome users from the Dalhousie community, other academic institutions, and external commercial groups.

Graduate Student Peer Support Network

The Peer Support Network offers peer support for fellow graduate students and postdoctoral fellows in the Faculty of Medicine by modelling skills to support positive personal coping strategies and academic success, facilitating self-reflection and growth, building confidence, and encouraging healthy lifestyle choices and positive coping strategies. We encourage the access of available resources including health, academic, and administrative services. Swing by our booth to learn more about what we have to offer and to meet our friendly peer supporters

Dal Innovates | Entrepreneurship Programming

Dal Innovates offers a suite of programs that are offered to students in any faculty or university in Atlantic Canada, and focuses on skills development, the commercialization of research and innovation, and the creation of new start-ups. The five diverse programs (Impactify, Path2Innovation, Scientist2Entrepreneur, Invention2Innovation, Lab2Market, and Ready2Launch) allow for participants to join at any level of their entrepreneurial journey. Lab2Market and Ready2Launch, are the most intensive entrepreneurship programs Dal Innovates offers, and are designed to lead into more advanced Atlantic accelerators. Thanks to these programs, many Dal Innovates alumni have created successful tech start-ups in the Atlantic region and have gone on to raise over 4.2 million in private and public funding! Come visit us at our table to learn more!

Student Presentation Schedule

Posters Presentations

Time		Poster #	Student	Department/ College/ School	Abstract Title	Research Area
Masters						
AM	10:50	M1	Alina Butova	Microbiology & Immunology	Investigating The Roles of Unfolded Protein Response Transcription Factors In Influenza A Virus Infection	Infection and Immunity
	10:57	M1	Jae Ho Han	Medical Neuroscience	A Small RNA Signature From Extracellular Vesicles In Patient Plasma Correlates With Recurrence Or Progression Of High-Grade Gliomas	Cancer
	11:04	M2	Katherine Purvis	Physiology & Biophysics	Optogenetic Tachypacing-Induced Heart Failure In Larval Zebrafish	Circulatory and Respiratory Health
	11:11	M2	Lara Virgilio	Biochemistry & Molecular Biology	Investigation Of The Molecular Basis For The Dual Role Of A Marine Antifreeze Protein	Natural Sciences and Engineering
	11:18	M3	Marley Blommers	Medical Neuroscience	Retinal Neuroblast Migration And Laminar Organization Requires The Cytoskeletal-Interacting Protein Mllt11	Neurosciences, Mental Health and Addiction
	11:25	M3	Meghan McLean	Pathology	Cancer Stem Cell Marker Aldh1A3 Mediates Invasion In Triple-Negative Breast Cancer By Inducing Plasminogen Activation	Cancer
PM	2:00	M4	Michaela Title	School of Health and Human Performance	Patients with acromegaly have regional differences in joint pain.	Musculoskeletal Health and Arthritis
	2:07	M4	Rachel Holland	Community Health and Epidemiology	The Contribution Of Socioeconomic Status To Racial Differences In Lung Function: A Systematic Review	Circulatory and Respiratory Health
	2:14	M5	Tony El-Rabahi	Physiology & Biophysics	Assessment Of Cardiac Electrical Remodelling In A Rat Model Of Severe Pulmonary Arterial Hypertension	Circulatory and Respiratory Health
	2:21	M5	Zachary Long	Physiology & Biophysics	Effects Of Autonomic Nervous System Activity On Atrial And Ventricular Myocyte Function In Zebrafish	Natural Sciences and Engineering
AM	10:50	M6	Anu Jose	Biochemistry & Molecular Biology	The Role Of Lipid Phosphate Phosphatase-3 In Cardiac Insulin Function And Energy Metabolism	Nutrition, Metabolism and Diabetes
	10:57	M6	Hannah Cahill	Pathology	Nrad1-Mir-4485-3P: A New Lncrna-Mirna Axis In Triple Negative Breast Cancer	Cancer
	11:04	M7	Jenna Bissonnette	Psychiatry	Complex Mismatch Negativity Deficits In Early Phase Psychosis Elicited By The Dual Rule Paradigm	Neurosciences, Mental Health and Addiction

Time		Poster #	Student	Department/ College/ School	Abstract Title	Research Area
AM	11:11	M7	Kirishani Kesavan	Physiology & Biophysics	Functional And Immuno-Characterization, And Distribution Of Cardiac Stem Cell Antigen-1 Or C-Kit Expressing Cells	Circulatory and Respiratory Health
	11:18	M8	Phoebe Phonchareon	Microbiology & Immunology	Interleukin-5 Induces A Selective Pattern Of Altered Gene Expression In Human Mast Cells	Cancer
	11:25	M8	Rhea Nickerson	Microbiology & Immunology	The Role Of The Cxcr3 Axis In The Efficacy Of Oncolytic Vesicular Stomatitis Virus Therapy In Combination With Natural Killer T Cell Immunotherapy In Melanoma	Cancer
PM	2:00	M9	Sarah Madeline Gallant	Nursing	Beyond these four walls: Exploring the experiences of mothers caring for babies going through withdrawal	Health Services and Policy Development
	2:07	M9	Adam Sunavsky	Medical Neuroscience	Dissociable Nucleus Accumbens Functional Connectivity Profiles In Adults With And Without Chronic Back Pain	Neurosciences, Mental Health and Addiction
	2:14	M10	Andrea Tomko	Pharmacology	Anti-Cancer Properties Of Cannflavin A And B In A Taxol-Resistant Model Of Breast Cancer	Cancer
	2:21	M10	David Burbidge	Medicine	Impact Of Exercise On Sod1G93A Disease Progression	Neurosciences, Mental Health and Addiction
AM	10:50	M11	Devin Manning	Community Health and Epidemiology	Changes In Publicly Funded Prescription Drugs Dispensed To Community-Dwelling New Brunswick Seniors Following Hospital Discharge For Myocardial Infarction Between 2008 And 2017.	Health Services and Policy Development
	10:57	M11	Eileigh Kadijk	Microbiology & Immunology	Influenza A Virus Host Shutoff Utilizes Interplay Between Ns1 And Pa-X	Infection and Immunity
	11:04	M12	Evan MacEachern	Physiotherapy	Cardiac Rehabilitation and Frailty: A Systematic Review	Aging
	11:11	M12	Jordan Dean Lukacs	Microbiology & Immunology	Natural Killer T Cell Immunotherapy Combined With Fast Expressing Oncolytic Viruses And Pd-1 Blockade Enhances Survival In A Mouse Model Of Spontaneous Lung Adenocarcinoma	Cancer
	11:18	M13	Maggie Hosmer	Microbiology and Immunology	Lime amendment to a chronically acidified forest soils results in shifts in microbial communities	Natural Sciences and Engineering
	11:25	M13	Michael Connolly	Physiology & Biophysics	Role Of Microtubules In Atrial Mechano-Arrhythmogenesis	Circulatory and Respiratory Health

Time		Poster #	Student	Department/ College/ School	Abstract Title	Research Area
PM	2:00	M14	Stacia Dolliver	Microbiology & Immunology	Coronaviruses Hcov-Oc43 And Sars-Cov2 Limit Stress Granule Formation To Promote Virus Replication	Infection and Immunity
	2:07	M14	Taylor Caddell	Microbiology & Immunology	Sars-Cov-2 Membrane And Envelope Proteins Inhibit Spike-Mediated Activation Of Atf6	Infection and Immunity
	2:14	M15	Yuqi Wang	Kinesiology	Functional impairment with arthropathy in acromegaly patients	Musculoskeletal Health and Arthritis
PhD						
AM	10:50	P1	Ashley Francis	Psychiatry	Differential Effects Of Cannabis Use On Event-Related Potential (Erp)-Indexes Of Cortical Inhibition In Cannabis Users And Non-Users.	Neurosciences, Mental Health and Addiction
	10:57	P1	Elise Bisset	Pharmacology	The Impact Of Dietary Nitrates On Cardiac Remodeling Is Age-Dependent In Male C57Bl/6 Mice	Aging
	11:04	P2	Julia Kontak	Health	peering in: Youth perspectives on Health Promoting Schools and youth engagement in Nova Scotia, Canada	Population and Public Health
	11:11	P2	Sarah Nersesian	Microbiology and Immunology	TCGA exploration reveals a relationship between NK cell ligand expression and tumour progression, genetics, and hypoxia in HGSC	Cancer
PM	2:00	P3	Ahmed Ramadan	Biomedical Engineering	Optogenetic Suppression Of Drug-Induced Early Afterdepolarisations In The Zebrafish Heart	Natural Sciences and Engineering
	2:07	P3	Alexa Wilson	Microbiology & Immunology	Stressed Out: Investigating How A Herpesvirus E3 Ubiquitin Ligase Modulates The Unfolded Protein Response.	Infection and Immunity
	2:14	P4	Sarah DeGrace	Psychiatry	A Scoping Review Of The Literature On Trauma Cue-Induced Drug Craving In Substance Users With Trauma Histories Or Ptsd	Neurosciences, Mental Health and Addiction
	2:21	P4	Stefan Hall	Physiology & Biophysics	Activation Of Cannabinoid Type Ii Receptor Attenuates Systemic Inflammation Secondary To Acute Lung Injury	Infection and Immunity
AM	10:50	P5	Anupama Ghimire	Biochemistry & Molecular Biology	Development And Characterization Of Recombinant Hybrid Spider Silks	Natural Sciences and Engineering
	10:57	P5	Kayle Dickson	Microbiology & Immunology	Beta-Caryophyllene As A Novel Adjunct Therapy For The Treatment Of Urinary Tract Infections	Infection and Immunity
	11:04	P6	Reynaldo Popoli	Medical Neuroscience	Pharmacological Cholinergic Inhibition As A Therapeutic Approach In Als.	Neurosciences, Mental Health and Addiction

Time		Poster #	Student	Department/ College/ School	Abstract Title	Research Area
	11:11	P6	Abhishek Mishra	Pharmacology	Atrial Natriuretic Peptide Promotes Vcs Cell Differentiation By Promoting Lipid Accumulation And Targeting Cellular Metabolic Pathways	Circulatory and Respiratory Health
PM	2:00	P7	Spencer Jones	Biochemistry & Molecular Biology	Swi/Snf Regulates The Inducibility Of Memory Genes During Ltm Formation	Neurosciences, Mental Health and Addiction
	2:07	P7	Trilok Neupane	Biochemistry & Molecular Biology	Investigating The Mechanism Of Rhodoquinone Biosynthesis	Natural Sciences and Engineering
	2:14	P8	Brendan McKeown	Pharmacology	Jadomycin B Acts Synergistically With Nsaids To Produce Cytotoxic Effects In Human Breast Cancer Cells In Vitro	Cancer
	2:21	P8	Edwin Leong	Infection and Immunity	Mast Cell Degranulation-Associated Products Modulate Progression And Resolution Of Skin Fibrosis	Infection and Immunity
AM	10:50	P9	Jonathan Baillie	Circulatory and Respiratory Health	Effects Of An Acute Increase In Hemodynamic Load On Cardiac Function During Cardiac Development	Circulatory and Respiratory Health
	10:57	P9	Kathleen Vergunst	Natural Sciences and Engineering	Characterizing The Structure And Assembly Of Hydrophobin Proteins	Natural Sciences and Engineering
	11:04	P10	Pooyan Moradi	Neurosciences, Mental Health and Addiction	Concussion Susceptibility And Neurovascular Dysfunction As A Predictor For Short- And Long-Term Complications Of Repetitive Mild Traumatic Brain Injury	Neurosciences, Mental Health and Addiction
	11:11	P10	Tam Pham	Circulatory and Respiratory Health	Applying And Expanding The Scope Of 19F-Nmr Spectroscopy To Probe Peptide-Membrane Interactions	Circulatory and Respiratory Health
	11:18	P11	Colin Pridy	Social Sciences and Humanities	Relaxing Music In The Dental Waiting Room Has Paradoxical Effects On Dental Anxiety In Patients With High Cognitive And Social Anxiety Sensitivity	Social Sciences and Humanities
PM	2:00	P11	Danielle Stanton-Turcotte	Genetics	Mllt11 Regulates Migration And Neurite Outgrowth Of Cortical Projection Neurons During Development	Genetics
	2:07	P12	Lauren Westhaver	Infection and Immunity	Mitochondrial Damage-Associated Molecular Patterns Trigger Arginase-Dependent Lymphocyte Immunoregulation	Infection and Immunity
	2:14	P12	Selena Maxwell	Aging	Cholinesterase-Associated Neuropathology In Octogenarians And Older	Aging

Platform presentations

Time	Student	Affiliation	Abstract Title	Research Area
Room: CHEB 170				
11:30	Haley Bernusky	Psychiatry	Is Anxiety A Mediator In The Relationship Between Cannabis Use And Psychotic-Like Experiences In Emerging Adults? Investigating A Mediation Model In A Multi-Site University Sample	Neurosciences, Mental Health and Addiction
11:45	Mia Schofield	Pharmacology	Circadian Clock Synchrony As A Mechanism For Regulating Behaviour In Drosophila	Neurosciences, Mental Health and Addiction
12:00	Yuqi Wang	Kinesiology	Functional impairment with arthropathy in acromegaly patients	Musculoskeletal Health and Arthritis
12:15	Joel Bierer	Surgery	Continuous Subzero-Balance Ultrafiltration Extracts Twenty-Two Inflammatory Mediators During Pediatric Cardiac Surgery With Cardiopulmonary Bypass	Circulatory and Respiratory Health
2:30	Tyler Wells	Medical Neuroscience	Activity Changes In The C-Boutons During Amyotrophic Lateral Sclerosis Disease Progression	Neurosciences, Mental Health and Addiction
2:45	Jessi Bak	Physiology & Biophysics	Role Of Microtubules And Transient Receptor Potential Ankyrin 1 (Trpa1) In Mechanically-Induced Arrhythmias	Circulatory and Respiratory Health
3:00	Marie-Claire Wasson	Pathology	Lncrna Linc01929 Is A Novel Mediator Of Critical Oncogenic Processes And Promotes An Immunosuppressive Tumor Microenvironment In Breast Cancer	Cancer
3:15	Taryn Jakub	Biochemistry & Molecular Biology	Clinically Identified Pathogenic Variants Disrupt The Enzymatic Activity Of The Epigenetic Regulator, Kdm6B, Resulting In A Novel Neurodevelopmental Disorder	Genetics
3:30	Animamalar Mayavannan	Microbiology & Immunology	Toll-Like Receptor 2 Signalling Is Essential For Steering Protective Host Immune Responses And Controlling Long Term Tissue Damage In Chlamydia Reproductive Tract Infection	Infection and Immunity
3:45	Nicholas Campbell	Biomedical Engineering	Development Of A Real-Time High Resolution Ultrasound System For Brain Imaging	Natural Sciences and Engineering

Excellence In Research – Oral Presentations

#	Time	Student	Affiliation	Abstract Title
	Room: CHEB 170			
1	9:20	Junzhe Young Wang	Biomedical Engineering	Development of an optical coherence tomography (OCT) system for middle ear imaging
2	9:35	Shannon Sibald	Biochemistry & Molecular Biology	Patterns and process of genome evolution in harmful algal bloom-forming protists.
3	9:50	Matthew Stoyek	Physiology and Biophysics	Role of the autonomic nervous system in control of the heart, in particular, using the zebrafish as a model for cardiac physiology and pathophysiology
4	10:05	Alamelu Bharadwaj	Pathology	Function of plasminogen activation system in cancer progression with specific emphasis on the function of S100A10 in breast cancer.
5	10:20	Jack Quach	Physiotherapy	The Impact of Frailty on Long-Term Outcomes of Cardiac Rehabilitation Patients
6	10:35	Martha Paynter	Nursing	Reproductive Injustice in Canadian Prisons for Women: A Multiple Methods Examination of the Mother Child Program

Student Abstracts by Research Area

Aging

The impact of dietary nitrates on cardiac remodeling is age-dependent in male C57Bl/6 mice

Elise S Bisset[1], Susan E Howlett[1,2]

1. Department of Pharmacology, Dalhousie University, Halifax, Nova Scotia

2. Department of Medicine (Geriatric Medicine), Dalhousie University, Halifax, Nova Scotia.

A significant health complication that arises with aging is adverse cardiac remodeling. One treatment that may improve cardiac health is dietary nitrates, however studies of the effects of nitrates generally focus on younger subjects. We therefore investigated the impact of chronic nitrate supplementation (1mM sodium nitrate) on heart structure and function in both young (7-month-old) and old (21-23-month-old) male mice after 12 weeks. In young and old mice, nitrate supplementation increased left ventricular size measured with echocardiography. The treated old mice had an increase in diastolic diameter from baseline while treated young mice had an increase in systolic diameter. When comparing the older and younger nitrate-treated mice, younger treated mice had thinner posterior walls than older mice (1.20 ± 0.04 mm vs 1.46 ± 0.04 mm: p=0.04). This resulted in older nitrate-treated mice having heavier left ventricles at endpoint compared to young, treated mice (133.5 ± 10 mg vs 187.7 ± 15 mg: p=0.01). While older mice treated with nitrates had larger left ventricles, there was no change in ejection fraction over time (66.9 ± 3.7% to 61.9 ± 4.4%: p=0.13). Conversely, younger mice exposed to nitrates had larger left ventricles with thinner walls and a reduction in ejection fraction when compared to age-matched controls (66.9 ± 3.4% to 55.8 ± 2.2%:p=0.02). To conclude, nitrate supplementation revealed age-specific cardiac remodeling in young and old mice. This raises questions about the use nitrates on cardiovascular health at all ages.

CARDIAC REHABILITATION AND FRAILTY: A SYSTEMATIC REVIEW

Evan MacEachern[1], Jack Quach[2], Nicholas Giacomantonio[3], Olga Theou[4], Wanda Firth[5], Ifedayo Abel-Adegbite[6], Mariana Gonzalez-Lara[7] & D. Scott Kehler[8]

1. School of Physiotherapy, Dalhousie University, Halifax, NS
2. School of Physiotherapy, Dalhousie University, Halifax, NS
3. Department of Cardiology, Dalhousie University, Halifax, NS
4. School of Physiotherapy, Division of Geriatric Medicine, Dalhousie University, Halifax, NS
5. Nova Scotia Health, Hearts and Health in Motion, Halifax, NS
6. Faculty of Health, Dalhousie University, Halifax, NS
7. Geriatric Epidemiology Research Department, Instituto Nacional de Geriatria, Mexico
8. School of Physiotherapy, Dalhousie University, Halifax, NS

Rationale: Research on frailty within cardiac rehabilitation (CR) is growing, however, there is no synthesis of the literature on frailty in CR. *Objectives:* Conduct a systematic review to understand: 1) patient frailty levels upon CR admission; 2) frailty's impact on CR completion; 3) changes in frailty level with CR and; 4) if frailty in CR impacts health outcomes. *Methods:* Eligible articles included measures of frailty in CR published in English. We searched databases (CINAHL, Embase, MEDLINE) from 2000-2022, selecting original research articles on frailty and CR. Two reviewers independently screened and synthesized data on article characteristics, CR characteristics, prevalence of frailty, and frailty predicting health outcomes in CR. *Results:* Our search identified 1,395 publications. Twenty-five cohort studies including 9,641 participants were synthesized. Seventeen studies assessed admission frailty (n=4,580), categorizing participants into robust (n=1,976, 43.1%), pre-frail (n=1,202, 26.2%), and frail (n=1,402, 30.6%). Five studies reported frailer patients are less likely to complete CR, while seven studies suggested frailer CR patients observe the greatest benefits from CR completion. Ten studies found frailty prevalence was reduced by 20.5-87.0% following CR completion; two studies reported no change. Frail CR participants at admission observed significant improvements in walking tests (studies=7) and grip and lower extremity strength (studies=2) upon completion of CR. Frailer participants had greater risk of hospital readmission or all-cause mortality (HR frail: HR=3.18[2.59-3.90]-3.93[3.29-4.70]; prefrail: HR=2.11[1.75-2.56]-2.19[1.00-4.79]) compared to non-frail participants (studies=2). *Conclusion*: CR improves frailty and physical function. However, frailty at CR admission was related to CR non-completion, risk of rehospitalization, and all-cause mortality.

The Impact of Frailty on Long-Term Outcomes of Cardiac Rehabilitation Patients

J Quach,[1,3] O Theou,[1,2,3] W Firth,[4] C McArthur,[1] N Giacomantonio,[4,5] DS Kehler[1,3]

1 - Physiotherapy, Dalhousie University, Halifax, NS, Canada
2 - Geriatric Medicine, Dalhousie University, Halifax, NS, Canada
3 - Geriatric Medicine, Nova Scotia Health, Halifax, NS, Canada
4 - Cardiology, Nova Scotia Health, Halifax, NS, Canada
5 - Cardiology, Dalhousie University, Halifax, NS, Canada

Purpose: Determine whether frailty status during cardiac rehabilitation (CR) are associated with long-term all-cause and cardiovascular disease (CVD) mortality, hospitalization, and emergency department (ED) visits. *Methods:* We analyzed data from patients admitted to CR in Halifax, Nova Scotia from May 2005 to April 2015 (N=3,371). The CR program included group-based exercise and education performed twice weekly for 12 weeks. A 25-item frailty index (FI) estimated frailty levels at CR admission and discharge. FI improvements were determined by calculating the difference between admission and discharge FI. CR data were linked to administrative health data to examine 5-year outcomes (all-cause and CVD mortality, hospitalization, and ED visits). Cox regression and Fine-Gray models were used to determine the association between FI and outcomes. Hazard ratios and confidence intervals correspond to a 1% change in the FI. *Results:* The mean (SD) age of the patients were 62 (11) years old; 74% were male. Mean admission FI scores were 0.34 (0.13). On average, FI improved by 0.07 (0.09) from CR admission to discharge. All-cause and CVD mortality rates were 6.9% and 2.8%, respectively. Admission FI was associated with time to mortality (all-cause=1.02[1.01,1.04]; CVD=1.03[1.02,1.05]), hospitalization (all-cause=1.02[1.01,1.02]; CVD=1.02[1.01,1.02]), and ED visit (all-cause=1.01[1.00,1.01]; CVD=1.02 [1.01,1.03]). FI improvements during CR had a protective effect regarding time to all-cause hospitalization (0.99[0.98,0.99]), but was not associated with other outcomes. *Conclusion:* Frailty status at CR admission was related to long-term adverse outcomes. Frailty improvements during CR was associated with delayed all-cause hospitalization.

Cholinesterase-associated Neuropathology in Octogenarians and Older

Selena P Maxwell, Meghan K Cash, Sultan Darvesh

A subset of octogenarians and older maintain normal cognitive function (CNOO) despite high prevalence and incidence of cognitive decline. The rostral prefrontal cortex (rPFC) and hippocampal formation are brain regions integral to cognition facilitated in part by cholinergic innervation. We hypothesized that preserved cholinergic neurotransmission in these regions contributes to intact cognition in CNOO. We evaluated neuropathological and cholinesterase-associated protein burden in the rPFC and hippocampal formation. Tissues from age- and sex-matched CNOO and Alzheimer's disease (AD) rPFC and hippocampal formation were stained for §-amyloid (A§), tau, o-synuclein, phosphorylated TAR DNA- binding protein 43 (pTDP-43), acetylcholinesterase (AChE), and butyrylcholinesterase (BChE). Relative abundance of neuropathological aggregates was semi-quantitatively scored. Deposition of A§ plaques, tau neurofibrillary tangles (NFT) and pTDP-43 inclusions were comparable between CNOO and AD cases in many regions. Intraneuronal A§ and tau-positive thorny astrocytes consistent with aging-related tau astrogliopathy, were also noted in CNOO rPFC. Abundance of BChE-positive plaque pathology was significantly higher in AD than in CNOO cases in most regions of interest, followed closely by abundance of AChE-positive plaques. BChE- and AChE-activities were also associated with varied NFT morphologies. CNOO cases maintained cognition despite high neuropathological burden in the rPFC and hippocampal formation. BChE-positive and, to a lesser extent, AChE-positive pathologies were significantly lower in most regions in CNOO compared to AD. This suggests specificity of cholinesterase-associated neuropathology with AD. We conclude that while CNOO have cholinesterase- associated neuropathology in the rPFC and hippocampal formation, abundance is significantly lower compared to AD which may contribute to their intact cognition.

Cancer

NATURAL KILLER T CELL IMMUNOTHERAPY COMBINED WITH FAST EXPRESSING ONCOLYTIC VIRUSES AND PD-1 BLOCKADE ENHANCES SURVIVAL IN A MOUSE MODEL OF SPONTANEOUS LUNG ADENOCARCINOMA.

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Aim: Non-small cell lung cancer (NSCLC) remains among Canada's leading cause of cancer deaths. Moreover, with a 5-year survival of 19%, improvements in treatment are crucial for reducing both morbidity and mortality. In this study, we examined the therapeutic benefit of combining oncolytic vesicular stomatitis virus (VSV) expressing fusion-associated small transmembrane (FAST) proteins p14 or p15, PD-1 checkpoint blockade, and natural killer T (NKT) cell immunotherapy on survival in a genetic mouse model of lung adenocarcinoma. **Methodology:** We generated mice that contain a tamoxifen-inducible Cre recombinase gene driven by the (Club cell-secretory protein) CCSP promoter, with *KP* mice (CCSP-KP mice) to enable the time-dependent activation of oncogenic $KRAS^{G12D}$ and ablation of one *p53* allele. CCSP-KP mice were treated with VSV-GFP, VSV-p14, or VSV-p15 on days 40, 42, and 44, followed by an iv. treatment of α-galactosylceramide-loaded dendritic cells to activate NKT cells on day 45. An ip. injection anti- PD-1 (300 µg) was given once a week for a total of 4 doses (days 48, 55, 62, and 69). **Results:** CCSP-KP mice receiving combinatorial treatment of VSV-p14 or VSV-p15, NKT cell activation and PD-1 blockade (n = 9-11) demonstrated increased overall survival in comparison with untreated CCSP-KP mice (n = 9). Furthermore, signs of morbidity (heavy or labored respirations, hunched posture, weight loss, etc.) were considerably delayed in treated mice. **Conclusion:** Our study demonstrates that combining multiple immunotherapies not only enhances and prolongs anti-tumor immune responses, ultimately increasing survival, but also minimizes treatment resistance due to the complex and distinct nature of each individual treatment.

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INTERLEUKIN-5 INDUCES A SELECTIVE PATTERN OF ALTERED GENE EXPRESSION IN HUMAN MAST CELLS

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Mast cells are immune effector resident cells that play important roles in host defense, inflammation, and immune regulation. Interleukin 5 (IL-5) is a type 2 cytokine that elevated in allergic disease and in parasitic infections. We observed that IL-5 treatment can modify the IFN production of human mast cells in response to viral infection without modifying the level of viral infection. Therefore, we explored broader impacts of IL-5 treatment on human mast cells. Human mast cells were cultured from cord blood derived stem cells and treated with IL-5. Total RNA was prepared from human cord blood derived mast cells (>95% pure) and sequenced using next generation techniques. A paired differential expression analysis was performed comparing untreated mast cells (8 donors) with cells treated with 10 ng/mL IL-5 for 42 hours. Upregulated or downregulated gene expression was identified using Salmon and DESeq2 in RStudio. Initial analysis indicated that genes in several classes (cytokine signaling, apoptosis, and protein phosphorylation) were modified upon IL-5 priming in mast cells. Some specific genes of interest with significantly upregulated expression (Padj<7.78E-8) following IL-5 treatment included Leukemia Inhibitory Factor (LIF) and Oncostatin M (OSM), which are IL-6 family members, but not IL-6 itself. Data from the transcriptome analysis was confirmed by quantitative PCR. LIF and OSM are currently being characterized. These studies demonstrate that IL-5 can have a profound impact on mast cell gene expression, even in the absence of viral stimulation. These observations also suggest that IL-5 blockade-based therapies may impact mast cell function.

Identifying the role of B cells in melanoma

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Melanoma is the most aggressive and deadly of skin cancers. B cells makeup a third of the immune cells in melanomas but their role is controversial. We are comprehensively studying the function of B cells and their interaction with mast cells in multiple murine melanoma models in wild-type and B cell-deficient mice, in addition to analysing melanoma patient samples. Knowledge of B cells and their cellular networks in melanoma is critical before B cell targeting strategies can be implemented/developed. The growth kinetics of melanoma in B cell-sufficient and -deficient mice was examined using the B16-F10 and inducible melanoma models. Immunological characterisation of tissues was conducted by high-parameter flow cytometry, immunohistochemistry, and qPCR. B cell cellular networks in patient melanoma tissue samples were investigated using tyramide signal amplification-based multiplex immunofluorescence. B cell-deficient mice developed melanomas slower than controls. Phenotyping by high-dimensional flow cytometry revealed high density of immature B2 cells in B16-F10 lesions. qPCR analysis showed reduced *Il10* expression in melanomas from B cell-deficient mice compared with controls. Mast cell-deficiency appeared to alter B cell density and phenotype in mice with B16-F10 tumours. Multiplex immunofluorescence showed B cells and mast cells in close proximity within human melanomas. Evaluation of B cell-mast cell aggregates as prognostic and diagnostic biomarkers using human melanoma samples is ongoing. Melanoma-resident B cells may support melanoma development and progression, potentially through interactions with neighbouring mast cells. Understanding of the role of B cells in melanoma is required before strategies can be devised to leverage or deplete them for clinical benefit.

LncRNA LINC01929 is a novel mediator of critical oncogenic processes and promotes an immunosuppressive tumor microenvironment in breast cancer

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Long non-coding RNAs (lncRNAs) are emerging as important epigenetic regulators of gene expression in cancer. While there are over 12,000 lncRNAs expressed in the human genome, the majority remain uncharacterized. Given that some lncRNAs exhibit critical functions in cancer development, metastasis, and drug resistance, we sought to expand the knowledge of how lncRNAs mediate these oncogenic processes. This led us to perform a genome-wide analysis to identify novel lncRNAs that regulate transcriptional processes required for breast cancer progression. Our bioinformatics analysis of 12,727 lncRNAs in 8000 tumors identified that LINC01929 is in the top 97th percentile of lncRNAs enriched in tumor versus normal tissue and is significantly associated with worse patient survival in breast, cervical, low-grade glioma, and kidney cancers. Our transcriptome analysis of breast cancer cell lines with knockdown of LINC01929 indicated that the lncRNA regulates the expression of hundreds of genes. These genes are overwhelmingly enriched in oncogenic pathways and associated with antigen presentation, T-cell regulation, apoptosis and proteasomal activity. Functional analyses support these gene expression data. LINC01929 knockdown increased MHC-I on the cell surface, protein levels of key immunoproteasome subunits and proteasomal activity. Moreover, CIBERSORTx analysis revealed that LINC01929 is associated with low T and B cell infiltration of breast tumors. Together, our findings suggest that we have identified a lncRNA that mediates critical oncogenic processes in breast cancer. LINC01929 regulates cancer-promoting gene expression networks that contribute to immune exclusion and tumor progression, and may serve as a therapeutic target for the treatment of breast cancer. BACKGROUND: Over the past thirty years, the young adult (YA; 18-39 years of age) cancer population has not seen progress in survival rates comparable to that of other oncology populations. Major gaps exist in YA oncology research and there is even less concerning those living with metastatic/advanced cancer. This systematic scoping review maps what is known about the experiences of YAs living

with metastatic/advanced cancer. METHODS: A systematic scoping review, guided by Arksey and O'Malley's methods, was conducted to examine the experiences of YAs living with metastatic/advanced cancer. The search strategy included relevant databases (MEDLINE, CINAHL, PsycINFO), ProQuest dissertations, grey literature and hand-searches of three journals. Applied key words included but were not limited to: palliative care; experience. These were used with Boolean operators AND and OR. The population included YA living with a metastatic/advanced cancer and the concept included their psychosocial experiences. The context was within both the hospital and community environments. Search terms were developed in collaboration with a medical research librarian. RESULTS: 2846 references were obtained, and 564 duplicates were removed. There were 10 included studies that were published from 2011-2018. Their findings covered four major themes: 1. Search to make meaning of their illness; 2. Relationships with others; 3. Mental health and psychosocial well-being; 4. Physical health. CONCLUSION: Three knowledge gaps were identified: 1. How YAs experience cancer care delivery; 2. Relationships with their children and partners; and 3. How socio-demographics (i.e. sex, gender, race, socio-economic status, sexuality) influence the experiences of YAs.

Jadomycin B Acts Synergistically with NSAIDs to Produce Cytotoxic Effects in Human Breast Cancer Cells in vitro

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Background: Breast cancer is the most prevalent cancer in North American women. Jadomycin B is effective in killing multidrug resistant, triple negative human breast cancer cells. The mechanism through which jadomycin B exerts its cytotoxic effect remains to be fully characterized. Cyclooxygenase-2 (COX-2) was identified as a target of interest in jadomycin B resistant breast cancer cells. *Objective:* To explore the effects of COX-2 signalling on jadomycin B cytotoxicity in triple-negative, human breast cancer cells requiring more effective treatments. *Methods and Results*: Control MDA-MB-231 (231-CON) cells exposed to jadomycin B (0-2.2 μM) over 7 months developed resistance to jadomycin B (231-JB) as determined using methyl-tetrazolium (MTT) cell viability assays. By qPCR, there was a significant increase in COX-2 (40 fold, $p < 0.05$) but not cyclooxygenase-1 (COX-1) (0.17 fold, $p < 0.05$), mRNA expression in 231-JB versus 231- CON cells. We therefore hypothesized that inhibition of COX-2 signalling would increase the susceptibility of breast cancer cells to jadomycin B. 231-CON and 231-JB cells were treated with jadomycin B with or without the COX-2 inhibitor celecoxib (CXB), or COX-1/2 inhibitors ibuprofen (IBU) or Naproxen (NAP). SynergyFinder 2.0 was used to analyze the cytotoxicity (MTT assays) of these combinations and calculate synergy scores using the Bliss model. IBU, NAP, and CXB were found to act synergistically with jadomycin B in both control and jadomycin resistant cells (Table 1). *Conclusions:* Jadomycin B acts synergistically with inhibitors of COX-2 in vitro, justifying further investigation into the COX-2 as a mechanism of action of jadomycin B.

Cancer Stem Cell Marker ALDH1A3 Mediates Invasion in Triple-Negative Breast Cancer by Inducing Plasminogen Activation

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Introduction: Triple-negative breast cancer (TNBC) is an aggressive form of breast cancer in need of an increased understanding and new therapies. TNBCs have high abundance of cancer stem cells defined by high aldehyde dehydrogenase 1A3 (ALDH1A3), which contributes to poor outcomes of TNBC patients. This study aims to investigate the mechanism for how ALDH1A3 increases invasion and metastasis of breast cancer cells through the plasminogen activation pathway. The plasminogen pathway produces plasmin, which can degrade fibrin in the extracellular matrix (ECM), promoting metastasis. Methods/Results: Proteomics on TNBC cells with low versus high ALDH1A3 levels showed changes in plasminogen activation pathway regulators, including tissue plasminogen activator (tPA) and plasminogen activator inhibitor (PAI-2). Western blots confirmed that ALDH1A3 increases tPA and decreased PAI-2 in a panel of breast cancer cells. In plasminogen activation assays, ALDH1A3 increased plasmin generation in TNBC cells. In transwell invasion assays, plasminogen is required for ALDH1A3-mediated invasion. In fixed breast cancer patient tumor samples, high ALDH1A3+/tPA+ and ALDH1A3+/PAI-2- cells were correlated with increased tumor grade. Conclusion: The plasminogen pathway in normal cells is used to break down fibrin clots, but when this system is put into overdrive due to the increased expression of ALDH1A3, cancer cells can use the pathway to break down fibrin in the ECM which promotes invasion and metastasis. The upregulation of tPA increases plasmin, making tPA a potential target to decrease plasmin's effects on the cells. Our results provide a new link between ALDH1A3 and the plasminogen activation system in TNBC progression.

The role of the CXCR3 axis in the efficacy of oncolytic Vesicular Stomatitis Virus therapy in combination with Natural Killer T cell immunotherapy in melanoma

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Background: Advanced melanoma is highly metastatic and resistant to traditional chemotherapies, resulting in a 5-year survival rate of <30%. This study investigated Natural Killer T (NKT) cell-based immunotherapy in combination with oncolytic Vesicular Stomatitis Virus (VSVΔM51) constructs. Oncolytic VSVΔM51 enhances NKT cell infiltration into tumors, increasing the efficacy of subsequent NKT cell immunotherapy. VSVΔM51 infection increases the production of CXCR3 chemokine receptor ligands, potentially recruiting CXCR3-expressing NKT cells into the tumor microenvironment; however, the specific role of the CXCR3 axis in treatment efficacy is unknown. Methods: Using the syngeneic B16-F10 melanoma model, responses to NKT cell immunotherapy, alone and in combination with recombinant VSVΔM51 constructs, were tested in wild-type and CXCR3-/-C57BL/6 mice. B16-F10 melanoma cells were inoculated subcutaneously. On days 9, 11, and 13, mice received intratumoral injections of oncolytic VSV-GFP (control) or VSV engineered to express reovirus membrane fusion protein p14 (VSV-p14). Dendritic cells loaded with α-galactosylceramide were delivered intravenously on day 14 to activate NKT cells. Tumor growth and overall survival were monitored. Results: Combined treatments enhanced survival compared to monotherapies. CXCR3-/- mice exhibited trends towards improved tumor regression and survival in response to VSV; however, survival and tumor growth were ultimately not significantly different between wild-type and CXCR3-/- mice across treatment groups.Conclusion: These results demonstrate that oncolytic VSV in combination with NKT cell immunotherapy provides superior survival benefit compared to monotherapies. The CXCR3 axis was dispensable in our combined therapy, but reduced viral clearance and enhanced oncolytic activity may compensate for the loss of CXCR3

A small RNA signature from extracellular vesicles in patient plasma correlates with recurrence or progression of high-grade gliomas

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Glial cell-derived tumours of the central nervous system make up the largest group of brain tumours. Most are high-grade gliomas (HGG) and are universally fatal despite multimodal therapy.With a suspected HGG, surgery is undertaken for tumour debulking and to make a diagnosis.While the tumour genetics provides some insight on prognosis, it rarely changes decision-making, nor does it predict recurrence.In managing patients with HGG,predicting recurrence, or differentiating between pseudoprogression(radiation necrosis) and true tumour progression would be invaluable in improving overall prognosis. Characterizing small RNA (sRNA) expression profiles from plasma-derived extracellular vesicles (EVs) over the course of a patient's treatments,may allow for patient-specific treatment modifications and improve outcomes.

Methods:

Plasma EVs were isolated using Vn96 capture from HGG patients perioperatively and with routine, follow-up surveillance imaging. sRNA sequencing was conducted and unsupervised hierarchal clustering of sRNA signatures were completed.Expression profiles were grouped longitudinally with the clinical status of patients.

Results:

Cluster analysis of nine HGG patients, has revealed a sRNA signature that is able to distinguish between tumours showing evidence of progression and those remaining stable over time.Those samples obtained from patients where a clinical diagnosis of tumour progression or pseudoprogression were uncertain, were found to cluster into progression vs. stable signatures. Clinical follow up of these patients will reveal the predictive value of these identified clusters.

Conclusion:

These preliminary findings demonstrate the potential utility of sRNA profiling of plasma-derived EVs obtained from patients with high-grade gliomas as non-invasive biomarkers for recurrent/progressive disease or stability/pseudoprogression.

Anti-cancer properties of cannflavin A and B in a taxol-resistant model of breast cancer

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1 in 8 women in Canada will be diagnosed with breast cancer in their lifetime and chemotherapeutic resistance can reduce survival rates revealing the need for novel treatment options. Studies have shown compounds found in Cannabis sativa can exert anti-cancer effects, but little is known about cannflavin A and B, two flavonoids present in Cannabis, and their role in chemotherapeutic breast cancer. Concentration curves for cannflavin A and B were generated in taxol-resistant cell lines to identify the range at which anti-tumor effects are observed.Maximal concentrations were assessed in a non-tumorigenic breast cell line. The activation of apoptosis and autophagy were assessed using annexin V staining, known autophagy inhibitors,and RT-qPCR.We also evaluated whether cannflavin A and B had the ability to reduce invasion. Cannflavin A and B reduced the cell viability of taxol-resistant breast cancer cell lines in a dose-dependent manner while not affecting the viability of a non-tumorigenic breast cell line. Cannflavin A and B produced variable responses when combined with THC, CBD, or paclitaxel-from antagonistic to additive, and even synergistic, depending on the concentrations used. Cannflavin A induced apoptosis, and both compounds partially exerted their effects through the induction of autophagy and reduced invasiveness. Results indicate that cannflavin A and B,two lesser characterized compounds from Cannabis, can reduce the viability of taxol-resistant breast cancer cells. These compounds can act synergistically with cannabinoids and paclitaxel. Future studies should be completed in in vivo models to confirm the anti-cancer effects of cannflavin A and B.

Nrad1-Mir-4485-3P: A New Lncrna-Mirna Axis In Triple Negative Breast Cancer

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Triple negative breast cancer (TNBC) is an aggressive breast cancer subtype in need of new treatments. TNBC is associated with worse patient survival and distinct gene expression profiles. Increased understanding of the factors that lead to aberrant gene expression in TNBC will lead to new treatments. Non-coding RNAs are among these factors. Both microRNAs (miRNAs) and the long non-coding RNAs (incRNAs) that regulate miRNAs are key contributors of breast cancer progression. Identifying key TNBC promoting IncRNA-miRNA are aces could result in the development of nucleotide-based therapies that target these molecules. Our work has identified a Inc-RNA-miRNA axis between TNBC-promoting IncRNA, non-coding RNA in the aldehyde dehydrogenase 1A pathway (NRAD1) and its interesting with mir-4485-3p. Gene miRNA microarray analyses revealed miR-44-85-3p as highly upregulated following knockdown of NRAD1 in TNBC cell lines. Sequence alignment between NRAD1 and mir-4485-3p revealed potential for binding interaction, which could result in sequestering of the miRNA by NRAD1 and resulting upregulation of mir-4485-3p upon NRAD1 knockdown. TaqMan quantitative polymerase chain reaction assays validated the microarray data and integrated analysis of our transcriptome data with predicted mRNA targets of miR-44-85-3p identified NRAD1 regulated miRNA axis in TNBC that is associated with cancer promoting gene expression changes. Ongoing experiments are confirming the interaction between NRAD1 and miR-4485-3p and the consequences of their interaction in TNBC growth, migration and stemness (features promoted by NRAD1)

Optogenetic tachypacing-induced heart failure in larval zebrafish

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Chronic tachypacing is commonly used in mammals to model heart failure (HF). Alternative methods of chronic tachypacing involving the use of light-activated ion channels ('optogenetics') have been explored in cultured heart tissue. However, this lacks the complexity of native myocardium. Recent efforts have explored zebrafish as a model for human cardiac dysfunction based on their electrophysiological similarities. Larval zebrafish offer a particularly attractive tool as they are translucent, allowing for in vivo measurement of cardiac activity. A study by Kossack et al. (2017) investigated the use of larval zebrafish as a model for HF using chronic sympathetic stimulation with isoproterenol. Differences in the genetic response were found in comparison to mammalian models, which were suggested to be due to different mechanisms of isoproterenol induced cardiac dysfunction. This study aims to establish a model of chronic tachypacing-induced HF in larval zebrafish using optogenetics to potentially overcome these limitations. The effects of chronic optogenetic tachypacing of larval zebrafish hearts between 2 to 6 days post fertilization (dpf) with two opsins (channelrhodopsin-2, ChR2, and anion channelrhodopsin-1, ACR1) will be compared. Morphological, functional, and genetic changes associated with cardiac remodelling during HF will be assessed. Cardiac morphology and function will be measured from in vivo brightfield microscopic recordings. Genetic responses will be evaluated by expression changes quantified using qRT-PCR. Thus far, it has been shown that chronic tachypacing with ChR2 results in cardiac development defects, while pacing with ACR1 results in morphological changes reminiscent of HR. Continuing studies will explore associated changes in cardiac function and genetics.

Assessment of Cardiac Electrical Remodeling in a Rat Model of Severe Pulmonary Arterial Hypertension

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Background: Pulmonary arterial hypertension (PAH) is a progressive incurable disease with unclear etiology. Primary cause of death in PAH patients is right (-sided) heart failure, occurring as a direct consequence of increased right ventricular (RV) afterload. Importantly, around 25% of these deaths have been linked to cardiac arrhythmias. However, mechanisms underlying arrhythmia susceptibility in patients with elevated pulmonary arterial and RV pressure remains unclear. Early studies provided evidence of RV ischemia in PAH patients as well as in animal models of PAH. Importantly, ischemia is a known pro-arrhythmic factor in the left ventricle; therefore, we hypothesize that RV ischemia may contribute to arrhythmia susceptibility in PAH. Methods and Results: Male and female Fischer CDF rats were treated with monocrotaline (MCT; 60 mg/kg, s.c.) to induce PAH or treated with vehicle as controls. Echocardiography was performed at 4 weeks post-MCT injection to assess disease progression. Electrocardiogram was recorded in anesthetized rats during echocardiography to study electrical abnormality and assess spontaneous arrhythmias during progressive PAH. At 4 weeks, hearts were collected, perfused in Langendorff mode, and electrical remodeling was assessed by optical mapping. The hearts were paced electrically with increasing frequency or treated with dobutamine (beta-1 adrenergic receptor agonist), and electrophysiological parameters were recorded. MCT treatment led to increase in RV systolic pressures and RV hypertrophy, compared to controls. Conclusion: We have established a model of severe PAH and acquired electrophysiological data to evaluate electrical remodeling in response to PAH. Electrophysiological data is currently being analyzed and will be completed before presentation.

Functional and Immuno-Characterization, and Distribution of Cardiac Stem Cell Antigen-1 or c-kit Expressing Cells

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Background: In the heart, stem cell antigen-1 (Sca-1) and c-kit were originally suggested to be markers cardiomyocyte precursor cells; however, a growing body of evidence now suggests that the majority (>90%) of Sca-1+ or c-kit+ cells in the heart express endothelial cell markers. In this project, we investigated endothelial cell characteristics of cardiac Sca-1+ or c-kit+ cells and assessed the spatial distribution of these cells in male and female rat hearts. Methods: Adult male and female Sprague Dawley (SD) and Fischer CDF rat hearts were excised and digested to obtain single-cell suspension. Cells were then stained with stem cell (Sca-1 and c-kit), and endothelial cell (CD31) markers, and analyzed using flow cytometry. To study the changes during pathological cardiac remodelling, flow cytometry analysis of the Fischer CDF rat hearts was performed at 4 weeks after monocrotaline injection (MCT; 60 mg/kg, sc). Results: Most Sca-1+ or c-kit+ cells in the heart are CD31+, demonstrate lectin binding and uptake acetylated low-density lipoprotein. The right ventricle (RV) of the heart has more c-kit+CD31+ and Sca-1+CD31+ cells than the left ventricle (LV). In normal healthy rats, no significant difference was observed in abundance of c-kit+CD31+ or Sca1+CD31+ cells in the RV of male and female rats. MCT treatment led to increase in RV systolic pressure and RV hypertrophy that was associated with marked reduction in abundance of c-kit+CD31+ or Sca-1+CD31+ cells in the RV. Conclusions: The c-kit or Sca-1 expressing cells in the heart may be resident endothelial progenitor-like cells. These cells are highly abundant in the RV that was reduced during pathological RV remodelling.

Role of Microtubules in Atrial Mechano-Arrhythmogenesis

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Background: In the heart, electrical excitation causes mechanical contraction, while feedback of the heart's mechanical state alters its electrical activity. With mechanical overload, this feedback can result in mechano-arrhythmogenesis (MA). In the ventricles, MA is driven by microtubule (MT) density/detyrosination in a transient receptor potential ankyrin 1 channel (TRPA1) dependent manner. In the atria, clinical evidence indicates arrhythmias are associated with increased TRP channels and in pressure overload with MT densification. Objectives: Determine if atrial MA is increased by MT density/detyrosination in a TRPA1-dependent manner. Methods: Rabbit isolated atrial myocytes underwent transient stretch with carbon fibres. MA incidence was assessed after pharmacologic manipulation of MT (densification/detyronsination by paclitaxel or reduced detyronsination by parthenolide) or TRPA1 (block by HC-030031). Contractile properties (rate and extent of contraction) were evaluated with sarcomere tracking. MT density/detyronsination was also measured in right atrial samples from cardiac surgery patients with normal or elevated right ventricle systolic pressures by western blot. Results: Increasing MT density/detyrosination with paclitaxel increases MA incidence above a threshold level of stretch ($p=0.0183$). Co-incubation of paclitaxel with parthenolide or HC-030031 mitigates the increase in MA ($p>0.999$ and $p=0.5640$, respectively). Myocyte contractile properties were improved by parthenolide. Patient pathologies may alter MT density/detyrosination. Conclusions: MT density/detyrosination may play a critical role in atrial MA, through activation of mechano-sensitive TRPA1. Parthenolide blocking detyrosination may decrease cytoskeletal linkages in atrial myocytes, thereby improving contraction. Future work will determine if pressure overload in patients is associated with MT density/detyrosination and leads to an increase atrial MA

Effects of an Acute Increase in Hemodynamic Load on Cardiac Function During Cardiac Development

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Cardiac function adapts on a beat-by-beat basis through extrinsic and intrinsic mechanisms. Stretch is a critical intrinsic modulator of cardiac function, as demonstrated by an increase in heart rate (HR) and stroke volume (SV) with an increase in venous return. In the developing heart, effects of acute changes in hemodynamic load on cardiac function are not well established but may be critical to the pre-neuronal control of cardiac excitation and contraction. Effects of an acute increase in hemodynamic load on cardiac function during development were investigated in vivo using 2-14 dpf zebrafish larvae. One advantage of this experimental model is that transparent larvae allow for measurement of cardiac function in intact animals. We have developed a micro-cannulation technique for in vivo infusion of solution directly into the venous system of zebrafish larvae with a flowcontrolled pressurisation system, allowing for acute changes of hemodynamic load. Cardiac volume and contraction are monitored by imaging a genetically-expressed cardiac-specific marker (GFP) and membrane potential and intracellular calcium using functional fluorescent proteins. The role of the autonomic nervous system (ANS) and stretch-activated channels (SAC) in observed responses are assessed by pharmacological and micro-surgical interventions. Results have shown that an acute increase in hemodynamic load at 2dpf causes a decrease in HR, which switches to an increase at 6dpf and is further increased at 14dpf. Interventions have indicated that effects on cardiac function are mediated by both intrinsic (SAC) and extrinsic (ANS) mechanisms. Our studies reveal factors involved in regulation of cardiac function in response to acute changes in hemodynamic load during development. This is essential for understanding cardiac activity in the developing heart and may help better understand disturbances that occur with congenital heart disease

Applying and expanding the scope of ^{19}F-NMR spectroscopy to probe peptide-membrane interactions

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Our understanding of G-protein coupled receptor (GPCR) interactions with peptide ligands has greatly expanded within the past few years. One important aspect of the peptide-GPCR binding process is hypothesized to be the role of the cell membrane as an intermediary to facilitate recognition and binding events. In the case of the apelin receptor, a class A GPCR, both of its endogenous peptide ligands - apelin and apela - have been shown to interact with a variety of membrane mimetics. The structural changes noted upon membrane interaction are hypothesized to be important precursors to apelin receptor binding. In order to test this hypothesis in physiological conditions, we are developing 19F nuclear magnetic resonance (NMR) spectroscopy approaches to probe peptide-membrane and, ultimately, peptide-receptor interactions. Initially, using solution-state NMR spectroscopy techniques, we have demonstrated interactions of fluorinated apelin analogues with membrane-mimetic bicelles. Through synthetic incorporation of 19F at specific positions along apelin, we show that the peptide-membrane interaction is specific to certain regions of apelin. Concurrently, we are exploring the potential of a designed synthetic trifluoromethyl-containing probe molecule to bind specifically to Histagged proteins. We demonstrate that this probe binds at high affinity to His-tagged proteins with observable changes. This opens the potential to take direct advantage of His-tags to carry out 19F NMR studies of membrane receptors and peptide ligands, instead of the typical requirement for chemical derivatization or biosynthetic 19F incorporation. Moving forward, we intend to apply both strategies to incorporate 19F to detangle peptide-membrane and peptide-receptor interactions in cellular context

Role of Microtubules and Transient Receptor Potential Ankyrin 1 (TRPA1) in Mechanically-Induced Arrhythmias

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Background: Disturbances of the heart's electrical activity ('arrhythmias') are thought to be driven in part by cardiac mechano-sensitivity. Clinical evidence shows that in cardiac disease, acute fluctuations in the heart's mechanical load alone is a strong predictor of arrhythmia incidence. Yet, the mechanisms underlying mechanically-induced arrhythmias (MIA) are poorly understood. Recent studies in rabbit left ventricular (LV) myocytes suggest that MIA are dependent on microtubules and the mechano-sensitive transient receptor potential ankyrin 1 channel (TRPA1). Objective: Determine the importance of microtubules and TRPA1 for MIA in the whole heart. Methods: Hearts isolated from rabbits (2kg, NZW) were instrumented with surface electrodes to monitor electrical activity and an intraventricular balloon to apply transient changes in LV volume and induce MIA. MIA incidence vs volume was fit with a Hill equation to calculate the volume that generated halfmaximal MIA incidence (V50). Paclitaxel (5μM) was applied to increase microtubule density and detyrosination, or with colchicine (10μM) to reduce density, parthenolide (10μM) to reduce detyrosination, or HC-030031 (10μM) to block TRPA1. Microtubule density was assessed in isolated LV myocytes by immunofluorescence. Results: Paclitaxel caused an increase in V50 compared to control, which was prevented by parthenolide or HC-030031. There was still a decrease in V50 after co-treatment with colchicine, however there was no decrease with colchicine alone. Microtubule density was increased by paclitaxel and decreased by colchicine compared to control, while colchicine prevented the paclitaxel-induced density increase. Conclusion: An increase in microtubule detyrosination increases MIA in the whole heart through a TRPA1-dependent mechanism.

Continuous Subzero-Balance Ultrafiltration Extracts Twenty-Two Inflammatory Mediators

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Background: Cardiopulmonary bypass (CPB) is associated with systemic inflammation (alternate complement pathway activation of C3a and C5a) in pediatric patients undergoing cardiac surgery. Intra-operative ultrafiltration has been hypothesized to remove inflammatory factors(<66 kDa) from the patient's circulation during CPB. This study aimed to identify a comprehensive collection of inflammatory mediators extracted by continuous subzero-balance ultrafiltration (SBUF). Methods: Pediatric patients undergoing cardiac surgery with CPB and SBUF were enrolled in a prospective observational cohort study. At the end of CPB, arterial blood(End-CPB Plasma) and ultrafiltration effluent samples (End-CPB Effluent) were analyzed with Luminex®to yield the concentrations of 39 inflammatory mediators from the complement, cytokine,chemokine, leukocyte adhesion and pulmonary vasoconstriction pathways. Sieving coefficients ([End-CPB Effluent Mediator]/[End-CPB Plasma Mediator] x 100%) were calculated to quantify the degree of mediator extraction. Results presented as median (IQR). Results: Twenty patients were enrolled with an age of 4.0 (0.2-12.0) months, weight of 5.2(3.4-8.1) kg and a spectrum of congenital heart diseases. Twenty-two mediators were extracted by SBUF with a range of Sieving coefficients (0.1%-1019%). Sieving coefficients for C3a and C5a were 1019% and 46% respectively. Mediator extraction by SBUF was significantly associated with molecular mass <66kDa (Chi2 with Yates' correction = 16.0, $p < 0.0001$). Conclusion: SBUF extracts twenty-two circulating inflammatory mediators from the complement, cytokine, chemokine, and leukocyte adhesion pathways throughout pediatric cardiac surgery with CPB. Further translational investigations are required and ongoing, to assess the clinical impact of this potentially therapeutic immunomodulatory mechanism.

Atrial Natriuretic Peptide promotes VCS cell differentiation by promoting lipid accumulation and targeting cellular metabolic pathways

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Atrial Natriuretic Peptide (ANP) is an important regulator of cardiovascular homeostasis. Mice lacking ANP high-affinity receptor (NPRA) revealed a hypoplastic phenotype in the ventricular conduction system (VCS) formation. However, the mechanism(s) underlying the effects ofANP/NPRA signaling in VCS development are not known. The role of metabolic adaptations in embryonic development is well documented. We hypothesize that ANP regulates metabolic changes in a subset of embryonic ventricular cells to promote VCS cell formation. In this study, cells were isolated from E11.5 cardiac ventricles which are yet to develop a fully functional VCS and cultured with or without exogenous ANP treatment. The expression of conduction cell marker Cx40 was analyzed by immunostaining and in-cell westerns. E11.5 cells revealed a significant increase in lipid accumulation and higher expression of 0x40 in response to the ANP treatment. Notably, the exogenous fatty acid treatment also promoted Cx40 expression in E11.5 cells. Seahorse assay confirmed significant increases in glycolytic rate (ECAR) and mitochondrial oxygen consumption rate (OCR) in cells treated with ANP. These results further indicated that ANP treatment promotes a switch in energy metabolism from an anaerobic to a more aerobic state in embryonic ventricular cells. RT-qPCR analyses showed significant increases in PPARy, PDK4 and LDHA gene expression and reductions in the expression of C/EBPa, PGC1a and B in ANP treated cultures. Collectively, these results suggest ANP mediated metabolic changes play a critical role in VCS cell differentiation. Future studies will focus on the role of PPARy, PDK4 and LDHA in VCS cell development.

Reproductive Injustice in Canadian Prisons for Women

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Introduction: Women are the fastest growing population in prison in Canada, with significant consequences for reproductive health. Almost 50% of incarcerated women are Indigenous; the prison system threatens public commitments to reconciliation. Pregnancy while incarcerated is associated with inadequate prenatal care, prematurity, and low birth weight; incarceration disrupts fertility and impedes parenting. The Correctional Services Canada al Mother Child Program aims to mitigate harms of separating mothers from babies. The program has never been subjected to independent study. The purpose of this study is to examine experiences of the program. Methods: Qualitative case study design and thematic analysis informed by abolition and reproductive justice. Data sources include quantitative participation data; public documents; and semi-structured interviews with nine mothers and 14 advocacy staff of Elizabeth Fry Societies. Results: Most lived experience respondents could not participate in the Mother Child Program due to eligibility criteria, or they chose alternatives to protect their children. Restricted access is disproportionately borne by Indigenous mothers. Respondents experienced debilitating trauma, denial of health services and punitive responses to poor mental health. They were subject to surveillance and deprecation of their parenting. Through personal agency and peer solidarity, they resisted institutional restrictions on access to care and to their children. Conclusion: Far from a panacea for mother-baby connection, this study demonstrates the Mother Child Program to inequitably available, qualifying is uncertain; continuous participation is precarious; and prisons are perceived as unsafe for babies. Further, addressing the disproportionate incarceration of Indigenous women is imperative for reconciliation and health equity.

Genetics

Mllt11 Regulates Migration and Neurite Outgrowth Of Cortical Projection Neurons During Development

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Mammalian cortical histogenesis relies heavily on cell-type specific gene expression programs and topographic targeting of axons to specific brain regions. The mechanisms that underlie this process are still poorly understood. Recent findings from our group have revealed a role for a novel, vertebrate-specific protein called Mllt11 in the regulation of the growth and stabilization of axonal projections within the cerebrum. It is expressed only in maturing post-mitotic neurons and its loss abrogates intrahemispheric axonal targeting. Interestingly, we also noted dysregulation of layer-specific projection neuron transcription factor expression in Mlltt11 mutant fetuses and neonates . Lastly, molecular and cellular analyses indicate a role for Mllt11 in regulating the stability of the axonal cytoskeleton during cortical development. Our study sheds light on the mechanism of how projection neurons connect to their targets and stabilize their transcriptional identity programs during brain maturation.

Clinically identified pathogenic variants disrupt the enzymatic activity of the epigenetic regulator, KDM6B, resulting in a novel neurodevelopmental disorder

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Development of the brain requires precise regulation of gene expression. Epigenetics plays a critical role in gene regulation, and disruption of epigenetic regulators frequently results in neurodevelopmental disorders (NDD), such as autism spectrum disorder (ASD) and Intellectual Disability (ID). KDM6B is a histone demethylase that specifically removes methyl groups from trimethylated histone H3 lysine 27 (H3K27me3), a well-established epigenetic modification for gene silencing. Through routine clinical whole genome sequencing diagnostics, *KDM6B* was identified for having a high prevalence of *de novo* truncating and missense variants in individuals presenting with NDDs. Here, we describe the clinical and molecular spectrum of a large cohort of 63 new and 12 published cases of individuals with *de novo KDM6B* mutations. Pathogenic variants of *KDM6B* result in a dominant NDD with varying phenotypes and severity including developmental delay, ID, ASD, dysmorphism, various neurological and gastrointestinal problems, and congenital anomalies. To understand the basic function of KDM6B in the nervous system we performed loss-of-function studies in flies, which demonstrated a role for the *Drosophila* KDM6B ortholog, Utx, in memory. *De novo KDM6B* missense variants found in our cohort were assessed using known 3D protein structures and *Drosophila* gain-of-function assays, which validated the predicted damaging effect of 11 unique missense variants on the enzymatic activity of KDM6B. Our results define the clinical spectrum of a novel *KDM6B*-related NDD and provide the first functional insight into clinically identified *KDM6B* variants. These studies provide a major advance towards understanding the molecular mechanisms underlying KDM6B-related NDDs.

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Beyond These Four Walls: Exploring The Experiences Of Mothers Caring For Babies Going Through Withdrawal

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Background: Neonatal Abstinence Syndrome (NAS) is a condition where an infant becomes dependent on an opioid that was exposed to them during pregnancy. There has been a significant increase in the number of babies diagnosed with NAS in Nova Scotia over the last decade. With this increase, nurses and the health care system are tasked with unique challenges to address this growing population. Current guidelines used to assess babies who are withdrawing are outdated. A new model of NAS care is being implemented at IWK Health – designed to improve the treatment and experience of babies, with the theme of mothers being the primary “treatment” for care. Although recent research has informed evidence-based practices in caring for babies going through the withdrawal process, there has been a lack of discussion on the experiences of mothers involved in this new model of care. Purpose: The primary aim of the proposed qualitative study is to explore the lived experience of mothers caring for their infants diagnosed with NAS to gain an understanding of their unique care needs. Methods: Conversational interviews will be completed with mothers who gave birth to an infant diagnosed with NAS. Data analysis will be completed using Max van Manen’s philosophical tenets of phenomenology. Implications: Findings will be translated to frontline nurses to better support and meet the unique needs of mothers, empowering their ability to care for their infants. Further, the findings will enhance the implementation and sustainability of the ESC model of care at IWK Health.

Changes in publicly funded prescription drugs dispensed to community dwelling New Brunswick seniors following hospital discharge for myocardial infarction between 2008 and 2017.

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Background: Secondary prevention after myocardial infarction (MI) requires long-term guideline-directed medical therapy including antiplatelets (clopidogrel), antihypertensives, lipid lowering agents, agents acting on the renin-angiotensin-aldosterone system (RAAS). Despite large increases in the dispensing of β-blockers, statins, and RAAS agents to elderly survivors of MI in Canada during the early 2000s, studies have shown that a significant proportion are not receiving the recommended therapies. Additionally, no studies have examined drug dispensations after MI in Canada since the approval of clopidogrel in 2011. Objective: To characterize the annual proportion of seniors (66 years and older) in New Brunswick (NB) discharged home following a hospitalization for MI who are dispensed including a β-blocker, statin, RAAS agent and clopidogrel within 30-days post-discharge between 2008 and 2017. Methods: A dynamic retrospective cohort will be assembled using administrative health claims data and include community-dwelling NB residents aged 66 years and older, who were covered by the NB Prescription Drug Program, and were discharged from hospital with MI between January 1, 2008, and December 31st, 2017. The proportion of patients who receive dispensations from community pharmacies for each drug class within 30-days of hospital discharge will be calculated for each calendar year. Data will be stratified by patient demographic and clinical characteristics. Expected Contributions: Results from this study will inform clinicians, government officials, and administrators at the health authorities on the quality of post-MI care provided in NB and how this has changed over time between 2008 and 2017. This study will assist in monitoring the community-based use of recommended interventions following an MI

SARS-CoV-2 Membrane and Envelope proteins inhibit Spike-mediated activation of ATF6

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Coronaviruses assemble at the ER-Golgi intermediate compartment (ERGIC). As its name suggests, the ERGIC participates in bidirectional vesicular traffic between the ER and Golgi. It is also a central hub for signaling pathways that traverse the secretory pathway and plays important roles in stress signaling, cholesterol regulation, interferon production, and inflammasome assembly. However, it is unknown how coronavirus assembly at the ERGIC affects these signaling pathways. Investigating the structural proteins of SARS-CoV-2, we found Spike selectively activates ATF6, an ER resident stress-sensing protein. However, the SARS-CoV2 membrane (M) and envelope (E) proteins both inhibit Spike-mediated ATF6 activation. We observed ATF6 is not activated during human coronavirus hCoV-OC43 infection, suggesting that M and/or E may prevent Spike-mediated ATF6 activation during infection. Chemical activation of ATF6 with AA147 reduced replication of human coronaviruses hCoV-OC43 and hCoV-229E. By studying interactions between CoV structural proteins and host signaling proteins at the ERGIC, we hope to better understand how CoV replication impacts host cell physiology and responses to infection. Many current SARS-CoV-2 vaccines direct Spike expression in the absence of other structural proteins like E and M. Based on our findings, we expect that vaccine-mediated Spike expression may activate ATF6, which might be important for generating robust antiviral immune responses. As next generation vaccines incorporate other CoV structural proteins, it will be important to determine how they affect Spike antigenicity, which could be influenced by multiple host signaling pathways that traverse the ERGIC

Investigating the roles of unfolded protein response transcription factors in influenza A virus infection

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All enveloped viruses encode transmembrane proteins that are synthesized, folded and processed at the endoplasmic reticulum (ER). The capacity of the ER to support these activities is tightly regulated by the unfolded protein response (UPR). The UPR is governed by three ER-localized sensor proteins (ATF6, IRE1 and PERK) that sense the accumulation of unfolded proteins in the ER and initiate synthesis of transcription factors (ATF6-N, XBP1s and ATF4, respectively) that coordinate a gene expression program that increases ER capacity to restore proteostasis. Influenza A virus (IAV) encodes transmembrane glycoproteins that are folded and processed in the ER. Studies to date suggest a complex relationship between IAV and the UPR, whereby viral replication can be arrested by UPR-inducing drugs, but IRE1 activity is required to support efficient viral replication. Overall, interactions between IAV and the UPR remain poorly characterized. My goal is to advance understanding of how UPR pathway components affect IAV infection and to elucidate mechanisms of viral control of the UPR. To provide focus for my preliminary studies, I investigated the effects of each UPR transcription factor on IAV replication. Lung epithelial A549 cells were transduced with lentiviral constructs encoding ATF6-N, XBP1s, ATF4 or an empty vector control, followed by selection of stable cell lines with puromycin. These cells were infected with IAV for 24 hours, at which point cell supernatants were collected for titering progeny virions. Consistent with previous observations of antiviral effects of strong UPR-inducing drugs, we observed that ectopic expression of each UPR transcription factor reduced the production of infectious virions, with XBP1s providing the strongest antiviral effect of an approximately 10-fold reduction. In ongoing studies, I am investigating the precise antiviral mechanism of action of these UPR transcription factors, with a special focus on XBP1s, to determine the stage of viral replication that is disrupted and to pinpoint host cell antiviral processes.

Influenza A Virus Host Shutoff Utilizes Interplay Between NS1 and PA-X

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Influenza A viruses (IAV) encode two host shutoff factors: polymerase acidic X (PA-X) and non-structural protein 1 (NS1). PA-X is an endonuclease that directly targets spliced host transcripts while NS1 interferes with maturation and/or nuclear export of messenger RNAs (mRNAs) through interaction with key host proteins. IAV host shutoff depletes cytoplasmic mRNA pools, which in turn results in nuclear accumulation of poly(A) binding protein (PABP) in infected cells. We examined PABP and poly(A) RNA distribution in cells infected with the wild-type (WT) IAV, PA-X deficient mutant (fs), or a panel of NS1 mutants. We confirmed that fs mutant did not cause nuclear accumulation of PABP, however many NS1 mutants had the same defect. To investigate which RNAs were being retained and hyperadenylated in the nucleus of infected cells, we used single molecule fluorescence in situ hybridization (FISH). This analysis revealed that GAPDH (abundant host mRNA) levels were decreased in the cytoplasm but not in the nucleus, while MALAT1 (abundant nuclear long non-coding RNA lacking poly(A) tail) was depleted. These dramatic depletion of MALAT1 was observed in WT, fs, and most NS1 mutant virus infected cells, but was not observed in cells infected with NS1 C-terminal deletion mutant virus. Our data reveals a novel NS1-dependent mechanism for the depletion of certain nuclear host RNAs. These experiments also suggest that contributions of PA-X and NS1 to host shutoff are not simply additive and indicate a functional link between NS1 and PA-X host shutoff activity.

Coronaviruses HCoV-OC43 and SARS-CoV2 limit stress granule formation to promote virus replication

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Stress granules (SGs) are cytoplasmic condensates that often form as part of the cellular antiviral response. Despite growing interest in SGs and other biological condensates, the role of SG formation during coronavirus infection is unclear. Herein, we analyzed SG formation during infection of human common cold coronavirus OC43 and highly pathogenic severe acute respiratory syndrome coronavirus 2 (SARS-CoV2). We did not observe SG induction in infected cells and both viruses inhibited eukaryotic translation initiation factor 2α (eIF2α) phosphorylation and SG formation induced by exogenous stress (e.g. sodium arsenite treatment). Furthermore, in SARS-CoV2 infected cells we observed a sharp decrease in the levels of G3BP1 protein which is often referred to as a master regulator of SG formation. Ectopic overexpression of nucleocapsid (N) and non-structural protein 1 (Nsp1) from both OC43 and SARS-CoV-2 inhibited SG formation. The Nsp1 proteins of both viruses inhibited arsenite-induced eIF2α phosphorylation, and the Nsp1 of SARS-CoV2 alone was sufficient to decrease G3BP1 levels. This phenotype was dependent on Nsp1-mediated depletion of cytoplasmic mRNAs and was associated with nuclear retention of TIAR. To test the role of G3BP1 in coronavirus replication, we infected cells overexpressing EGFP-tagged G3BP1 with OC43 and observed a significant decrease in infection compared to control cells expressing EGFP. The antiviral role of G3BP1 and the existence of multiple SG suppression mechanisms that are conserved between the common cold OC43 and the pandemic SARSCoV2 suggests that SG formation may represent an important antiviral host defense that coronaviruses target to ensure efficient replication.

BETA-CARYOPHYLLENE AS A NOVEL ADJUNCT THERAPY FOR THE TREATMENT OF URINARY TRACT INFECTIONS

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Introduction: Urinary tract infections (UTIs) are a very common type of infection. Symptoms include urinary frequency, urgency and painful urination. While UTIs are manageable with antibiotics, painful symptoms may persist. Beta-caryophyllene (beta-C) is a terpene found in several plants, including cloves, black pepper and Cannabis sativa. It has local anesthetic and anti-inflammatory activity, mediated through cannabinoid receptor 2. In addition, anti-bacterial activities have been described. We hypothesized that beta-C may be a potential adjunct therapy for UTI management. Methods: UTI was induced in a murine model via transurethral inoculation of uropathogenic Escherichia coli. Animals received intraperitoneal treatment with beta-C (100mg/kg), or an antibiotic comparator following induction (six hour model) or after six hours (24 hour model). Animals were evaluated for changes in bacterial burden, behavioral parameters, and inflammatory responses after six or 24 hours. Results: A localized infection results from UTI induction and persists from six to 24 hours post induction with limited ascension into the kidneys and no systemic infection. After 24 hours, betaC demonstrated significant anti-bacterial activity in both the urine and bladder tissues. Beta-C significantly reduced the response to evoked pain 24 hours post induction. Non-evoked pain responses were also significantly improved over the course of the infection. UTI induction resulted in a significant increase in adherent leukocytes (24 hour timepoint) and impaired microcirculation within the bladder, which were both restored with beta-C treatment. Conclusion: Beta-C modulates the bacterial burden, pain responses and inflammation levels in murine UTIs, suggesting possible utility as an adjunct therapy for UTI.

Stressed out: Investigating how a herpesvirus E3 ubiquitin ligase modulates the unfolded protein response.

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The unfolded protein response (UPR) senses the accumulation of misfolded proteins in the endoplasmic reticulum (ER) and initiates transcriptional responses to support ER proteostasis. It is supported by three stress-sensing proteins, PERK, IRE1 and ATF6. Kaposi's sarcomaassociated herpesvirus (KSHV) usurps the UPR to reactivate from latency, whereby IRE1 activation causes synthesis of the XBP1s transcription factor that transactivates the promoter the viral lytic switch gene RTA. We discovered that following reactivation from latency, progression through the lytic replication cycle features UPR sensor activation coupled with inhibition of downstream transcriptional responses; this UPR inhibition is required for generation of viral progeny. However, the viral gene products that regulate the UPR remain unknown. I discovered that steady-state levels of PERK protein diminish during KSHV lytic replication. KSHV encodes two E3 ubiquitin ligases, K3 and K5, that interfere with immune responses by directing the ubiquitination of a semi-overlapping set of host immune synapse proteins that are endocytosed and traffic to the lysosome for degradation. I have shown that K3 is sufficient to downregulate PERK, and preliminary studies show that hydroxychloroquine, an inhibitor of lysosomal acidification, prevents PERK degradation in K3-expressing cells. In ongoing studies, I am investigating the molecular determinants of K3-mediated PERK downregulation.

Activation Of Cannabinoid Type Ii Receptor Attenuates Systemic Inflammation Secondary To Acute Lung Injury

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The COVID-19 pandemic has emphasized the danger of immune dysregulation in severe cases of lung infection. These cases are characterized by life-threatening complications including pneumonia, acute respiratory distress syndrome, and multi organ failure. Elevated pro-inflammatory cytokine levels are described as contributing to disease progression. The cannabinoid type 2 receptor (CB2R) is a G protein-coupled receptor with high levels of expression on immune cells. Activation of CB2R exerts immunomodulatory effects in numerous pre-clinical models, including protective effects in lung inflammation. Thus, we hypothesized that experimental CB2R activation could reduce systemic inflammation in a murine model of acute lung injury (ALI). To test this hypothesis, 12-week-old C57BL/6 mice were challenged with intranasal Pseudomonas aeruginosa, followed by treatment with HU-308, a selective activator of CB2R. At 6 hours, tissue samples were collected to assess lung histopathology and plasma cytokine release. In separate groups, intravital microscopy (IVM) of the intestinal or pulmonary microcirculation, respectively, was performed to quantify leukocyte activation and capillary perfusion. Untreated LPS mice displayed marked increases in lung histopathology score, plasma cytokine levels, intestinal submucosal leukocyte adhesion, and reduction in submucosal functional capillary density. HU-308 treatment significantly reduced leukocyte adhesion in submucosal collecting venules, and modestly but significantly reduced lung histopathology score. In summary, treatment with selective activator of CB2R, HU-308, reduced pulmonary and systemic inflammatory responses induced by intranasal LPS administration.

MAST CELL DEGRANULATION-ASSOCIATED PRODUCTS MODULATE PROGRESSION AND RESOLUTION OF SKIN FIBROSIS

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Fibrosis is a feature of many chronic inflammatory diseases. Mast cells (MC) are resident immune effector cells in most tissues and increase in density during fibrosis. MC involvement in fibrosis progression has been well-studied, but their roles in resolving fibrosis remain unelucidated. Our research aims to determine MC roles and approaches to exploit mast cell activities to promote resolution of fibrotic injury.

Bleomycin (Blm) or saline (control) was injected locally for up to 21 days to induce skin fibrosis in MC-deficient and wild-type (WT) mice, and tissues sampled during fibrosis progression and a subsequent 21day resolution phase. Ketotifen was administered in drinking water to impair MC degranulation. Skin tissues were examined for selected gene expression and for changes in histology. Changes in dermal thickness (ΔDT) were used as a key indicator of fibrotic change.

Blm-treated skin showed substantial ΔDT which was reduced in MC-deficient mice. MC density increased with Blm treatment, further elevating during resolution. Significant reductions in ΔDT towards baseline were seen only in WT mice during resolution. Ketotifen treatment during Blm reduced ΔDT at the peak of fibrosis, however, continuous ketotifen inhibited resolution. Gene expression of remodeling-associated enzymes was modified during fibrosis.

MCs have important roles in fibrotic progression and resolution in this skin fibrosis model. MC mediators released during degranulation may play key roles in fibrosis resolution and tissue remodelling. Selectively modifying MC activities may provide novel approaches to promote fibrosis resolution.

Recalls of Foods due to Microbiological Contamination Classified by the Canadian Food Inspection Agency, 2000-2017

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It is estimated that four million Canadians experience foodborne illness every year. The mishandling of raw meat is partially to blame, but the greater concern is with contaminated foods that are assumed to be safe. In Canada, the Canadian Food Inspection Agency (CFIA) facilitates the recall of contaminated food products to protect consumers from foodborne illness. Microbiological-contaminated food is responsible for a large amount of these food-related recalls and is a major contributor to the transmission of foodborne illness. While the CFIA documents all food recall events, no study has consolidated microbiological-related food recall data from Canada to examine annual recall trends. We obtained microbiological-related food recall data for the years 2000-2017 from the CFIA to characterize the number recalls and the nature of each event. We classified each recall event by the contaminating pathogen, the degree of risk associated with the contamination, the type of food contaminated, and the recall year. Meat and meat products, followed by nuts/edible seeds and fishery/seafood products were the food products most commonly recalled for microbiological contamination. Additionally, Salmonella spp., Listeria monocytogenes, and E. coli O157:H7 were the three foodborne pathogens responsible for a majority of the microbiological-related food events examined. Major food recalls events were also linked to foodborne outbreaks in Canada to examine recall effectiveness. Trends identified from this study on microbiological-related food recall events in Canada will assist future health risk assessments and implementation processes associated with food recalls.

Mast cells roles in resolution of fibrosis: insights from human cardiac surgical patients

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Introduction: After injury in the heart, improper resolution of inflammation leads to fibrosis and heart failure. Mast cells (MCs) respond to damage via selective production of granule products, lipid mediators and cytokines. IL-33 is increased in the heart after damage and promotes proper healing, and MCs can respond to IL-33. We hypothesized that MC responses will improve resolution of cardiac inflammation with reduced fibrosis, potentially through IL-33 activation.

Methods: Human cord blood-derived MCs (CBMCs) were activated with IL-33. Mediator production and gene expression of analytes was evaluated. Human atrial tissue and plasma samples from cardiac surgical patients were analyzed. MC density was evaluated via toluidine blue staining of tissues and confirmed by droplet digital PCR (ddPCR) quantitation of MC-specific transcripts. Fibrosis was quantified via Sirius red/fast green staining.

Results: IL-33 activated CBMCs produced mediators such as IL-10 ($p = 0.031$, $n = 6$), IL-13 ($p < 0.0001$, $n = 17$) and VEGF-A ($p < 0.0001$, $n = 17$). CBMCs did not degranulate or produce pro-fibrotic mediators TGF-β, PGD2, or Amphiregulin. Atrial samples from cardiac surgical patients with higher MC content had lower collagen content ($p = 0.0073$, $n = 99$), suggesting MCs may reduce fibrosis. Patients with high MC content had improved functional outcomes at post-operative follow-up ($p=0.0007$, n-33), while low MC patients did not ($p=0.074$, $n=49$).

Conclusion: Our findings demonstrate that increased mast cell density is associated with reduced fibrosis and better recovery after tissue injury, potentially involving IL-33 activation.

TOLL-LIKE RECEPTOR 2 SIGNALLING IS ESSENTIAL FOR STEERING PROTECTIVE HOST IMMUNE RESPONSES AND CONTROLLING LONG TERM TISSUE DAMAGE IN CHLAMYDIA REPRODUCTIVE TRACT INFECTION

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Introduction: Chlamydia trachomatis (Ct) is the most common STI and causes serious complications in women such as chronic pelvic pain,Pelvic Inflammatory Disease(PID),ectopic pregnancy and infertility.Toll-Like Receptor 2(TLR2) is a pattern recognition receptor expressed widely on immune cells and non-immune cells. TLR2 binds to Ct and activates innate and adaptive host immune responses. Certain TLR2 polymorphisms have been shown to confer risk to Ct-associated infertility in women.The reported roles of TLR2 in protecting from reproductive tract tissue damage has been conflicting and its functional role in host responses to Ct infection remains an unresolved question. We hypothesized that TLR2 signaling is essential for steering protective immune responses and controlling tissue damage. Methods:To characterize the functional role of TLR2, mice with or without the expression of TLR2, (WT and TLR2KO respectively),were infected with Chlamydia muridarum (Cm),and innate and adaptive immune responses were examined by different immunological assays including ELISAs,flow cytometry,protein array,and ex vivo antigen recall assay. Results: Cysts formed in the oviduct of mice; a characteristic representation of cysts formed in the fallopian tubes of humans were comparable between the strains early on and interestingly the absence of TLR2 resulted in the formation of significantly larger cysts at 70-72 days post infection, indicating an essential role for the protein to protect from long term tubal blockage. TLR2KOs demonstrated divergent macrophage and B cell frequencies,dysregulated local immune responses with attenuated IL-6 response,increased Type 1 and Type 2 responses and longer-term inflammation compared to the WT controls. Strikingly,TLR2KOs had deficient infiltration of T cells into the cysts, characterized by spatial phenotyping.Additionally, TLR2KOs had dampened type 1 and type 2 systemic responses and were especially incapable of producing type 17 response.Type 17 response was recovered when mice were reconstituted with TLR2+/+ bone marrow derived myeloid cells. Significance: These results together show a critical role for TLR2 in steering protective local and systemic immune responses and controlling the development of chronic cysts and could be a potential target for therapeutic interventions.

Mitochondrial damage-associated molecular patterns trigger arginase-dependent lymphocyte immunoregulation

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Tissue damage leads to loss of cellular and mitochondrial membrane integrity and release of damage associated molecular patterns, including those of mitochondrial origin(mitoDAMPs).We investigated the lymphocyte response to mitoDAMPs. Using primary cells from mice and human donors,we found that natural killer (NK) cells and T cells adopt regulatory phenotypes and functions in response to mitoDAMPs. NK cell-mediated cytotoxicity, IFN-y production,T cell proliferation and in vivo anti-viral T cell activation were all interrupted in the presence of mitoDAMPs or mitoDAMP-rich irradiated cells in in vitro and in vivo assays. Mass spectrometry analysis of mitoDAMPs revealed enrichment for arginase and products of its enzymatic activity. Functional validation by arginase inhibition and/or arginine add-back revealed that arginine depletion was responsible for this alteration in immunologic polarity. We conclude that lymphocyte responses to mitoDAMPs reflect a highly conserved mechanism that regulates inflammation in response to tissue injury.

Functional impairment with arthropathy in patients with acromegaly

Chen, Kevin; Wang, Yuqi; Title, Michaela; Steeves, Keillor; Ibrahim, Aisha Y; Van Uum, Stan; Chik, Constance L; Ladouceur, Michel; Imran, Syed Ali

Objective: The aim of this study was to compare the physical function between patients with either acromegaly or nonfunctioning pituitary adenomas (NFA). Methods: Participants (acromegaly: n=100, NFA: n=77) were recruited from Halifax, NS, London, ON, and Edmonton, AB. Potential NFA participants were recruited to have similar age, sex and BMI distribution to the acromegaly sample. Participants completed questionnaires about musculoskeletal disability of the upper extremity (QuickDASH), hips (HOOS-JR), knees (KOOS-JR), and ankles (Quick-FAAM). In addition, level of self-confidence to mai2ntain balance (ABC-6), and number of falls in past 12 months were recorded. Independent samples t-tests (HOOS, KOOS, number of falls) and Mann-Whitney tests (DASH, DASH-Work, DASHInstrument, QuickFAAM, ABC-6) were used to assess statistical significance. Results: Acromegaly patients had significantly higher DASH (Mdn: 18.18 vs 6.82, $p<0.001$), lower functional scores for the hip ($\bar{x}$: 71.86 vs 87.01, $p = 0.022$) and ankle joints (Mdn: 79.69 vs 97.92, $p<0.001$) whereas no difference were found in the knee functional score ($\bar{x}$: 74.27 vs 81.93, $p=0.316$). The acromegaly group experienced more falls in the previous 12 months ($\bar{x}$: 1.35 vs 0.53, $p=0.001$) and lower ABC-6 (Mdn: 67 vs 88, $p<0.001$). Conclusion: Acromegaly patients showed increased functional impairment of their upper extremities, hips, and ankles joints but not for their knee joints. In addition, acromegaly patients had a decreased confidence to maintain balance, and fell more often. The result from this study provides the impetus to further study how the balance mechanisms of acromegaly patients may be impaired.

Patients with acromegaly have regional differences in joint pain.

Chen, Kevin; Title, Michaela; Wang, Yuqi; Steeves, Keillor; Ibrahim, Aisha Y; Van Uum, Stan; Chik, Constance L; Ladouceur, Michel; Imran, Syed Ali

Introduction: The aim of this study was to compare joint pain mapping between patients with acromegaly and controls. Methods: Participants [acromegaly: n=100; non-functioning pituitary adenoma (NFA): n=76] were recruited from neuro-pituitary programs in Halifax, NS; London, ON; and Edmonton, AB. Participants with NFA were recruited for similar age-, sex-, and BMI-distribution between groups. Joint pain was measured using an anchored visual analog scale (0-100 mm). History of joint surgery and pain medication usage were also collected. Joint pain scores (transformed) were analyzed using a group (acromegaly/NFA) x region (axial/appendicular) mixed ANOVA. Posthoc analysis of the interaction effect consisted of pairwise independent and dependent t tests with Bonferroni correction. Significance was set at $p<0.05$. Results: There was a significant interaction effect between group and region on joint pain scores ($p=0.020$). Post-hoc tests indicated that only the acromegaly group had regional differences in joint pain, with significantly higher pain in the axial joints compared to appendicular joints ($p<0.001$). Main effects of group and region were significant, with higher pain scores in the acromegaly group ($p<0.001$) and axial region ($p<0.001$). Furthermore, the acromegaly group had significantly higher pain medication usage ($p=0.033$) and history of joint surgeries ($p=0.002$). Conclusion: Patients with acromegaly have higher joint pain and greater regional differences in joint pain than patients with NFA. Axial joints are associated with greater pain than appendicular joints in acromegaly. This greater level of pain despite higher usage of pain medication and history of joint surgeries stresses the urgency in developing effective treatments for acromegalic arthropathy.

Optogenetic Suppression of Drug-induced Early After depolarisations in the Zebrafish Heart

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Early after-depolarisations (EADs) are electrical disturbances of cardiomyocytes that interrupt the repolarisation phase of the cardiac action potential (AP) and can lead to premature excitation and sustained arrhythmias. Optogenetics has the potential to prevent EADs by using genetically-expressed light-activated ion channels to aid in AP repolarisation. Our goal was to investigate the use of optogenetics to modulate membrane potential (Vm) of ventricular cardiomyocytes for the suppression of EADs in the whole zebrafish heart. Hearts were isolated from adult zebrafish with cardiac-specific expression of the cation-nonselective light-activated channel channelrhodopsin2 (ChR2) or anion-selective channelrhodopsin-1 (ACR1). ChR2 or ACR1 were activated by blue (470nm) or green (530nm) light of varying intensity (0.02-0.167mW/mm2) focused on the ventricle with a fibre-optic cannula. Vm and AP characteristics were measured by intracellular microelectrode recordings in the illuminated region. EADs were induced by pharmacological activation of L-type calcium channels and block of rapid delayed rectifier potassium channels. It was found that activation of ACR1 caused a shortening of the AP (-27±6%; p=0.009), while activation of ChR2 resulted in no change (-6±3%; p=0.106). Activation of ACR1 or ChR2 caused a similar change of resting Vm (+26±6 vs +21±8%, with the greatest light intensity; p=0.606), rate of AP upstroke (-40±10 vs -32±12%; p=0.623), and AP amplitude (-29±7 vs -24±9 %; p=0.666). AP shortening with ACR1 enabled suppression of the drug-induced EADs. Overall, these results suggest that ACR1 may be a useful means to prevent arrhythmias in the whole heart, warranting further exploration of its utility as an anti-arrhythmic tool

Development and characterization of recombinant hybrid spider silks

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Spider silks are natural protein-based biomaterials secreted by spiders for purposes such as web construction, locomotion, wrapping of prey and protection of eggs. They are renowned for their mechanical properties and hold great promise for applications ranging from highperformance textiles to the regenerative medicine. This study focuses on the development and comparative characterization of hybrid silk fibres made by two different strategies: mixing aciniform and pyriform silk proteins prior to spinning (mixed fibres) and using a fused protein containing modules from aciniform and pyriform silks (fused fibres). Each silk on its own has distinctive mechanical behaviour and physicochemical properties, with materials produced using combinations of these silks currently unstudied. Recombinant aciniform, pyriform, and fused silk proteins were expressed in Escherichia coli, with downstream purification achieved by Ni2+-NTA affinity chromatography. The mixture of aciniform and pyriform proteins, and the fused protein showed alpha helicity in both an aqueous buffer and in fluorinated acid- and alcohol-based dope solution, as observed by far-UV circular dichroism spectroscopy. Building on methods previously introduced in our lab, wet-spinning was used to spin both mixed and fused fibres. Mixed fibres exhibited a larger diameter and higher strength than fused fibres. In contrast, fused fibres showed relatively smaller diameters and higher extensibility. Fibre-state secondary structuring was evaluated by Fourier transform infrared spectromicroscopy, with differences in proportions of a-helix, b-sheet, and other structures being observed from one type of fibre to another. These structural differences varied as a function of post-stretching conditions and are directly related back to mechanical behaviour measured through tensile testing. Through the investigation and characterization of structural and mechanical properties of mixed and fused aciniform-pyriform silk materials, their suitability and tunability for disparate applications will be determined.

Investigating the mechanism of rhodoquinone biosynthesis

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The lipophilic electron-transport cofactor rhodoquinone (RQ) plays an essential role in the bioenergetics of a variety of bacteria and selected eukaryotic organisms that survive in a low oxygen environment. RQ allows the electron transport chain to function with fumarate as a final electron acceptor instead of oxygen. Rhodoquinone biosynthesis enzyme A (RquA), homologous to S-adenosyl-L-methionine (SAM)-dependent methyltransferases, is necessary for RQ biosynthesis. Both RquA and RQ are absent in humans or other mammals, making RquA a drug target specific to pathogens that require RQ for survival. Ubiquinone (UQ), structurally similar to RQ, is known to be a substrate for RQ biosynthesis via in vivo studies. However, the mechanism of UQ to RQ conversion is not known. In this study, we are characterizing the mechanism of in vitro RQ biosynthesis. RquA from Rhodospirillum rubrum was recombinantly overexpressed in Escherichia coli. RquA was solubilized in Brij-35 detergent and purified by affinity and size-exclusion chromatography. Upon titration of RquA with a synthetic UQ3 or SAM, the intrinsic fluorescence intensity of RquA decreased, suggesting that UQ3 and SAM bind to RquA. An in vitro functional assay was established to assess the RquA activity where UQ3 and SAM were the substrates, and the RQ3 produced was monitored by HPLC or LC-MS. Using 15N-SAM in the assay produced RQ3 with a 15N-amino group, confirming SAM as the amino donor in RQ biosynthesis. Similarly, methanol and methylthioadenosine were identified as UQ3- and SAM-derived products formed during the reaction, respectively. Unlike known aminotransferases, RquA does not use pyridoxal 5'-phosphate (PLP) as a coenzyme. As these findings reveal, RquA provides an entirely new example of a non-canonical SAM-dependent enzyme that does not catalyze methyl transfer; instead, it uses SAM in an atypical amino transfer mechanism.

Investigation of the molecular basis for the dual role of a marine antifreeze protein

Lara Virgillio

Antifreeze proteins (AFPs) are found across diverse taxa and they allow survival in freezing environments. AFPs protect organisms by binding to ice crystals, thereby preventing crystal growth and recrystallization. The most thoroughly studied of these proteins is AFP6, a 37- residue alpha-helical protein found in the blood plasma of winter flounder, Pseudopleuronectes americanus. The natural role of AFP6 in flounder is to lower the freezing point. However, recent results using recombinant AFP6 have shown that it can trigger ice formation in vitro (Chang & Ewart, unpublished). The transition of AFP6 from an ice growth inhibitor to an ice growth stimulator would require a change in the solution conditions or in the conformation or assembly of the protein. Our current hypothesis is that AFP6 oligomerizes to form an ice crystal template, which would allow ice nucleation to occur. In this study, synthetic AFP6 oligomerization was investigated by crosslinking with glutaraldehyde. This protein was found to associate at both natural temperatures and following repeated freezing and thawing cycles. These results provide insight into the effect of native AFP6 assembly on its dual behaviour as an ice growth inhibitor at high sub-zero temperatures and as an ice nucleator at lower temperatures

Effects of Autonomic Nervous System Activity on Atrial and Ventricular Myocyte Function in Zebrafish

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Background: A principal driver of cardiac adaptation is the autonomic nervous system (ANS), which projects sympathetic and parasympathetic nerves to neural plexi in the heart, comprising the intracardiac nervous system (IcNS). The IcNS is the final pathway for neural control of the heart and classically has been considered simply a 'relay station' for ANS inputs. It is now appreciated that the IcNS may also combine and processes extracardiac inputs and intracardiac sensory information for rapid modulation of cardiac function. The zebrafish has emerged as a powerful experimental model to study the IcNS based on the experimental accessibility of the entire IcNS in the live, whole heart (a limitation of mammalian models), providing an opportunity to study integrated IcNS function and determine its importance for cardiac adaptation. Objectives: My initial goal is to define the effects of sympathetic and parasympathetic receptor activation on atrial and ventricular cardiomyocyte function in the zebrafish heart. Methods: Isolated, paced hearts from adult zebrafish with major IcNS components removed are exposed to varying concentrations of pharmacological agonists and antagonists of sympathetic (isoproterenol and timolol) and parasympathetic (muscarine and atropine) IcNS receptors on cardiomyocytes. Individual cardiomyocyte function is measured by intracellular electrode recordings of membrane potential and fluorescence imaging of intracellular calcium, while electrical conduction and mechanical function are assessed by voltage optical mapping and videographic analysis. Conclusions: Ultimately, my research will help us understand IcNS function and its involvement in the adaptation of cardiac activity to physiological changes

Characterizing the structure and assembly of hydrophobin proteins

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Hydrophobins are small, globular proteins with amphiphilic character that are produced and secreted by filamentous fungi. At hydrophobic-hydrophilic interfaces they self-assemble into durable amyloid-containing structures, called rodlets, which create protective, water repellent coatings for fungal spores. Hydrophobins have diverse sequences and tertiary structures, complicating attempts to characterize how they function. However, there is a subset of hydrophobins (class IB) that have been observed to share a similar structure. To investigate this class of hydrophobins we carried out structural and functional studies with SC16 and SLH4, hydrophobins isolated from *Schizophyllum commune* and *Serpula lacrymans*, respectively. SC16 and SLH4 were recombinantly expressed using *E. coli* and purified by immobilized Ni^{2+} affinity chromatography. Secondary structure analysis of both SC16 and SLH4 before and after assembly suggest that they undergo a similar conformational change. While these hydrophobins share a similar structure they possess different patterns of surface hydrophobicity, assemble into distinct rodlet morphologies, and have a varied level of reliance on assembly conditions. Determining how hydrophobin surface properties affect self-assembly will allow the rational selection and future modification of hydrophobins to fulfil a variety of commercial applications as emulsifiers and surface modifiers.

Lime amendment to a chronically acidified forest soils results in shifts in microbial communities.

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Nova Scotian forests are still enduring the consequences of past acidic precipitation (Keys et al., 2015; Sterling et al., 2020; Clair et al., 2007). Acidification causes a decrease in essential nutrients, primarily base cations, and a release of toxic metals such as aluminum into soils. Subsequently resulting in decreased forest productivity, biodiversity, and carbon capture. The only current solution to mitigate the acidification is to supplement the environment with crushed carbonate rock by a process called “liming” to reintroduce the necessary base cations to the soils and raise the pH. Tree generation time is used to evaluate if liming is effective, however this is a slow process. Utilizing the soil microbes which have rapid generation time to evaluate liming could offer a faster alternative method. These microbial communities (made up of bacteria, fungi and viruses) are known as “microbiomes” and change as a result of any changes in nutrient availability and pH. Therefore, by characterizing the microbiomes of both lime amended and non-amended soils we can identify differences that could potentially be used for diagnostics.

Development Of A Real-Time High Resolution Ultrasound System For Brain Imaging

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Ultrafast ultrasound imaging is rapidly becoming a key diagnostic tool in medical imaging. Its improved temporal resolution compared to focused imaging enables ultrafast power Doppler imaging. The power ratio compared to a focused Doppler image. This allows small vascular and slow-moving blood flow to be detected over the entire imaging region. The detection of vasculature has been shown to be effective in defining the boundaries of glioblastoma tumors. This is due to the large amount of vasculature surrounding the tumor required to feed its growth. However, B-Mode images generated using ultra-fast imaging do not have equivalent axial resolution or contrast as compared to line-by-line focused imaging. This prompted our development of a hybrid ultrasound imaging system capable of performing ultrafast power Doppler and focused B-mode imaging. The aim is to combine the best features of both imaging models in one system to aid in the detection of a tumors boundaries.

The system generates a focused image with 128 lines, 768 pixels per line and an ultrafast imagine with 64 lines, 384 pixels per line. A total of 1 focused frame and 68 ultrafast frames are generated by the ultrasound system at a 10Hz frame rate. The ultrafast power Doppler image is generated in software and is overlayed on the conventional B-image model.

Retinal Neuroblast Migration And Laminar Organization Requires The Cytoskeletal-Interacting Protein Mllt11

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The vertebrate retina is an organized laminar structure comprised of distinct cell types populating three nuclear layers. During development, each retinal cell type follows a stereotypical temporal order of genesis, differentiation, and migration, giving rise to its stratified organization. Once born, the precise positioning of cells along the apico-basal (radial) axis of the retina is critical for subsequent connections to form, relying on orchestrated migratory processes. While these processes are critical for visual function to arise, the regulators of cellular migration and retinal lamination remain largely unexplored. Here, we report a role for a microtubule-interacting protein, Mllt11 (Myeloid/lymphoid or mixed-lineage leukemia; translocated to chromosome 11/All1 Fused Gene From Chromosome 1q) in mammalian retinal cell migration during retinogenesis. We show that Mllt11 loss-of-function in mouse retinal neuroblasts affected the migration of ganglion, astroglial, and amacrine cells into the ganglion cell layer and led to their ectopic accumulation in the inner plexiform and nuclear layers. We demonstrate that Mllt11 plays a critical role in the migration and lamination of neurons in the retina, and its loss impacted formation of the basal-most retinal layers. The formation of functional neuronal circuitry relies on precise positioning of cells in their respective layers; thus, the ectopic positioning of retinal neuroblasts, attributed to Mllt11 loss, may disrupt functional connectivity in the retina and produce visual defects.

Is Anxiety a Mediator in the Relationship Between Cannabis Use and Psychotic-Like Experiences in Emerging Adults? Investigating a Mediation Model in a Multi-Site University Sample

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Cannabis is commonly used by Canadian emerging adults (ages 18-25 years), many of whom attend post-secondary institutions. Frequent cannabis use has been linked with psychotic-like experiences (PLEs), but the exact nature of this relationship is not fully understood. Anxiety is also prevalent in the emerging adult population, and anxiety has been independently linked with both cannabis use and PLEs. The present study evaluated whether anxiety mediates the relationship between cannabis use frequency and PLEs in emerging adult undergraduates. We hypothesized that consuming cannabis more frequently would be associated with more anxiety which, in turn, would be associated with greater PLEs. Specifically, we expected anxiety to mediate the relationship between cannabis use frequency and PLEs. One-thousand-five-hundred-and-seven first- and second-year emerging adult university students (mean [SD] age = 19.2 [1.52] years; 67% female) were recruited. Cross-sectional, self-report survey data were collected throughout fall 2021 from five Canadian universities as part of the UniVenture study. Validated measures capturing demographics, cannabis use frequency, anxiety, and PLEs were administered. A mediation model with frequency of cannabis use as the predictor, PLEs as the outcome, and anxiety as the mediating variable was tested using the PROCESS macro for SPSS with bootstrapping. Using 95% confidence intervals, we found evidence of a significant indirect effect of cannabis use frequency on PLEs through anxiety. Assuming replication in future longitudinal research, the present findings suggest anxiety as an important intervention target in cannabis users in order to potentially prevent the development of PLEs, and in turn psychosis, in emerging adults.

Circadian clock synchrony as a mechanism for regulating behaviour in Drosophila

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Most patients suffering from neuropsychiatric disorders (NDs) cannot consolidate their sleep into the nighttime. Thus, circadian rhythms may offer a mechanism that we can exploit to explain how NDs may develop. Circadian rhythms are behavioural and physiological responses today/night cycles, regulated by a transcription negative feedback loop called the circadian clock. We have shown that mutations in circadian genes cause circadian clocks to oscillate differently in different regions in the brain. We believe that such circadian clock misalignment across the brain may underlie ND development. However, we do not know which neuronal clusters require synchrony for coherent behaviour. We therefore developed a novel assay (LABL) to measure clock oscillations directly in distinct neuronal clusters in the Drosophila brain, in vivo and in real time. Since the eye is the primary light input point for both mammals and flies, I will begin by altering the eye clock and measuring clock oscillations in different parts of the brain using LABL. Thus, we will build a communication map of circadian clocks across the brain. This data will guide us in identifying the neuronal clusters associated with ND-like symptoms in the fly when their synchrony is disrupted. Preliminary data shows that when altering the eye clock, the clock of the DN1p cluster remains unchanged, whereas the clock of the LNd cluster is affected. Given the high homology of both circadian clocks, circadian genes and neuronal communication pathways between humans and flies, we expect our discoveries to be directly testable in mouse and human models.

Dissociable nucleus accumbens functional connectivity profiles in adults with and without chronic back pain

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The nucleus accumbens (NAc) is a critical structure implicated in the aetiology of chronic pain. The respective roles of the two NAc substructures, the shell and core, in mediating chronic pain have not been studied. Resting state fMRI scans in 71 healthy controls (HC) and 75 patients with chronic back pain (CBP) were acquired. Thirty HC and 18 CBP patients' data were held out from the initial analyses to be used as a validation dataset. We mapped shell and core whole-brain resting state functional connectivity (rsFC) within and between HC and CBP. Significant connections from the CBP>HC and CBP <HC contrasts were used to predict Neuropathic Pain Scale (NPS) scores and to assess if they could accurately classify between groups. In both groups, the core was more connected to salience and language/memory regions; the shell was more connected to default mode regions. HC had greater NAc connectivity with language/memory, sensory, and sub-cortical regions relative to CBP; CBP patients had greater connectivity with attention, and default mode regions. NAc connectivity with eight regions, including the dorsolateral prefrontal cortex (dlPFC) was significantly correlated to the NPS; five of these were moderate predictors of classifying between groups. CBP had higher rsFC in the left NAc–right dlPFC relative to HC in the validation data. These findings show similar patterns of NAc shell and core rsFC within HC and CBP participants while highlighting the dlPFC as a particular region of interest that can distinguish between groups.

A Scoping Review Of The Literature On Trauma Cue-Induced Drug Craving In Substance Users With Trauma Histories Or PTSD

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Among trauma-exposed individuals, substances may be used as a means of obtaining symptom relief following exposure to trauma reminders. Repeated pairing of trauma cues with substance use may lead to the development of classically-conditioned craving to trauma cues. Conditioned craving following cue exposure can be studied in-lab using the cue-reactivity paradigm. To map cue-reactivity research conducted with trauma-exposed substance users, we aimed to synthesize research which studied our population of interest, used a cue-reactivity paradigm, and measured craving as an outcome. Three databases were searched using relevant keywords. Twenty-eight studies met our criteria. Four key themes are discussed in our review of these scoped studies: 1) craving as an outcome; 2) methodological subtypes across paradigms; 3) affect as an additional outcome or as a mediator of cueinduced craving; and 4) cue-reactivity paradigms as an intervention outcome assessment tool. Overall, there is strong evidence for cue-reactivity paradigms as a useful means of eliciting craving in response to trauma cues. Our scoping review suggests the need for a meta-analysis to determine the magnitude of the trauma cue-induced craving effect in substance users with trauma histories, and to determine significant moderators (e.g., PTSD symptom severity) and mediators of this effect (e.g., negative affect)

Complex Mismatch Negativity Deficits in Early Phase Psychosis Elicited by the Duat Rule Paradigm

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Electroencephalogram (EEG) technology has great potential for use in a clinical environment considering its time-and cost-effective nature. Using EEG to examine the simple mismatch negativity (sMMN), a marker of auditory cortex function,has been of great interest in the exploration of biomarkers for psychotic illness. Despite many studies reporting sMMN deficits in chronic schizophrenia,there are not reliable reports of sMMN reductions in the early phase of the illness, suggesting the sMMN is not a sensitive enough measure of vulnerability to be used as a biomarker. Recently,a more computationally complex measure of auditory cortex function(the complex mismatch negativity; cMMN) has been hypothesized to provide a more sensitive marker of illness vulnerability. The current study employed the novel dual rule cMMN paradigm to examine the cMMN in 14 individuals with early phase psychosis (EPP) and 15 healthy controls (HC).We found significant reductions of cMMN amplitudes at the frontal region in EPP ($p=.014$)with large effect sizes ($g=1.03$), as well as correlations between higher cMMN amplitudes and multiple positive psychosis symptoms indexed by the Scale of Prodromal Symptoms. This study is an early step in the exploration of the cMMN as a biomarker for psychosis risk and provides evidence that the dual rule cMMN paradigm is an excellent method for cMMN elicitation. Future studies must utilize this paradigm to examine the cMMN in a sample of high-risk individuals while employing a longitudinal design to determine the predictive capability of this measure.

Concussion susceptibility and neurovascular dysfunction as a predictor for short- and long-term complications of repetitive mild traumatic brain injury

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Mild traumatic brain injury (TBI) is the most common type of head trauma in humans. The underlying mechanisms of post-concussion syndrome, post-impact catastrophic death, and post-traumatic epilepsy remain poorly understood. Establishing novel diagnostic and prognostic biomarkers requires an in-depth understanding of these mechanisms. We combined neurobehavioral, molecular, electrophysiological and imaging techniques with a rodent TBI model and in humans to assess the effects of brain injury. Cortical spreading depolarizations were dominant electrophysiological events immediately after repetitive TBI and were associated with longer post-trauma recovery. Rats with a longer recovery time also showed lower neurological scores and higher mortality, and were termed “susceptible” to injury. At one week after initial injury, blood-brain barrier opening and neuroinflammation were higher in susceptible rats compared to resilient animals. One to five months following injury, susceptible rats were more likely to develop post-traumatic epilepsy and performed worse in cognitive tasks. In humans, we used dynamic contrast-enhanced MRI to quantify blood-brain barrier dysfunction after exposure to sport-related mild traumatic brain injury. Together, we provide evidence that cortical spreading depolarizations, blood-brain barrier dysfunction, and pro-inflammatory transforming growth factor β signaling are early outcomes following repetitive mild TBI that correlate with delayed cognitive decline and abnormal brain activity. Finally, we demonstrate the feasibility and applicability of blood-brain barrier imaging in human patients following mild TBI.

Extended and replicated white matter changes in obesity: Spatial and effect size meta-analyses of diffusion tensor imaging studies

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Obesity has become a global public health issue, with an impact spanning increased health care costs, and serious health conditions both mental and physical. Associations between obesity and brain structure are frequently reported for gray matter but understudied in white matter, where associations as measured by fractional anisotropy (FA) are less replicated and more heterogeneous. We analyzed the location of brain changes in obesity using seed-based d mapping in a spatial meta-analysis, and then validated the extent of obesity related changes in a region of interest effect size meta-analysis. Spatial meta-analysis results indicated obesity measures were related to reduced FA in several white matter regions including the genu and splenium of the corpus callosum, middle cerebellar peduncles, anterior thalamic radiation, cortico-spinal projections, and cerebellum. The effect-size meta-analysis validated some of the spatial metaanalysis results, where obesity was related to lower FA in the genu and splenium of the corpus callosum, middle cerebellar peduncles, and the superior longitudinal fasciculus which was not represented in the spatial results. The extent of these obesity related brain changes was a small to medium effect. Our findings demonstrate that brain changes related to obesity involve specific regions replicated in our effect size meta-analysis. Keywords: diffusion tensor imaging; white matter; obesity; fractional anisotropy

SWI/SNF regulates the inducibility of memory genes during LTM formation

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Long-term memory requires gene expression in distinct temporal waves. Immediate-early genes (IEG) are transcribed rapidly, within minutes after neuron stimulation, followed by secondary response genes (SRG) several hours later. The pathways leading to IEGs induction during LTM are well understood, however, we still have much to learn about the function and regulation of downstream SRGs. Here, we show that the SWI/SNF chromatin remodelling complex is required for normal LTM by knocking down a core SWI/SNF subunit, Bap60, in memory neurons of the Drosophila mushroom body (MB). Using MBspecific transcriptomic and epigenomic profiling in SWI/SNF knockdown flies before and after memory formation we establish that SWI/SNF is required for most chromatin accessibility and gene expression changes that occur in MB memory neurons after LTM formation. Interestingly, SWI/SNF appears to primarily effect LTM-induced SRGs, since known IEGs are induced normally in response to LTM. Further, we identify direct binding sites for SWI/SNF during LTM formation and show that SWI/SNF may cooperate with the IEG HR38 to induce expression of a novel memory induced SRG, the transcription factor Prospero. Disruption of these direct SWI/SNF-dependent mechanisms during LTM coincides with an almost complete loss of the inducible expression of genes with known memory-related functions. Our data is the first to provide mechanistic information about SWI/SNF in memory neurons during memory formation. The SWI/SNF complex is one of the most frequently disrupted cellular components in autism and intellectual disability, so this work may provide insight into the molecular mechanisms underlying these poorly understood neurodevelopmental disorders.

Differential effects of cannabis use on event-related potential (ERP)-indexes of cortical inhibition in cannabis users and non-users.

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Cannabis has psychoactive properties and is thought to be associated with potential structural and functional changes with early and heavy use. Previous research suggests cannabis users (CU) vs. non-users (NU) have deficits on EEG-derived event-related potentials elicited by paired click and visual Go/NoGo paradigms. We used these paradigms to examine inhibitory functioning in CUs (n = 14; 9 male) vs. NUs (n=16,4 male). Effect sizes suggest CUs had impaired N100 measures of sensory gating compared to NUs. Additionally, a trend level interaction and latency findings for the P200 suggested CUs had smaller amplitudes and quicker latencies to S, compared to NUs.Go/NoGo findings revealed enhanced P100 amplitudes in CUs (vs. NUs). No other between-group differences or sex differences were observed. This study provides further support for cannabis-induced deficits on early-attentional processing as indexed by the N100 and novel findings regarding enhanced P100 amplitudes to the Go/NoGo paradigm.

Impact Of Exercise On SOD1^{G93A} Disease Progression

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Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disease characterized by progressive motor neuron death leading to muscle atrophy and paralysis. There are currently no cures for ALS with current medication-based treatment only extending patients lives by a few months. Some studies have correlated a life of high-intensity exercise with the development of ALS, whereas on the other end exercise is often prescribed as a nonpharmacological treatment to reduce ALS pathology. Research on the topic has been very controversial with differing levels of exercise intensity, different time points to that animal models underwent their training programs, and highly variable methods to identify positive or negative effects. To investigate the variability in the results of previous research we subjected 3 groups of mice expressing SOD1G93A mutation, as a model of ALS, with their littermate controls to an intensive exercise regimen consisting of 1 hour of incline running 5 days a week and 1 group as a sedentary control. The 3 groups began training at different time points, young, adult, and post symptomatic mice. With lateral recording of the mice walking on a flat and incline treadmill biweekly, tis study used a kinematic approach to identify any early behavioural biomarkers of ALS disease and how exercise impacts the progression of the disease with the differing timepoints. Early results indicate an early change in hip range of motion in the SOD1G93A mice compared to the wild type, and exercise seems to help maintain ankle strength during the weight bearing phase of movement.

Pharmacological Cholinergic Inhibition As A Therapeutic Approach In ALS

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Amyotrophic Lateral Sclerosis is a neurodegenerative disease characterized by muscle denervation and motor neuron death which lead to muscle weakness and eventually paralysis. Interestingly, onset of behavioural symptoms occur later than motor neuron death and muscle denervation. C-boutons are cholinergic synapses from a subset of V0 interneurons called V0c. C-boutons release acetylcholine, which binds to post-synaptic muscarinic receptors and subsequently modulate motor neuron excitability. Previous research has shown that genetically silencing C-boutons in ALS mutant mSOD1^{G93A} mice leads to earlier symptom onset and worsening of behavioural performance, suggesting that they are involved in the delayed symptom onset of relative to motor neuron death. However, when these mice are exercised three times a week, behavioural performance is improved. In order to investigate clinically-relevant approaches, we aimed to reduce the effect of cholinergic activity through the use of two cholinergic antagonists (atropine and methoctramine) in two conditions: frequent exercise and resting conditions. Both atropine and methoctramine improved maximum speed on a treadmill during muscle denervation and early symptomatic stages compared to controls Moreover, the use of methoctramine improved the weight of mice starting at symptom onset stages. Methoctramine also improved grip strength starting at symptom onset stages, although this difference was only seen in the resting condition during early symptomatic stages, Lastly, the lifespan of both atropine and methoctramine resting groups was increased by nearly 8% compared to controls. Our research suggests that cholinergic antagonists may offer a therapeutic approach to ALS.

Activity Changes In The C-Boutons During Amyotrophic Lateral Sclerosis Disease Progression

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Amyotrophic Lateral Sclerosis (ALS) is an adult-onset neurodegenerative disease with progressive motor neuron death, where patients usually die within 5 years of diagnosis. In ALS, symptoms manifest only after significant muscle denervation has occurred, which suggests that surving motor neurons can compensate for those that have died, known as behavioural compensation. Previously we showed that the C-bouttons, which are cholinergic synaptses onto motor neurons that modulate their activity, are necessary for this behavioural compensation in mSOD1^{G93A} ALS Model mice. We hypothesized that, since the C-boutons are contributing to behavioural compensation, then the C-boutons must be more active during ALS. To investigate this, we histologically measured the number of motor neurons and V0c interneurons (the neuronal source of the C-boutons) that express c-FOs (an immediate early gene and marker for neuronal acitivyt) in mSOD1^{g93a} mice after they walk on a treadmill for one hour. This was done at four stages of the disease: presymptomatic, progressive muscle denervation, symptom onset, which corrlated with a similar increase in motor nauron activity. Interestingly, the V0c interneurons experience significant death and reduced activity at the early symptomatic timepoint which correlates with motor neuron death and reduced activity. Our observations suggest that the C-boutons controbute to behavioural compensation at symptom onset, but due to the death and reduced activity of the C-boutons and motor neurons at early symptomatic ages, are unable to compensate as the disease progresses.

The Role of Lipid Phosphate Phosphatase-3 in Cardiac Insulin Function and Energy Metabolism

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Background: Dysregulated energy metabolism contributes to obesity-induced heart disease. Lysophosphatidic acid (LPA) signaling has been implicated in obesity-related metabolic dysfunction. Lipid phosphate phosphatase 3 (LPP3) degrades LPA, thereby arresting LPA signaling. Cardiac-specific LPP3 deficiency causes heart failure in mice. It remains unclear whether LPP3 expressed in cardiomyocytes influences cardiac nutrient metabolism at baseline and during obesity. Aim: To examine whether LPP3 modulation in cardiomyocytes alters insulin signaling, energy metabolism, and cardiac function in health and obesity. Methods: Mice with cardiomyocyte specific LPP3 overexpression (LPP3 OE) were subjected to intraperitoneal injection of insulin or saline to determine cardiac insulin signaling using immunoblot analysis. Mitochondrial substrate oxidation was determined in cardiac myofibers using respirometry. Cardiac function was assessed using Doppler flow analysis. Plasma LPA levels were determined using ELISA. Results: LPP3 OE mice had an 8- and 7-fold increase in cardiomyocyte LPP3 mRNA and protein content, respectively, compared to wild type, which resulted in a ~50% reduction in circulating LPA in LPP3 OE mice. In vivo cardiac function was similar between LPP3 OE and wild type mice as was determined by measuring aortic outflow, mitral inflow, and E/A. Moreover, glucose and fatty acid oxidation and insulin signaling were unchanged between genotypes at baseline. Conclusion and Future Objectives: Cardiomyocyte-specific LPP3 overexpression in mice does not alter cardiac function, energy metabolism and insulin signaling at baseline. We will subject these mice to high fat feeding to determine whether LPP3 overexpression can mitigate LPA signaling activation and metabolic and cardiac dysfunction during obesity.

Peering in: Youth perspectives on Health Promoting Schools and youth engagement in Nova Scotia, Canada

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Background: Health Promoting Schools (HPS) is a whole school approach that shapes the conditions necessary to support student health and well-being. Youth engagement is recognized as key to HPS implementation, yet research related to the involvement of youth voice in school health promotion initiatives is limited. The purpose of this study was to understand youth perspectives on HPS and school youth engagement. Methods Ten youth (grades 9-10, ages 14-16) were trained as peer researchers using a Youth Participatory Action Research approach. The peer researchers interviewed 23 of their peers (grades 7-10, ages 12-16) on perspectives related to HPS and school youth engagement. All interviews were audiorecorded, transcribed, and data were analyzed using inductive 'codebook' thematic analysis. Results Themes related to a healthy school community were mapped onto the pillars of HPS:1) Social and Physical Environment, 2) Teaching and Learning, 3) Partnerships and Services, and 4) School Policies. Participants placed more importance on the social and physical environment of the school including respect, inclusivity, supportive relationships, and the design of spaces. Key factors for youth engagement were: 1) safe and supportive spaces, 2) passion and interest, 3) using their voice, 4) power dynamics, 5) accessibility, and 6) awareness. Conclusion With recognition that youth engagement is a crucial part of HPS, this work provides relevant and applicable information on areas of the healthy school community that are important to youth, and if/how they are meaningfully engaged in school decision-making.

Relaxing Music In The Dental Waiting Room Has Paradoxical Effects On Dental Anxiety In Patients With High Cognitive And Social Anxiety Sensitivity

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Given that anxiety sensitivity (AS: fear of arousal-based body sensations) is a known risk factor for anxiety-related concerns and specific phobias (e.g., dental phobia), and music is an anxiety reducing technique with the ability to reduce state anxiety, this study sought to determine the efficacy of a music intervention in decreasing dental related anxiety among patients awaiting dental clinic services, particularly those with high AS-physical concerns (i.e., fear of adverse physical consequences of arousal sensations). Forty-six dental patients between the ages of 20 and 78 years (61% female) participated in the intervention. While awaiting dental procedures, patients were exposed to music intended to be either relaxing (n=24) or neutral (n=22). During the exposure period, participants completed the State-Trait Anxiety Inventory-State Form-6, and the Dental Anxiety Scale-4 as outcome variables. They also completed the Anxiety Sensitivity Index-3 to determine their trait AS levels. Results: Contrary to predictions, participants exposed to relaxing (vs neutral) music did not report lower levels of dental or state anxiety. Paradoxically, unlike in the neutral music condition, participants in the relaxing music condition showed a significant correlation between AS-cognitive concerns (e.g., fear of losing control) and AS-social concerns (e.g., fear of public embarrassment), and dental anxiety. Conclusion: Results suggestion that dental clinics be more intentional in their selection of music for the purpose of aiding in relaxation, as patients with high AS-cognitive and/or high AS social concerns may experience paradoxical effect of increased dental anxiety.