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UNDERGRADUATE SUMMER RESEARCH SHOWCASE | Abstracts

2024

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A Message From The Vice-Dean

Dear Colleagues,

Welcome to the 2023 Virtual Undergraduate Summer Research Showcase.

This is the twentieth iteration of our undergraduate summer student research programming, which has grown to be a very important event in the University of Saskatchewan College of Medicine research calendar.

This year, we have poster submissions from 11 different biomedical and clinical research categories, for a total of 17 competition categories.

I am delighted to acknowledge the exceptional dedication and hard work of students, mentors, adjudicators and all who facilitated undergraduate student research programs. Our staff have worked incredibly hard to ensure all students gained the research experience they desired.

I wish all of us in our college yet another unforgettable research experience!

With kind regards,

Anatomy, Physiology & Pharmacology

Chenkun (Steve) Zheng (Dr. Asmahan AbuArish)

Elucidating the downregulation of stress granules formation in cystic fibrosis airway epithelial cells

Cystic fibrosis (CF) is a genetically inherited hyperinflammatory pulmonary disease resulting from a mutation in the gene encoding the cystic fibrosis transmembrane conductance regulator (CFTR) channel. ΔF508 (ΔF) is the most common CF-causing mutation where a single phenylalanine deletion results in a misfolded CFTR protein, unable to perform its channel function. ΔF-CFTR is retained in the endoplasmic reticulum (ER) leading to chronic ER stress. Previous experiments in the lab have shown that cells expressing ΔF-CFTR (ΔF-cells) form significantly fewer stress granules (SGs) than those expressing wild type (WT)-CFTR when exposed to cigarette smoke extract (CSE). We hypothesize that chronic ER stress in ΔF-cells impairs the cell's integrated stress response (less phospho-eIF2α) leading to less SGs formation and hyperinflammation. As ΔF-cells are subject to chronic ER stress, we tested if a difference in the activation of the eIF2α pathway which responds to ER stress could help to explain the difference in SGs formation. Our results show that phospho-eIF2α levels are significantly lower in ΔF-cells in response to CSE. Furthermore, inhibiting the actions of phospho-eIF2α inhibits SGs formation in WT-cells. These findings suggest that the difference in eIF2α phosphorylation explains the different responses of WT- and ΔF-cells to CSE.

Jared Stevenson (Dr. Michelle Collins)

Investigating the Role of PITX2C on Cardiometabolic Pathways in the Neonatal Rat Heart

Introduction: Atrial fibrillation (AF), the most common arrhythmia, is highly associated with genetic risk variants near the paired-like homeodomain transcription factor 2 (PITX2) gene. This transcription factor regulates cardiac development, metabolism, and calcium handling. It has been shown that loss of Pitx2c function in zebrafish increases oxidative stress, however, we do not know how this promotes arrhythmia. Therefore, we are exploring calcium/calmodulin-dependent protein kinase II (CaMKII) as a candidate pro-arrhythmic factor, as it plays a central role in AF initiation and pathogenesis and can be induced by increases in reactive oxygen species (ROS) and sustained increases in intracellular calcium.

Hypothesis: We hypothesize that CaMKII is constitutively active in the absence of PITX2C function owing to increased ROS.

Methods & Results: We treated neonatal rat atrial cardiomyocytes (NRAMs) with siRNA to create a Pitx2c knockdown (KD) model. qPCR revealed a robust KD of Pitx2c. We observed increased CellROX staining in Pitx2c KD cells, indicating elevated ROS levels. Immunostaining of phosphorylated CaMKII, a modified version of CaMKII known to exhibit constitutive activity, revealed no difference between control and KD cells.

Conclusion: Thus far, we have identified an effective Pitx2c KD method and provided evidence of oxidative stress in cells lacking Pitx2c.

Syed Ali Raza Rizvi (Dr. David Cooper)

Time-Lapsed 4D Synchrotron Imaging of early PTH-induced Changes in Trabecular Bone of the Rabbit Calcaneus

The overarching goal of this project was to understand the relationship between mechanical strain and trabecular bone remodeling via time-lapsed imaging techniques, as the complex three-dimensional nature of trabecular bone remodeling has traditionally been less well-defined than linear remodeling in dense cortical bone. Using synchrotron microcomputed tomography (micro-CT), this project sequentially imaged calcanei from female New Zealand white rabbits to track individual trabecular bone changes with three in vivo scans and one ex vivo scan spaced five days apart each. The rabbits were administered 30 μg/kg/day of parathyroid hormone (PTH) over these fifteen days to increase remodeling activity for later examination, with another project aim being to understand the role of PTH in early bone morphology changes in vivo. After imaging, the successful registration of each scan and subsequent visualizations established the success of the multiple time point imaging technique, with observed examples including trabecular rods increasing in length and gradual resorption over trabecular surfaces. Our results also showed a significant increase in bone volume fraction in the trabecular region over fifteen days of PTH administration ($p=0.026$). With these results, our next aim moving forward will be to focus on better understanding the relationship between mechanical strain and trabecular bone remodeling.

Aiden Glass (Dr. John Howland)

Exploring the role of tau in cognitive flexibility: Pairwise discrimination and reversal learning in MAPT-/- rats

The neuronal microtubule associated protein tau (Mapt) gene encodes the protein tau, which is involved in neuroplasticity, neuronal function, and is implicated in neurodegenerative disease. Tau pathologies such as Alzheimer's disease (AD) affect many cognitive processes, including cognitive flexibility, which is the ability to shift attention between strategies and adapt to new information. The present experiment uses a novel rat Mapt knockout model to assess cognitive flexibility using the operant-based touchscreen tasks pairwise discrimination (PD) and reversal learning (RL). In PD, adult male and female Mapt-/- and litter-matched wildtype controls were simultaneously presented with two images and trained to reliably respond to only the rewarded image and avoid responding to the punished image. Animals then moved onto RL, in which the rewarded and punished images were swapped, necessitating the use of cognitive flexibility. Mapt-/- rats showed impairment on both PD and RL acquisition, as measured by number of sessions required to reach criterion, though this effect was significant only in females. These results reveal a nonspecific cognitive deficit in Mapt-/- rats, and a possible sex difference with females being more affected. Since PD acquisition is impaired, future experiments should investigate the influence of tau on neuroplasticity in the dorsal striatum.

Kaylen Young (Dr. John Howland)

Exploring the role of Tau protein in age-related spatial memory decline in rats

The microtubule-associated protein tau (Mapt) gene encodes for the tau protein which is involved in neuronal stability and synaptic plasticity in the hippocampus, as well as neurodegenerative diseases like Alzheimer's disease and other dementias. The purpose of this study was to assess the potential role of tau in hippocampal-dependent cognition using a novel Mapt knockout (Mapt-/-) rat. We used the Object Location Task (OLT) to assess hippocampal-dependent incidental spatial memory. The OLT involves a novelty discrimination procedure with objects without the need for reward or other motivational stimuli. Testing was conducted on young (2 month old) and aged (12 month old) male and female rats. Our results show that aged Mapt-/- rats have conserved spatial memory in the OLT while the wild-type rats demonstrate a decline in performance. This difference cannot be explained by altered object exploration times or overall health of the rats. Ongoing experiments will further assess cognition and behaviour of the Mapt-/- rat strain with a particular focus on cortico-limbic circuits.

Aidan Hydomako (Dr. Scott Widenmaier)

Investigating the influence of the hepatic stress-defending transcription factor NRF1 on VLDL composition in the context of sepsis

Sepsis is a life-threatening condition marked by a dysregulated immune response to infection, leading to acute inflammation, tissue damage, and multi-organ dysfunction. The liver mediates immunometabolic adaptations that promote survival during sepsis. Notably, infection and inflammation stimulate increased VLDL secretion by the liver, causing hypertriglyceridemia and supplying abundant lipids for immune cells and thermogenic tissues. We previously demonstrated that the hepatocyte stress-defence transcription factor NRF1 enhances sepsis tolerance by increasing VLDL secretion. Hepatic NRF1 deficiency in mice led to relative hypotriglyceridemia, hypothermia, and increased mortality. Conversely, overexpression promoted relative hypertriglyceridemia, prevented hypothermia, and improved survival. Here, we investigated the influence of hepatic NRF1 gain and loss of function on plasma APOB levels, the primary apolipoprotein on VLDL, during lipopolysaccharide-induced sepsis. We found that hepatocyte-specific NRF1 knockout reduces plasma APOB levels under both control and septic conditions, suggesting NRF1 plays a role in maintaining baseline VLDL secretion. Additionally, relative plasma APOB levels in NRF1-overexpressing mice were comparable to controls under septic conditions, despite elevated plasma triglycerides, suggesting that hepatic NRF1 promotes the formation of triglyceride-rich VLDL particles. Further investigation into hepatic NRF1-mediated tolerance mechanisms could reveal novel therapeutic approaches to addressing the global health burden of sepsis.

Carter Johnson (Dr. Darell Mousseau)

Using Autopsy Brain to Establish Whether Markers of Type 2 Diabetes Align with Markers of Alzheimer Disease Pathology

Insulin resistance, a hallmark of Type 2 diabetes (T2D), has been linked to Alzheimer's disease (AD) through immune dysfunction resulting in neuroinflammation. This study investigates the correlation between insulin resistance markers and AD pathology in human brain cortex samples to develop a baseline comparator for screening of a cutting-edge brain organoid neurodegenerative model involving innate host microglia in Dr. Mousseau's laboratory. This aims to provide a more effective model of neurodegenerative disease screening. Along with the model of interest, the relationship between monoamine oxidase A (MAO-A) activity and the insulin receptor pathway was assessed, exploring its direct relationship with insulin resistance and AD pathology. Fifty-five cortex samples from control, early-onset AD (EOAD), and late-onset AD (LOAD) groups were analyzed for phosphorylated insulin receptor substrate-1 (p-IRS-1: Ser307, Ser616, Tyr895), total IRS-1, and insulin receptor (IR) using western blotting and fluorescent densitometry. A decrease in pSer307-IRS-1 was observed in EOAD and LOAD, suggesting a link with T2D and AD. An unexpected strong correlation between IR and AD pathology was identified with MAO-A, while MAO-A activity also aligned with p-IRS-1 in healthy controls but not in AD patients. The results collected provide a strong foundation to further examine the brain organoid model effectiveness.

Aaron Su (Dr. Scott Widenmaier)

Investigating the Effect of Cholesterol Crystals on Cytokine Expression in Hepatic Cell Culture Models

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a condition where fat accumulates in the liver, and can progress into the more severe state of metabolic dysfunction-associated steatohepatitis (MASH), which is emerging as the most common cause of liver failure and liver cancer. MASLD progression to MASH is due, in part, to excess liver storage of cholesterol, which then precipitates into cholesterol crystals. In the liver of mouse models, such crystals are positively correlated with inflammatory cytokines, and sequestosome-1 (an autophagy substrate). Therefore, it is hypothesized that in cell culture models of hepatocytes and macrophages respectively, the blockage of cholesterol crystal formation will decrease inflammatory cytokines and sequestosome-1 expression. In addition, the synergistic effect of cholesterol crystals and palmitate (saturated fatty acid) induced lipotoxicity may exacerbate cytokine and sequestosome-1 features in cells. Gene and protein expression results show that cholesterol crystals in such models had virtually no effect on features of interest, suggesting that cholesterol crystals influence these two MASH features through different mechanisms. Further steps include repeating the experiment in a model of co-culturing hepatocytes and macrophages to simulate a more realistic environment of the liver.

Ario Safaeian (Dr. Changting Xiao)

Establishing a Protocol for Visualizing Lipid Droplets in Rat Gut Enterocytes

Dysregulated lipid processing in intestinal absorptive cells (Enterocytes) leads to lipid and lipoprotein abnormalities accompanied by an increased risk of cardiovascular disease in patients. This project aims to establish a protocol for visualizing enterocyte LDs with BODIPY staining in rat intestinal tissues. Jejunum tissue was collected after the rats were provided with lipids into the small intestine lumen and sectioned using Cryostat at -20 ℃ with 5μm thickness. Using a protocol adopted from mice, LDs seemed disrupted, dislocated or not clearly visible. Further, we tested several modifications to this protocol, including with and without permeabilization (with various reagents, e.g. Saponin, Tween 20, and Digitonin), sample collection and fixation methods. Preliminary results indicate that permeabilization did not disrupt the LDs. Clear LD images were obtained with tissues collected using the Swiss Roll (SR) method with fixation at the time of collection. The stained LDs in SR samples were mostly contained and not disrupted. Furthermore, their locations in the intestinal tissue and enterocytes were consistent with LD biology. Further refining of the protocol is ongoing. An optimal protocol for visualizing rat enterocyte LDs with BODIPY staining would likely include the collection of intestinal tissues with the SR method along with fixation at the time of collection and with optional permeabilization.

Royce Hermanson (Dr. Justin Botterill)

Measuring the activity of dorsal and ventral mossy cells during hippocampal-dependent behaviours via fluorescent calcium indicators

The hippocampus has historically been implicated in learning and memory, but emerging research suggests it also has functions in affective behaviours1,2. It consists of areas CA1, CA2, CA3, and the dentate gyrus (DG)3. The DG is a major point of entry for information4. It has a primary glutamatergic principal cell type known as granule cells, and an additional glutamatergic cell type known as mossy cells (MCs)3. MCs are large, excitatory neurons that form complex connections within the hippocampus, but their overall effect remains difficult to elucidate as they form both excitatory and inhibitory circuits3. MCs have been implicated in hippocampal-dependent learning and memory1,5, spatial exploration6, novelty detection7,8, and affective behaviours1,9. They have historically been viewed as a homogenous cell population, but recent studies suggest that dorsal and ventral MCs differ in gene expression10, morphology11, and axonal projections11,12. Recent cell-selective methods such as designer receptors exclusively activated by designer drugs (DREADDs) have probed MCs1, but not dorsal-ventral differences, as they target all MCs. Our study probes physiological activities of dorsal and ventral MCs simultaneously as mice carry out affect-related tasks. We utilized fiber photometry in conjunction with genetically-encoded calcium indicators to simultaneously record from dorsal and ventral MCs in behaving mice.

Zachary Berardi (Dr. Justin Botterill)

Investigating the Roles of Dorsal and Ventral Mossy Cells in Hippocampal-dependent Cognitive Behaviours

The hippocampus is broadly implicated in learning and memory, but many cells and circuits that influence cognition remain poorly characterized. Mossy cells (MCs) are a relatively understudied cell type in the main input region of the hippocampus called the dentate gyrus. Recent work has shown that MC activity influences hippocampal-dependent cognitive behaviours, yet most research has examined only artificial manipulation of MC activity. With advances in cell-selective tools, a growing body of literature has reported differences in gene expression, morphology, firing patterns, and axonal projections between MCs in the dorsal and ventral subdivisions of the hippocampus. Importantly, it is poorly understood whether dorsal and ventral MCs serve different roles in cognition. This project utilized dopamine receptor type 2 (Drd2-Cre) mice and fiber photometry to genetically target and selectively record the activity of dorsal and ventral MCs during cognitive behavioural tasks (novel object tests, contextual fear conditioning). Behavioural results revealed sex differences in both object tests, but effects are limited by a small sample size. Thus, future cohorts will be incorporated. We have collected time-synced fiber photometry data and analysis is currently underway. Our next steps are to compare dorsal and ventral MC activity and correlate MC activity with behaviour.

Hetvi Darji (Dr. Asmahan AbuArish)

Characterizing Stress Granules in Cystic Fibrosis Bronchial Epithelial (CFBE) Cells

To protect against stress, cells activate protective mechanisms such as the integrated stress response (ISR) by phosphorylating the eIF2α (p-eIF2α) resulting in stress granules (SGs) formation. SGs sequester proteins and mRNA to inhibit general protein synthesis to help cells cope. It was established in the lab and for the first time that cigarette smoke (CS) exposure induces robust SGs formation in healthy airway epithelial cells but not as well in cystic fibrosis (CF)-related cells. This can potentially explain some aspects of hyperinflammation in CF airways. In this project, we characterize SGs formation under CS exposure in healthy and CF-related cells treated with different inhibitors of the ISR pathway. To characterize SGs, we use ImageJ code to measure their individual size, number of SGs per cell, and the level of phospho-eIF2α (p-eIF2α) incorporated into every SG. Our analysis shows there are fewer and smaller SGs in CF-related cells, and they incorporate less p-eIF2α. Inhibiting the effect of p-eIF2α in healthy cells using ISRIB inhibits SGs formation. Inhibiting the phosphorylation of PERK which is upstream of eIF2α also halts SGs formation. This demonstrates that the PERK/eIF2α pathway is responsible for SGs formation in healthy airway epithelium which is disrupted in CF-related epithelium.

Malia Gee (Dr. Julian Tam)

Contribution of Bicarbonate Secretion to Mucociliary Clearance in Swine Distal Airway

Cystic Fibrosis (CF) is a chronic disorder resulting from a mutation in the cystic fibrosis conductance transmembrane regulator (CFTR). CFTR is an anion exchanger responsible for chloride, and bicarbonate secretion in the airways. The anion exchange protein 2 (AE2) and CFTR are found on the apical membrane of ionocytes where they collaborate to contribute to bicarbonate secretion. Ionocytes are responsible for 60% of CFTR-dependent ion flux despite constituting ~1% of epithelial cells. Inhibiting ionocyte function has been presented as sufficient to produce phenotypes consistent with CF. There have been debates about the significance of bicarbonate secretion to mucociliary clearance (MCC). If bicarbonate influences MCC in the distal airway, MCC will differ in a bicarbonate-scarce environment. To test this hypothesis, we tracked the movement of 250μm tantalum discs on distal airway samples in one control and two experimental conditions. Both experimental conditions inhibit ionocyte bicarbonate secretion however, they differ as only one condition includes a bicarbonate addition to the apical membrane at the five-minute mark. Our results show a significant MCC reduction in bicarbonate-scarce environments that is restored when bicarbonate is subsequently added. We hope to assess these properties in CF swine and human tissue, further analyzing bicarbonate's effect on MCC.

Grayson Tourney (Dr. Michael Levin)

hnRNP A1 dysfunction-induced exon skipping may impact neurodegeneration

Neuronal dysfunction of heterogeneous nuclear ribonucleoprotein A1 (A1) is associated with neurodegeneration in multiple sclerosis. A1 mediates the alternative splicing of mRNA, so we hypothesized that A1 dysfunction-mediated changes in splicing would result in transcript-level changes in neuronal targets with functional consequences. Short- and long-read sequencing of RNA from mouse primary embryonic neurons with dysfunctional A1 revealed differential transcript usage for App (encoding amyloid beta precursor protein; a change also observed in Alzheimer's disease) and Klc1 (encoding kinesin light chain-1, involved in transport and axonal growth). Mouse neuroblastoma cells (Neuro-2a) were transfected with plasmids encoding eGFP-tagged full-length (FL) or skipped-exon (SE) isoforms of each transcript and imaged to assess neurite length changes as a measure of neurodegeneration. Preliminary data suggests that Klc1-SE overexpression decreased neurite length relative to Klc1-FL, but expression efficiency of all constructs was low due to regulatory elements in their 3' UTRs, and efforts are underway to generate new ΔUTR constructs for both Klc1 and App. We are also developing a live-cell kinesin transport assay to evaluate the differential effects of Klc1-SE versus FL on neuronal cargo transport as a separate metric. Together these analyses will show whether A1 dysfunction-induced alternatively-spliced isoforms impact neuronal function and neurodegeneration.

Maya Wilson (Dr. Valerie Verge)

Can a Novel Non-Invasive Therapy, Acute Intermittent Hypoxia, Rapidly Sensitize Neural Tissue to the Repair-Promoting Neurotrophin - NGF?

The neurotrophin nerve growth factor (NGF) and its receptor trkA are important for maintenance and regulation of axon growth in sensory neurons. We have found that drops in pH and ultimately neuron depolarization can rapidly mobilize trkA receptors to sensory neuron membranes, increasing the neuron's responsiveness to NGF. We have also shown that Acute Intermittent Hypoxia (AIH), a novel non-invasive therapy involving breathing normal oxygen levels alternating with lower oxygen levels, increases neuronal activity and nerve regeneration akin to invasive electrical nerve stimulation. This made us posit whether AIH's ability to increase neuronal activity alters sensory neuron responsiveness to NGF by rapidly mobilizing more trkA to the plasma membrane (PM). To investigate this, primary neuronal cultures of adult male Lewis rat dorsal root ganglia were established and underwent AIH or Normoxia treatment. Immunofluorescence under non-permeabilizing conditions assessed AIH treatment's impact on PM trkA levels. Preliminary evidence supports that AIH treatment results in increased presentation of PM trkA. These findings remain to be quantified, but suggest that sensory neurons are able to rapidly alter a neuron's responsiveness to NGF by mobilizing receptors already formed in the cytosol to the cell surface; the mechanisms of which are the focus of future experiments.

Nathaniel Aubynn (Dr. Michael Levin)

Establishing MS-relevant in vitro model systems for assessing small molecule therapeutics

Multiple Sclerosis (MS) is a neurodegenerative disease marked by significant neuronal cell loss. Neuronal dysfunction of the RNA binding protein heterogeneous nuclear ribonucleoprotein A1 (hnRNP A1) is a pathologic feature of MS, characterized by hnRNP A1's mislocalization from the homeostatic nuclear location to the cytoplasm in neurons. We hypothesized that oxidative stress, significant in MS pathogenesis, would induce mislocalization of neuronal hnRNP A1, creating an MS-relevant in vitro stress model. This model could then be used to test novel small molecules for their ability to correct hnRNP A1 mislocalization. Primary embryonic cortical neurons were exposed to varying doses (0.5-10mM of3–morpholinosydnonimine hydrochloride (SIN-1), a reactive oxygen species generator, to induce oxidative stress. The treatment led to hnRNP A1 mislocalization at both 4 and 24 hours, with significant effects observed starting at 2 mM SIN-1. The optimal condition for testing small molecules was determined to be 2 mM SIN-1 for 4 hours. Neurons pre-treated with small molecules were then exposed to the optimal condition. Out of four small molecules tested, two demonstrated partial effectiveness in correcting hnRNP A1 mislocalization. This model provides a valuable tool for studying oxidative stress in MS and evaluating potential therapeutic agents targeting hnRNP A1 mislocalization.

Yun Hei (Isaac) Lo (Dr. Veronica Campanucci)

Effects of ETI therapy on sensory neurons from △F508 mice

Cystic fibrosis (CF) is a lethal pulmonary disease caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) channel, which is responsible for chloride and bicarbonate transport. Preliminary results from our lab revealed that sensory neurons from DF508 mice had impaired chloride homeostasis. We hypothesized that treatment of cultured sensory neurons with CFTR modulators (ETI) would restore normal chloride levels. To test this hypothesis, we used mice (male and females) carrying the most common CFTR mutation-causing CF, △ F508, and wild-type (WT) littermates to study the intracellular chloride levels with the help of the MQAE chloride-sensitive dye. Our findings show that in both males and females, there was a significant difference in the levels of mean MQAE fluorescent between the genotypes, but ETI did not restore chloride homeostasis. Our data suggests that ETI fails to rescue normal sensory neuron function in a mouse model of CF.

Ethan Minier (Dr. Changting Xiao)

Characterization of immune cell distribution in mesenteric lymph during fat absorption in rats

Dysregulated gut functions, including lipid handling, are associated with metabolic diseases, including type-2 diabetes and obesity. Various biological factors are present during dietary fat absorption and lipoprotein secretion in the gut; however, very little has been studied regarding their amounts, identities and implications in lipid metabolism and disease development. This project aimed to quantify and characterize these live cells.

Sprague-Dawley rats were surgically implanted with catheters into the mesenteric lymph duct (for collecting lymph fluid), the duodenum (for providing fats), and the peritoneum (for giving drug treatments). Total cells in rat lymph samples collected before and after providing fats into the duodenum were counted. An abundance of cells was observed. We next analyzed the quantity and subtypes of immune cells in the lymph fluid collected. Lymph samples were incubated with rat-specific antibodies against several immune cell markers and analyzed using flow cytometry. A wide variety of immune cells was observed.

These results indicate that live cells, including multiple subtypes of immune cells, are present in the mesenteric lymph during fat absorption. Future research is warranted to investigate the functional roles of such cells as they relate to lipid handling in the gut and systemic health in healthy and disease conditions.

Mahboubeh Pordeli (Dr. Francisco Cayabyab)

Perampanel as a Neuroprotective Agent: Investigating Its Potential in Cerebral Ischemia Through AMPAR Blockade

AMPA receptors (AMPARs) play a critical role in synaptic plasticity and neurotransmission but are also implicated in neuroinflammation. AMPARs on microglia and astrocytes contribute to the release of pro-inflammatory cytokines during excitotoxic events, such as ischemic stroke. In this study, we explored the neuroprotective effects of Perampanel, an AMPAR antagonist, in a pial vessel disruption (PVD) model of cerebral ischemia. We hypothesize that Perampanel reduces glutamate-induced excitotoxicity by blocking AMPARs on neurons and modulates neuroinflammation by inhibiting AMPARs on glial cells.

Our results demonstrate that Perampanel significantly reduces neurodegeneration, as evidenced by reduced Fluoro-Jade C (FJC) staining. Moreover, Perampanel attenuates microglia and astrocyte activation, as reflected by reduced Iba1 and GFAP expression and reduced pro-inflammatory mediators. These findings suggest that Perampanel's neuroprotective effects are partly mediated by the suppression of pro-inflammatory cytokines, likely derived from activated glial cells.

In conclusion, Perampanel mitigates both neuronal excitotoxicity and neuroinflammation, providing a potential therapeutic approach for limiting neuronal damage and improving outcomes in ischemic stroke.

Elina Setork (Drs. Francisco Cayabyab & Changiz Taghibiglou)

Istradefylline, an adenosine A2A receptor antagonist, promotes neuroprotection in an animal model of ischemic stroke

Stroke is the second-leading cause of death globally, with 16 million cases in 2020 and with half of the stroke survivors having long-term disability. Current treatments focus on acute care, with limited attention to neuroprotection and prevention. After a stroke, extracellular adenosine levels rise rapidly, leading to desensitization of neuroprotective A1 receptors (A1Rs) and upregulation of A2A receptors (A2ARs). This elevation of A2ARs after ischemic insult is mediated by protein kinase CK2. A2AR hyperactivation is also linked to neurodegenerative diseases like Alzheimer's and Parkinson's disease, making it a target for reducing neuronal damage after adenosine elevation. Since A1R and A2AR are abundantly expressed in hippocampal neurons and glial cells, we investigated the neuroprotective potential of Istradefylline, a selective A2AR antagonist, in reducing hippocampal neuronal death and glial activation. Using a pial vessel disruption (PVD) stroke model, we analyzed hippocampal tissues from sham, PVD + vehicle, and PVD + Istradefylline groups. Using propidium iodide staining and confocal microscopy, the neuronal death observed after PVD was significantly reduced by Istradefylline. The PVD-induced enhancement of microglia and astrocyte markers was also attenuated by Istradefylline. These results suggest that blocking A2AR activity with Istradefylline promotes neuroprotection by reducing neuroinflammation from astrocytes and microglia.

Satyam Singh (Dr. Wendie Marks)

Examining the Effects of Early vs. Late Maternal Separation Stress on Physical & Neurodevelopmental Outcomes in Protein-Restricted Neonatal Wistar Rats

This study examined the effects of early and late maternal separation stress combined with protein-restriction (PR) diets on developmental, behavioral, and neurobiological outcomes in neonatal Wistar rat pups. The Early Maternal Separation Stress (EMS + PR) group (PND 2-12), exhibited increased anxiety-like behavior, characterized by higher outer arena time (thigmotaxis) and lower inner arena time in the Open Field Test (OFT) compared to the Late Maternal Separation Stress (LMS + PR) group (PND 10-17). These anxiety-related and exploratory differences were significant in male pups. The EMS group also displayed significantly longer reversal times in the Negative Geotaxis test on postnatal day 11 (PND 11), suggesting delayed motor development at this time point. On PND 16, ultrasonic vocalizations (USVs) were significantly reduced in the LMS group, indicating potential social communicative deficits. Additionally, ear and eye opening were on average slightly delayed in the EMS group. No significant differences were found in hippocampal BDNF expression between the EMS and LMS groups. These findings highlight the combined impact of different maternal separation stress periods and PR diets on physical, behavioral and physiological outcomes in neonatal Wistar Pups.

Joanne Jibu Zachariah (Dr. Heather Szabo-Rogers)

Role of genes involved in midfacial morphogenesis

Orofacial clefting is the most common congenital anomaly that affects 1/700 Saskatchewan babies. Midfacial clefting, a subset of orofacial clefting, affects the development of the nasal septum and the medial nasal prominences. However, less is known about the mechanisms underlying midfacial clefting. Our lab models midfacial clefting using two different mouse lines – the Unicorn and the Prickle1Beetlejuice (Prickle1Bj) mouse lines. We did cell lineage tracing to track Sox9 expressing chondrocytes in early development of Unicorn embryos and observed decreased Sox9 expression in the medial nasal prominence (mnp) of the mutants. We also performed whole mount in-situ hybridization experiments on wildtype and mutant embryos to compare the expression domains of the morphogen Sonic hedgehog (Shh) and the medial nasal prominence specifier Alx3. The results demonstrate the decreased Alx3 expression in the proximal regions of the frontonasal prominences and wider medial expression domains of Shh in the Unicorn and the Prickle1Beetlejuice mutants. Together these results suggest the roles of Alx3 and Shh in the proper merging of the midline.

Fatma Younis (Dr. David Cooper)

Is Intra-Trabecular Bone Remodelling Induced by Parathyroid Hormone A Consequence of Trabecular Thickening?

Osteoporosis is a chronic condition characterized by the loss of bone volume and detrimental changes to bone microarchitecture. Parathyroid hormone (PTH) is currently used in the treatment of osteoporosis due to its significant role in regulating bone remodeling. Bone remodeling removes microdamage, helps maintain bone mineral levels through the creation of new bone and aids in maintaining Ca homeostasis. This project aimed to elucidate the relationship between the increased trabecular thickness induced by parathyroid hormone and intra-trabecular bone remodeling. New Zealand White rabbit calcanei from a 4-week trial, which included a PTH-dosed group and a control group, were imaged by synchrotron micro-CT. It was hypothesized that as trabecular thickness increases, an associated increase in intra-trabecular bone remodeling would be observed. A trend of increasing trabecular thickness ($p = 0.11$), percent bone volume ($p = 0.10$), and volume ($p = 0.11$) and length ($p = 0.31$) of intra-trabecular remodeling events was observed in the PTH dosed group. However, contrary to the hypothesis, no correlation was found between trabecular thickness and intra-trabecular remodeling. Future research could investigate the thickness of trabeculae at individual intra-trabecular remodeling events to determine the threshold of trabecular thickness necessary for remodeling to occur.

Jenna Reding (Dr. Michael Levin)

Investigating the Role of NeuN in Neurodegeneration

Neuronal Nuclei (NeuN), also known as RNA binding fox-1 homolog 3 (RBFOX3), is an RNA-binding protein that has been used as a neuron-specific marker to evaluate neuronal death. NeuN contributes to neuronal homeostasis through the regulation of RNA metabolism and is thought to regulate synaptic function. Studies have found that NeuN is altered in Alzheimer's Disease, Amyotrophic Lateral Sclerosis, and Multiple Sclerosis, indicating that NeuN dysfunction may be related to neurodegeneration. To investigate the role of NeuN in the pathogenesis of neurodegenerative diseases, we established a NeuN knockout (KO) model in a neuronal cell line using CRISPR-Cas. We designed and tested three single guide RNAs (sgRNAs) targeting NeuN in neuronal cells to determine their KO efficiency. The first sgRNA (sgNeuN1) had an 86% KO efficiency compared to 78% and 73% for the other sgRNAs. The first sgRNA demonstrated successful NeuN KO (~46%, ***P ≤ 0.001). Next, we investigated how NeuN KO might impact seven synaptic RNA targets using RT-qPCR; we found that NeuN KO did not change the abundance of any, suggesting that NeuN affects synapses in another mechanism. Our research provides a basis for further investigation into the functional consequences of NeuN and how it may contribute to neurodegeneration.

Erwin Zhu (Dr. Juan Ianowski)

IInvestigation of Different Mechanisms of Mucociliary Clearance in Healthy and Bicarbonate-Scarce Swine Distal Airways

Cystic Fibrosis (CF) is an autosomal genetic mutation where the cystic fibrosis transmembrane regulator (CFTR) anion channel is dysfunctional. Major pulmonary pathologies of CF include pH disruptions, reduced bicarbonate (HCO3-) secretion and impaired ciliated clearance of objects by the airways (mucociliary clearance). The impaired HCO3- secretion in CF is proposed to be a major factor of dysfunctional mucociliary clearance (MCC), due to bicarbonate's mucin-unpacking properties and contribution to airway pH. Recent research presented the existence of distinct mechanisms for clearance based on different airway substrate-object interactions. In this study, two different MCC measurement methods (tantalum discs and Alcian blue dye) were performed to determine the existence of distinct clearance velocities between discs and dye in healthy and in CF-like bicarbonate-defective distal swine airways. Provided we see distinct movements for different MCC experiments, results may give way for research on the molecular interactions governing clearance, research on molecular therapies for better clearance in CF conditions and give insight to how different respiratory infections are cleared. We also investigate whether distinct clearance velocities, if found, are maintained or become indistinguishable in CF-like conditions. Results will also emphasize the implications of using different MCC measurement methods for future CF and pulmonary research.

Sanskriti Shrestha (Dr. Anand Krishnan)

Screening of lncRNA-encoded microproteins as potential therapeutic candidates for prostate cancer

Prostate cancer (PC) is the most diagnosed and the third leading cause of cancer-related death in men in Canada. An advanced stage of PC is called neuroendocrine prostate cancer (NEPC), which is a treatment-resistant subtype of PC because of its transdifferentiated neuroendocrine status. Long non-coding RNAs (lncRNA) are RNAs that have more than 200 nucleotides. They were initially considered to have no translation potential, but recent studies demonstrated that they can encode microproteins. Advanced studies showed that the lncRNA-encoded microproteins have prognostic implications and therapeutic potentials in several diseases, including cancer. In this work, we screened nine lncRNA-encoded microproteins for their antineoplastic roles in PC and NEPC cells in vitro. Our results showed that three of the nine lncRNAs-encoded microproteins tested (LINC00116, EIF1B, and EIF3J-AS1) induce cytotoxicity in PC cells. In contrast, they promoted NEPC cell proliferation. The differential responses of PC and NEPC cells to lncRNA-encoded microproteins may be attributed to the differential molecular signature of PC and NEPC cells. Overall, our study showed that the microproteins encoded by LINC00116, EIF1B, and EIF3J-AS1 are potential suppressors of PC.

Uday Chhina (Dr. Darrell Mousseau)

Investigating the effect of SSRIs on an organoid model of the human brain in Alzheimer's disease

Alzheimer's disease (AD) is an irreversible dementia that leads to neuronal loss, caused by buildup of beta-amyloid (A13) plaques. Brain derived neurotrophic factor (BDNF) supports learning and memory by maintaining synaptic plasticity, and is a biomarker typically depleted in AD. SSRIs, like Fluoxetine, have been mainstays in treating depression but there is limited knowledge on their efficacy for reversing the neurodegeneration in AD. Brain organoids (BORGs) are 3D aggregates consisting of both neurons and glial cells, and we hypothesized that they could be used to assess the effects of SSRIs on AD biomarkers such as BDNF and A13. Male and female BORGs derived from both healthy and AD donors were grown for 90 days and treated with Fluoxetine for 1 week, and then tissue lysates were assessed for various AD biomarkers via western blotting. Treatment results show that Fluoxetine decreases BDNF over time and exerts variable effects on A13 based on the AD subtype. Overall, BORGs may be an applicable model to study neurodegenerative diseases and associated treatments like SSRIs. Future studies should utilize multiple concentrations of SSRIs and check if biological sex modifies the effects of SSRIs on AD biomarkers.

Jordan Bairos (Dr. Scott Widenmaier)

SOAT/ACAT activity is required to form cholesterol crystals in hepatocyte lipid droplets

Background: Excess cholesterol is toxic and can exert stress that promotes disease. Accumulation of unesterified or "free" cholesterol (FC) within the endoplasmic reticulum membrane triggers the conversion of FC into cholesteryl esters (CE) by sterol O-acyltransferase (SOAT, also known as ACAT). A severe consequence of prolonged cholesterol storage is the formation of cholesterol crystals (CC). Recent studies in patients with metabolic dysfunction-associated steatohepatitis (MASH) indicate that CC in hepatocyte lipid droplets distinguish MASH from simple steatosis, and that CC nucleate intracellularly on lipid droplet surfaces. Although CC are present in MASH, the mechanistic factors that contribute to their formation are not well understood. Here, we investigated the role of SOAT activity on CC formation in lipid droplets.

Hypothesis: SOAT-mediated esterification of cholesterol is required for CC formation in lipid droplets of cholesterol loaded cells.

Methods and Results: CC were detected in live cells using polarized light microscopy. CC formed in a dose-dependent manner exclusively at hepatocyte lipid droplets and not in the lysosome. Inhibition of SOAT drastically reduced CC formation in human hepatocytes and mouse macrophage. Remarkably, the formation of three-dimensional CC clefts required SOAT activity in hepatocytes.

Conclusion: SOAT-mediated esterification may underlie CC by concentrating CE in lipid droplets.

Chase Ellingson (Dr. Payam Dehghani)

Seismocardiogram-derived hemodynamics of patients presenting to the cardiac catheterization laboratory

Left ventricular end-diastolic pressure (LVEDP), an important hemodynamic parameter, is obtained during cardiac catheterization. Seismocardiography (SCG) measures the vibrations produced by the heart to evaluate cardiac cycle timing intervals and contractility noninvasively. This exploratory study aimed to derive LVEDP noninvasively using SCG.

Patients presenting for non-emergent cardiac catheterization (n=100) had LVEDP assessed during cardiac catheterization and completed a one-minute SCG measurement before and after catheterization. A predictive LVEDP model was developed using the first 52 participants' SCG data, which underwent validation using the remaining 48 participants.

The SCG-derived diastolic E-wave, mitral valve opening, isovolumic relaxation and contraction, and rapid ejection intervals were used to predict LVEDP. For LVEDP intervals of <8mmHg, 8-12mmHg, 13-18mmHg, and >18mmHg, the negative predictive value was 84, 71, 54, and 87, respectively. For the same intervals, specificity was 93, 74, 43, and 87, respectively. However, sensitivity and positive predictive value were poor.

This is the first study to demonstrate high specificity and negative predictive value for deriving LVEDP using SCG in a blinded analysis. However, considerable variability in our results suggests more research with a larger sample size is needed. This research provides a theoretical framework for future efforts to obtain hemodynamic parameters using SCG.

Max Bodnarchuk (Dr. Julian Tam)

Contribution of the pulmonary ionocyte to the process of mucocilliary clearance for the treatment of cystic fibrosis

Pulmonary ionocytes are a recently discovered cell type believed to play a role in the pathogenesis of cystic fibrosis (CF). It has been shown in animal models that while ionocytes comprise less than 1% of the total airway, they are responsible for approximately 60% of the total CFTR dependent ion flux [1]. Our lab has previously discovered that pulmonary ionocytes are responsible for the regulation of airway surface liquid (ASL) pH, and abnormalities in this mechanism result in acidic and dehydrated ASL [2]. Based on this observation, we believed that this would negatively impact the antimicrobial properties of the ASL and the ability to clear the airways. This project sought to quantify the effect of inhibiting ionocytes on the efficacy of mucocilliary clearance. We measured mucociliary clearance using dissected wild-type (Cftr +/+) swine bronchioles, and ionocyte inhibition was accomplished using the potent anion exchange inhibitor 4,4′-diisothiocyano-2,2′-stilbenedisulfonic acid (DIDS). Our results showed that DIDS had a significant inhibitory effect on mucociliary clearance rates ($p = 0.0015$) as compared to the control group. Based on this finding, we conclude that the pulmonary ionocyte plays a role in maintaining the normal functioning of mucociliary clearance.

Jay Patel (Dr. Anand Krishnan)

Exploring the Role of Autonomic Neurotransmitters in Androgen-Deprivation Induced Neuroendocrine Prostate Cancer

Neuroendocrine Prostate Cancer (NEPC) is a lethal and highly metastatic subtype of prostate cancer (PC) that arises due to neuroendocrine differentiation (NED) of PC cells. Although the exact underlying mechanism transitioning PC to NEPC is unknown, anti-androgen therapy resulting in androgen deprivation is a well-known trigger for NEPC. The PC cells undergoing NED display increased neurite-like outgrowth and express NED markers, such as, Chromogranin-A, Neuron-Specific Enolase, and Synaptophysin. Innervation of prostate tumors by sympathetic and parasympathetic nerves promotes prostate cancer growth via the neurotransmitters, Norepinephrine (NE) and Acetylcholine (ACh). In this study, we examined if these neurotransmitters promote NEPC in androgen-deprived conditions. We cultured LNCaP cells with Testosterone+ACh or Testosterone+NE or Testosterone+ACh+NE for 14 days, followed by Testosterone deprivation for 48 hours or 72 hours. Bright-field imaging showed increased neurite-like outgrowth in ACh groups. RT-qPCR analysis showed variable expression across neuroendocrine biomarkers with CHG-A significantly upregulated in ACh groups. Overall, this study suggests that parasympathetic signaling driven by ACh has the potential to promote androgen-deprivation induced NEPC.

Annika Dixon (Dr. Michael Levin)

pFlareA reporter does not detect exon skipping due to dysfunctional hnRNP A1

Heterogeneous nuclear ribonucleoprotein A1 (A1), a protein that modulates RNA splicing, is dysfunctional in multiple sclerosis (MS) neurons. Our lab has shown that alternative splicing (AS) changes mediated by dysfunctional A1 mechanistically contribute to the pathogenesis of MS. To test whether exons in transcripts of interest (EOIs; from Macf1, Klc1, Baz2b) identified by RNAseq are alternatively spliced, EOIs and their flanking regulatory regions were cloned into a pFlare reporter plasmid, where red fluorescence indicates EOI retention and green fluorescence indicates EOI skipping. Neuro2a cells co-transfected with each pFlare plasmid and either wild-type A1 or a dysfunctional mutant A1 did not reveal a significant difference in AS in any of the targets of interest, suggesting that either dysfunctional mutants do not fully model MS-associated A1 dysfunction, or the EOI and flanking regions in pFlare did not encompass regions regulated by A1. Thus, we will next (1) validate the AS events using a PCR-based assay, (2) test our pFlares in a loss-of-function model of A1 dysfunction, and (3) mutate the putative A1 binding sites in the pFlare plasmids. Together these will validate both the observed events and the pFlare experimental system for future studies exploring AS, A1 dysfunction, and MS.

Ethan Done (Dr. Jo-Anne Dillon)

Characterizing the SHARP PCR Helicase

Helicases are replicative enzymes that unwind duplex DNA (dsDNA) that are powered by Adenosine Tri-Phosphate (ATP) hydrolysis. Plasmid Copy Number Reduction (PcrA) is one such helicase. Recently, a super helicase called PcrA M6 was engineered from the thermostable PcrA of Geobacillus stearothermophilus. This helicase features a stabilized active conformation due to the translation of a disulfide bond. The speed of this enzyme makes it compatible with novel diagnostic and sequencing techniques, namely, SSB-Helicase Assisted Rapid Polymerase Chain Reaction (SHARP PCR). While it was initially reported that disulfide bond stabilization is spontaneous, some researchers, including Dr. Taekjip Ha, have questioned this and suggested an additional crosslinker is needed. To address this uncertainty and the lack of clear protocols, this study presents an optimized method for purifying PcrA M6 using nickel affinity and ssDNA affinity chromatography. To confirm PcrA M6 activity, a Fluorescence Resonance Energy Transfer (FRET) DNA unwinding assay was used to visualize dsDNA unwinding.

Maheen Zafar (Dr. Michael Wu)

Tissue and temporal requirement of the Integrator in C. elegans development

The integrator is a protein complex that is involved in the maturation of small nuclear RNAs. To investigate the importance of the integrator in C. elegans, CRISPR/Cas9 genome editing was utilized to attach an auxin-inducible degradation (AID) tag to a subunit of the integrator loci which when accompanied with the auxin receptor protein TIR1 in the presence of auxin, resulted in its degradation. Previously, the ubiquitous expression of the TIR1 protein in the presence of auxin resulted in significant developmental defects in C. elegans. In this study we hypothesized that systemically expressing TIR1 protein in major C. elegans tissues (hypodermis, intestine, muscle and neurons) in the presence of auxin would reveal the tissue for which the integrator is most critical. Approximately 100 age synchronized worms were grown on solid NGM plates of varying concentrations of auxin (0,1, 2 and 4 mM). The worms were imaged 24, 48 and 72 hours after auxin exposure using a stereomicroscope. The body lengths were measured in ImageJ. The results demonstrated that degrading the integrator complex in the muscle, hypodermis and intestine leads to significant developmental defects by the 72-hour mark. Degradation of the integrator in the neurons did not lead to significant developmental defects.

Eric Luo (Dr. Jenny Wachter)

Investigating the prophylactic potential of Borrelia burgdorferi outer membrane vesicles

The causative agent of Lyme disease, Borrelia burgdorferi (Bb), is responsible for the most prevalent tick-borne illness in the Northern Hemisphere. Bb exists in an enzootic cycle, transitioning between an Ixodes tick vector and vertebrate hosts. These environments require Bb to express different surface-exposed proteins to allow for survival in the tick and vertebrate host, which includes persistent infection. Bb has been shown to produce outer membrane vesicles (OMVs) in vivo and in vitro. However, during in vitro culture, Bb typically expresses genes involved in survival in the tick vector. We used a strain we recently developed that produces large amounts of OMVs and over-expresses proteins involved in vertebrate infection through the induction of the alternative sigma factor RpoS. Our results from mass-spectrometry and western blot showed that when RpoS is induced, BbOMVs contain outer-surface proteins such as OspC, which is vital for vertebrate infection. OspA, a tick specific protein, was detected in BbOMVs during RpoS over-expression. As OspA, along with other tick-specific proteins can induce autoimmune pathologies, we engineered suicide vectors to knock out ospA, ospD, and napA and vlsE which is required for persistent infection. These findings will help further studies to determine the prophylactic potential of BbOMVs.

Rylan Bahrey (Dr. Aaron White)

Using Transposon Sequencing to identify genes involved in Salmonella survival

Gastroenteritis causing Salmonella were recently ranked as the most significant food borne pathogens in terms of global disease impact. 'Survival in' and 'Transmission from' water sources are known to be important for the pathogenic success of gastroenteritis-causing Salmonella. A Tn-Seq library in S. Typhimurium 14028 was generated and will be used to identify Salmonella genes that are important for survival in water. Tn-Seq works on the principle that an entire population of knockout mutant strains ('a transposon library') can be tracked and quantified using Illumina DNA sequencing. This was done by using an E. coli donor strain with a transposon-delivery plasmid, that upon mating with S. Typhimurium 14028, generated a saturated transposon library. Prior to the water survival experiment, even distribution of mutants will be confirmed by sequencing. A culture of the Tn-Seq library will be inoculated into water and characterized on Day 1 as the "input" library. On Day 42, the population of surviving cells (~10%) will be analyzed by sequencing and compared to the starting input. Performing this sequence comparison on multiple replicates will allow us to identify mutants that are consistently missing from the Day 42 samples, versus strains that are missing due to chance.

Allison Novecosky (Dr. Wei Xiao)

Dissecting Rad5 Functions in DNA-damage Tolerance through protein-protein interaction network

DNA damage tolerance (DDT) promotes survival in eukaryotic cells despite damage to their genetic material. Within the DDT pathway, stalled replication forks result in monoubiquitination of proliferating cell nuclear antigen (PCNA) by the Rad6-Rad18 complex, and monoubiquitinated PCNA can be further polyubiquitinated by the Mms2/Ubc13-Rad5 complex to promote error-free lesion bypass. Recent research in our laboratory indicates that both E3 ligases Rad5 and Rad18 share a novel PCNA-binding motif; however, only Rad5 preferentially binds monoubiquitinated PCNA. The goal of this research is to map the Ub-binding motif within Rad5 to better characterize Rad5's preferential binding to monoubiquitinated PCNA. Yeast two-hybrid assays were used to determine the strength of interaction between Rad5 and various Rad5 truncations with PCNA and ubiquitinated PCNA. Rad5 truncations showing preferential binding of Ub-PCNA are thought to contain a Ub-binding motif. Rad5-N431 consistently showed preferential binding for ubiquitinated PCNA at a degree indistinguishable from intact Rad5, suggesting that Rad5's Ub-binding motif is located within the N-terminal 431 amino acids. Furthermore, Rad5 truncations containing aa31-431 and aa100-431 show interactions comparable to that of intact Rad5 or Rad5-N431. Further assays showed that the Rad5 truncation containing aa80-160 binds ubiquitin alone, indicating that this region contains Rad5's Ub-binding motif.

Maria Zafar (Dr. Yuliang Wu)

Role of DDX41 Helicase in MDS/AML through P-bodies and Stress Granule Formation

DDX41 (DEAD-box helicase 41) is an RNA helicase required for essential aspects of RNA metabolism including ribosome biogenesis, pre-mRNA splicing, and translation. Mutations in DDX41 are linked to blood cancers, myelodysplastic syndrome (MDS), and acute myeloid leukemia (AML). Despite clinically reported increases in DDX41 mutations, the mechanisms resulting in MDS/AML remain unclear. Processing (P)-bodies and Stress Granules (SG) are organelles composed of RNA that play a role in regulating mRNAs under environmental stress. Wu lab has recently found that P-body formation is associated with DDX41, here we investigate the role of DDX41 in the formation of both P-bodies and stress granule formation. Using immunofluorescence and Western blot, we found that DDX41 is required for P – bodies formation but not for stress granules. This was indicated by a significant reduction in PB marker expression, whereas SG marker expression was not significantly affected. Using a GFP-tagged P-body marker (4-ET), we determined that DDX41 may play a role in mRNA splicing of P – body genes, which may be the potential mechanism behind changes in P-body dynamics. Further research is required to elucidate the precise mechanism linking mutated-DDX41, P-body dynamics, and MDS/AML.

Enrique Aburto Arreguin (Dr. Jessica Sheldon)

Investigating mechanisms of environmental persistence in clinical isolates of Acinetobacter baumannii

The bacterium Acinetobacter baumannii has gained notoriety over recent decades as a major cause of antibiotic-resistant nosocomial infections. The prevalence of A. baumannii here can be attributed to its ability to survive harsh conditions characterized by desiccation and exposure to commonly used biocides. Here, A. baumannii can readily survive on various medical devices such as breathing tubes, feeding tubes, and catheters — subsequently causing infections, particularly in immunocompromised patients and those experiencing extended hospital stays. Although this may explain the existence of A. baumannii reservoirs in hospitals, direct assessment of clinical isolates' ability to withstand various stressors is lacking in the literature. We hypothesized that the clinical isolate survival under biocide exposure is due to expression of factors not present in historical laboratory strains of the bacterium. Antibiotic susceptibility assessments of 10 isolates showed varying degrees of resistance, including two isolates that were resistant to last-resort carbapenem antibiotics. Growth analyses with ethanol, bleach, and benzalkonium chloride showed no substantial survival differences between clinical isolates and laboratory strain AB17978 when comparing within biocide concentrations. Whole-genome sequencing showed a conservation of 4/5 identified biocide resistance genes amongst isolates and AB17978. Future experiments will involve generating mutants in identified genes to assess individual contributions to biocide resistance.

Jing Liu (Drs. Ahmed Mostafa, Fang Wu & Cody Lewis)

Personalized Medicine: The effect of tacrolimus level on kidney allograft rejection outcomes

Study in Manitoba (Wiebe et al.) showed that kidney transplant patients who develop donor-specific antibodies (DSA), commonly associated with antibody-mediated rejection (AMR), exhibit lower tacrolimus trough levels compared to patients without DSA. This retroactive study investigates whether lower tacrolimus levels are correlated with AMR or cell-mediated rejection (CMR). Tacrolimus results from 329 patients were pulled from the laboratory information system [(LIS), SoftLab] from 2012 to 2024. Patients were grouped as AMR, CMR, and no evidence of AMR or CMR based their renal biopsy reports. Median tacrolimus levels were calculated at 0-3, 4-6, and 10-12 months post-transplant, and 6 months before the first documented AMR or CMR. No significant differences were found in the median tacrolimus levels during the first year of treatment, suggesting no significant impact on rejection. However, in the 6 months leading up to the development of AMR, patients had lower tacrolimus levels compared to those who did not develop AMR ($P < 0.05$, Šídák's multiple comparisons test). No differences in tacrolimus levels were observed in patients with or without CMR. Findings were consistent with the Manitoba study, suggesting that lower tacrolimus trough levels may be a predictor for AMR development.

Erica Andres (Dr. Aaron White)

Purification of the Bacterial Amyloid Curli from Escherichia coli

Neurodegenerative diseases (ND) are a class of disorders that feature the accumulation and aggregation of normal human proteins, called amyloids, in the central nervous system. ND is highly prevalent with 1 in 6 individuals becoming affected. Salmonella and E. coli are pathogenic bacteria that are able to form biofilms in the digestive tract. One component of these biofilms is the protein curli. This protein has a similar structure to human amyloid beta, the amyloid plaque that accumulates in the brain of Alzheimer's patients. Work in our lab has shown that Salmonella curli can interact with human amyloid beta peptides, causing aggregation. Our hypothesis is that E. coli curli behaves similarly. As over 95% of the population has E. coli in their gut, this could have significant implications for the progression and frequency of ND. In order to run assays to test our hypothesis we need to purify E. coli curli, a process that had only been done in Salmonella thus far.

Jian Park (Dr. Jeff Dong)

Investigating the Response of Macrophages to Oxidized Phosphatidylcholine in the Context of Trem2 Expression

Multiple sclerosis (MS) is a chronic neuroinflammatory disease characterized by demyelination and neurodegeneration in the central nervous system (CNS). At steady state, axons are myelinated by sheaths of lipids that aid in electrical conduction but during MS the oxidation of myelin associated lipids can lead to the production of cytotoxic molecules such as oxidized phosphatidylcholines (OXPC). Our previous research found OXPC elevation in MS lesions and OXPC injections into the spinal cord white matter of mice induced lesions containing clusters of microglia/macrophages, innate immune cells. Triggering receptor expressed on myeloid cells 2 (TREM2) is a lipid sensing receptor expressed by myeloid cells including macrophages. Previous literature has shown TREM2 expressing microglia better protects neurons from OXPC-mediated neurotoxicity than TREM2 knockout microglia in vitro, potentially indicating the role of TREM2 in OXPC neutralization. Yet, how microglia/macrophages respond to OXPC-induced lesions requires further investigation. To assess the response of microglia/macrophages to OXPC, we stimulated microglia/macrophages in vitro with OXPC and observed cellular changes over 20 hours in a live cell imager. Over the period of 20 hours, we observed changes in cellular morphology, cell death, and increase in lipid peroxidation in OXPC treated macrophages.

Griffin Lehnert (Dr. Jo-Anne Dillon)

IMethods for Investigating Critical Cell Division Proteins in Neisseria gonorrhoeae

FtsI is a critical cell division protein in Neisseria gonorrhoeae (Ng) and the primary target of β-lactam antibiotics. Previous studies in the Dillon laboratory found four conserved amino acid residues in the uncharacterized N-terminus of FtsI. Single substitution mutations at these residues not only disrupt the interaction between cell division proteins FtsI and FtsW, but also alter FtsI's affinity for penicillin.

The objectives for this project were to develop methodologies to: 1) transform host Ng cells with FtsI mutations and 2) overexpress and purify FtsW by nickel-affinity chromatography.

The agar spot transformation method was validated by transforming a streptomycin susceptible Ng isolate with Ng DNA containing streptomycin resistance markers. As a result, transformants gained high streptomycin resistance. In testing multiple protocols, I have begun optimizing the isolation and purification of FtsW. Interestingly, through bioinformatic analysis of FtsW, two potential transcription start sites were identified. While long and short transcripts been observed in Escherichia coli FtsW, these dual start sites have never been described in Ng. Further investigations into their functionality and transcription in vivo are still required.

This project not only established protocols for future Ng cell division studies, but also elucidated previously undescribed start sites in FtsWNg.

Darby Liebrecht (Dr. Peter Pioli)

Sex and Age Differences in Thymic B Cells

T cells are white blood cells that destroy harmful pathogens. When a pathogen is encountered, the T cell becomes activated and aids in the immune response. To ensure proper functioning of T cells, they undergo negative selection with the help of B cells. Upon activation, thymic B cells can differentiate into antibody-secreting cells (ASCs). If autoreactive, these ASCs secrete pathogenic autoantibodies against self-antigens, as seen in many autoimmune diseases such as myasthenia gravis. Autoimmune diseases are heavily skewed towards females and display age of onset differences, which raises the question of how these two variables affect thymic B cells. To answer this question, the spleen and thymus were extracted from young and old male and female mice and examined using flow cytometry.
Our experiments revealed a decreased in thymic CD38 of old male and female mice in Germinal Center B cells (GCBs) compared to their younger counterparts. We also observed increased CD11c in the thymus of old female mice compared to young female mice. Male mice, however, did not display any age-related differences. Lastly, we noticed an increase in thymic Ki-67 and BCL-6 in GCBs of male and female mice.

Francisca Lopez Molina (Dr. Jeffrey Chen)

Verification of the genetic determinants of acid pH-mediated control of Mycobacterium tuberculosis type-7 ESX-1 secretion activity

The Type VII ESAT-6 secretion system 1 (ESX-1), spanning the cell envelope of Mycobacterium tuberculosis (M. tb), is a key virulence factor involved in evading and modulating the host immune response. It facilitates the secretion of multiple proteins, including the highly immunogenic proteins EsxA and EsxB. Wild type M. tb possesses the ability to reversibly suppress secretion of EsxA and EsxB when exposed to acid pH (<5). An M. tb transposon mutant library screen showed that interruption of four genes (mgtC, Rv1894c, sugI, fadE20) renders M. tb unable to cease secretion in acid pH. Four constructs consisting of a functional copy of these genes were cloned into a vector (pNBV1) using PCR and restriction enzyme cloning, to complement the M. tb transposon mutants and assess whether these genes are responsible for their ability to sense pH changes and halt secretion. Three constructs (Rv1894c-pNBV1, sugI-pNBV1, fadE20-pNBV1) were successfully made and verified by whole plasmid sequencing. These were electroporated into M. tb transposon mutants, but due to the slow-growing nature of Mycobacterium species, the transformants are currently growing. Immunoblot analysis of culture supernatant proteins secreted by the complemented mutants in acid pH will be used to assess reversion to the wild-type phenotype.

Diya Patel (Dr. Oleg Dmitriev)

Investigating the metal binding properties of MEMO1

MEMO1 is an evolutionarily conserved protein involved in various biological processes, notably playing a crucial role in breast cancer cell metastasis, as demonstrated in both in vivo and in vitro studies (MacDonald et al, 2014). Recent findings suggest that MEMO1 binds to both iron and copper in vitro (Dolgova et al, 2024). However, during MEMO1 purification, the affinity chromatography column turned pink-a phenomenon not observed with the C244S mutant, which is unable to bind metal. It was hypothesized that this colour change was due to MEMO1 forming a complex with either cobalt or manganese, the two biologically significant metals that commonly form pink-coloured complexes. To test this hypothesis, both MEMO1 and the C244S variant were purified using affinity chromatography, and the protein-metal complex containing fractions were analyzed using inductively coupled plasma mass spectrometry (ICP-MS). With the purified protein, metal binding assays using UV-Vis spectroscopy were also conducted. However, no significant shifts in the absorbance peaks were detected, indicating that MEMO1 may not bind manganese or cobalt as initially hypothesized.

Osman Badawi (Dr. Lalenthra Naidoo)

The Effect of the COVID-19 Pandemic on Head and Neck Abscess Admissions: A Retrospective Chart Review

Objective: During the COVID-19 pandemic, otolaryngologists noticed a rise in head and neck abscess cases, though limited research exists on this trend. This study examined whether the pandemic influenced abscess cases by reviewing patient records from Jim Pattison Children's Hospital (JPCH) and Royal University Hospital (RUH). The goal is to identify changes in prevalence and inform future healthcare strategies.

Methods: A retrospective review of patient charts from March 1, 2017, to February 28, 2023, was conducted using the SCM database. ICD-10 codes identified cases of head and neck abscesses, and data on patient demographics, COVID-19 and vaccination status, diagnosis, treatment, and admission were recorded. Diagnoses were verified via hospital notes. A t-test compared incidence rates before and after the pandemic.

Results: Abscess rates rose from 4.96 E-3 pre-pandemic to 5.86 E-3 post-pandemic, but the increase was not statistically significant. No significant differences were seen across age or gender. The largest difference was between the year before (4.93 E-3) and during the pandemic (7.13 E-3), a statistically significant increase.

Genevieve Dietrich (Dr. Ernesto Figueiro)

Perinatal outcomes associated with Placental Growth Factor (PlGF) assessed in pregnant patients from 12w-20w6d gestational age, in a population with high prevalence of Diabetes

Purpose: This study aimed to investigate the association between placental growth factor (PlGF) levels and the occurrence of adverse maternal and fetal outcomes during the first 21 weeks of pregnancy.
Methods: Data were collected from women receiving care between June 2022 and August 2024. Patients were followed throughout their pregnancy and delivery. PlGF levels, maternal diabetes status, and pregnancy outcomes were recorded. PlGF levels were interpreted based on gestational age, according to previously established criteria. Adverse outcomes were defined as preterm birth before 37 weeks of gestation, preeclampsia, intrauterine growth restriction (IUGR), and low birthweight.
Results: Data was collected for 57 women. Women with low/very low PlGF levels had a higher prevalence of Type 2 Diabetes (44% vs 10%). While rates of preterm birth were higher in the low/very low PlGF group (56% vs 29%), the difference was not statistically significant. Only one case of IUGR was reported during the study period. Low/very low PlGF levels were significantly associated with preeclampsia (p=0.03; NPV=95.23%).
Conclusion: Low PlGF levels in the first 21 weeks of pregnancy can aid in the prediction of preeclampsia. Inclusion of PlGF screening into early pregnancy assessments could enhance the prediction of adverse pregnancy outcomes.

Eric Wang (Drs. Pouneh Dokouhaki, Ahmed Mostafa, Cody Lewis & Fang Wu)

Utilization of in silico analysis for prediction of graft failure in kidney transplant

In kidney transplantation, HLA epitope mismatch based on high resolution HLA sequencing provides an advantage for risk stratification. We had analysed HLA surface epitopes to evaluate immunological compatibility between donors and recipients. Now, we explore how T-cell epitopes, and the indirect pathway are involved in graft rejection.

Methods: We obtained HLA and pathology data from 613 patients followed post renal transplant in Saskatchewan. Analysis for mismatch scores were calculated through HLAMatchmaker and PIRCHE. Banff criteria were extracted from renal biopsy reports.

Results: Overall and locus specific HLAMatchmaker and PIRCHE scores are correlated with DSA formation ($p=0.003$). CMR is more common than AMR ($p=0.0151$) and tends to occur earlier following transplant. Significant risk cutoff for Matchmaker scores were found at the following loci: A=14.5, B=11.5, C=8.5, DR345=7.5, DQ=10.5 and total 54.5 ($p<0.05$). PIRCHE values were significant for the following: A=15.5, DR345=24.5, DQ=25.5, and total 118.5 ($p<0.05$). DSA free survival showed significant difference between stratified groups ($p<0.0010$).

Conclusion: HLA epitope analysis is more predictive of DSA formation than for CMR or AMR. However, patients who developed CMR, AMR, and DSA consistently had higher scores for both HLAMatchmaker and PIRCHE. Overall, there are valuable clinical applications for epitope-based analysis post-transplant with multiple immune recognition pathways playing a role.

Noah Lim (Dr. Kerry Lavender)

Indirect effects of IFNα2/14 treatment of CD4+ T cells on CD8+ T cell proliferation

The type 1 interferon (IFN) response is a critical component of innate immunity, with the ability to regulate immune functions and restrict infections. IFNα, a subtype of type 1 IFN, is produced ubiquitously by most cells, making it essential for immune response studies. IFNα consists of 12 subtypes, previously thought to have similar effects on target cells. However, recent findings reveal different infections induce the release of distinct IFNα subtypes, emphasizing the significance of subtype-specific immune modulation. This research investigates the effects of IFNα14 and IFNα2 on CD8+ T cell proliferation. Previous studies by the Lavender Lab indicated that IFNα14 had a more potent suppressive effect on CD8+ T cell proliferation than IFNα2 in total immune cells. Our study assessed whether these effects were mediated directly on CD8+ T cells or indirectly through CD4+ T cells by further isolating CD8+/CD4+ T cells from total immune cells. Using flow cytometry, results showed no significant differences in the treatment groups, suggesting IFNα's effects on CD8+ T cells are not mediated through CD4+ T cells. Variations between individual donors contributed to variability in the data, preventing statistical significance. Future research will explore mechanisms driving subtype-specific effects with potential implications for targeted therapeutic development.

Jacob Pilon (Drs. Camille Hamula & Ninad Mehta)

Determining PCR performance for detection of Staphylococcus aureus Small Colony Variants

Background: Staphylococcus aureus (SA) is a bacterium that can cause a wide range of infections, from minor skin conditions to severe, life-threatening disease. Small Colony Variants (SCVs) of Staphylococcus aureus are often associated with chronic and recurrent infections. Their altered metabolism and slow growth makes it difficult to perform conventional antimicrobial susceptibility testing.

Objective: To compare capabilities of two PCR methods (GeneXpert with the Hologic Panther System) in identifying methicillin resistance in SCVs.

Methods: Previously identified SCVs were cultured. The samples of bacteria where then processed to be analysed GeneXpert and Panther PCR systems to determine the presence or absence of the methicillin resistance gene. Their results will be compared with each other.

Results: Currently the GeneXpert has been shown to have a sensitivity of 91.9% and a specificity of 92.3% in identifying MRSA from SCVs when compared to traditional method. Results of the Panther system are yet to be determined.

Conclusions: Our data shows, that molecular methods is a viable alternative to traditional culture methods, and greatly improves the turn around time for the result.

Justin Klassen (Drs. Anil Kumar & Victoria Ansalem)

Human microproteins as dependency factors for Zika virus

Zika virus is a mosquito-transmitted human pathogen endemic to tropical and subtropical areas. Infection with Zika virus results in a flu-like illness in most cases. However, during infection in pregnant women, the virus can cross through the placenta and infect the brain of the fetus, severely affecting brain development. Currently there are no vaccines or drugs available to manage Zika infection. Like many viruses, Zika depends extensively on human proteins to successfully infect cells. Relatedly, a recently discovered group of human proteins termed 'microproteins' that are less than 100 amino acids in length have been shown to play important roles in cell cycle regulation, host signalling pathways and diseases like cancer. To assess the role of microproteins in Zika infection, we cloned CRISPR gRNA against 10 microprotein genes into lentiviral vector plasmids and used those plasmids to produce cell lines with stable microprotein knockouts. We then infected each cell line with ZIKV and used viral titration by plaque assay and qPCR methods to assess the strength of each infection relative to an unedited control. We found that 3 genes: LINC00662, ZNF599, and EMC6 appear to be dependency factors for ZIKV as their removal led to significantly less effective ZIKV infections.

Community & Indigenous Health

Kit Stern (Dr. Hassan Vatanparast)

Ground Work: Bone Health Investigations vs. Randomized Control Trials

Osteoporosis is a metabolic bone disease characterized by loss of bone mineral and increased risk of fracture. While it is understood that nutrition and physical activity can impact the development and maintenance of bone tissue the approximate dosing of important foods and modes of activity are not yet well understood. This Summer Project involved working on a well-established randomized controlled trial (RCT) and beginning the set up for another. The effects of milk and yogurt supplementation on bone health and body composition in Canadian young adults RCT was set up over the summer and seeks to perform a nutritional intervention in young adults. The Fortify Bone Study is an RCT nearing completion and involves exercise interventions of differing intensities in older adults. By elucidating increased knowledge of bone health factors across lifespan more effective recommendations can be made by health professionals. The Summer Project focused on research rigor in bone health RCTs from set up to data collection stages.

Samantha Mannala (Dr. Jacob Alhassan)

Anti-Black Racism in Canada and its Effects on Health

Anti-Black racism in Canada profoundly impacts the health outcomes of Black patients, reflecting a complex interplay of socioeconomic and environmental factors. Despite Canada's reputation as a multicultural society, systemic racism continues to influence various life aspects, including health. This scoping review aims to identify and analyze literature on the health impacts of anti-Black racism in Canada.

Search terms related to anti-Black racism, Black populations in Canada, and health were used to query multiple databases. Studies were screened for inclusion based on their focus on anti-Black racism in Canada and its effects on health, resulting in 21 studies for analysis.

Our review reveals that anti-Black racism adversely impacts Canadian Black patients in four key areas: healthcare access, mental health, noncommunicable diseases, and communicable diseases. Black patients report challenges in accessing healthcare due to prejudice from healthcare workers and denial of services. Additionally, racism contributes to poorer mental health outcomes and exacerbates noncommunicable diseases like hypertension, diabetes, and substance use, as well as communicable diseases such as HIV and COVID-19. Proposed solutions include enhanced training for healthcare workers, increasing the representation of Black healthcare workers, developing culturally appropriate mental health services, and implementing collaborative approaches to combat racism and improve health outcomes.

Kevin Entwistle (Dr. Nazeem Muhajarine)

Trust Dynamics in Health Scientists Throughout the Covid-19 Pandemic

One of the largest lasting effects of the COVID-19 pandemic has been the public's overall change in trust in scientific authorities and communications. This study aimed to investigate the evolution of public trust in scientists during the pandemic by quantifying the change and identifying factors that influenced its erosion or maintenance. These findings are part of the larger study titled the Trust Dynamics and Equity in Public Health Project, led by the Coronavirus Variants Rapid Response Network (CoVaRR-Net). The study found that age, gender, ethnicity, spirituality, place of residence, education, and socioeconomic status all had a significant connection with whether an individual experienced a change in trust in scientists since the pandemic. Further research in this project's qualitative phase will reveal areas for improvement in policy to aid the rebuilding of trust in our scientific community.

Tayah (Xinyi) Zhang (Dr. Stacey Lovo)

First Nation and Métis Peoples' Experiences Accessing Care for Neuropathic Pain

Background: Indigenous Peoples living in remote areas face many barriers to accessing healthcare. Studies on the lived experiences of neuropathic pain from perspectives of Indigenous Peoples are lacking. The goal of this phase two research was to understand First Nations and Métis experiences of neuropathic pain and accessing care, as part of a three-phase project exploring community-directed virtual care strategies for managing neuropathic pain in remote Indigenous communities in Saskatchewan.

Methods: The study used a community-based participatory action framework with the collaboration of Indigenous Elders to ensure findings are community-directed and culturally responsive. Seven individuals participated in semi-structured interviews. Interviews were audio recorded, transcribed, and analyzed using thematic analysis.

Results: The following themes were identified: 1) Accessing healthcare for neuropathic pain, 2) Barriers to healthcare and healing, 3) Communication of neuropathic pain, 4) Impact on quality of life, 5) Strength-based solutions, and 6) Thoughts on virtual healthcare.

Conclusion: First Nations and Métis Peoples living with neuropathic pain reported experiences of impersonal and inequitable healthcare. They identified culturally responsive preferences that could aid in neuropathic pain management. They offered tentative support for virtual care with caveats. Participants' voices have informed the ongoing interventional study.

Kenzie Halter (Dr. Jacob Alhassan)

From Disadvantage to Innovation: A Health Impact Evaluation of the Benefits of a Free Rural Transportation Service in Northern Saskatchewan

Social factors such as transportation are strong determinants of health. The Kikinahk Friendship Center free bus service in La Ronge is an interesting example of the positive effects transportation can have on one's health; especially for those living rurally. We interviewed 16 bus riders and 6 bus drivers to learn more about the bus's functioning, its overall impact on health, and the state of transportation in northern Saskatchewan without the bus. Data analysis thus far has revealed that the bus service had a positive impact on spiritual, emotional, physical, and mental health. Bus users used the bus for various reasons, including but not limited to, attending medical appointments and visiting family. It has provided an alternative to hitchhiking and allowed community members to save money and gain independence. Our data suggests that free transportation in a powerful vehicle for ensuring access to care, improving social participation, and supporting the mobility rights of those rendered the most vulnerable. This is important in the context of policymaking and infrastructure planning, as it has strong potential to prevent illness and disease and keep Saskatchewan's population healthy.

Terri Thunder (Dr. Benjamin Leis)

ācimok: Using Story to Improve Wrap-around Supports for Patients with Infective Endocarditis (a MENDO project)

Infective endocarditis (IE) is a life-threatening condition, often caused by bacteria, with over 60% of cases at Royal University Hospital, Saskatoon involving people who use injection drugs (PWID). PWID face significant challenges in the healthcare system, including stigma, patient-initiated discharges, incomplete treatment, and loss to follow-up. Many also experience homelessness, low socioeconomic status, and are disproportionately Indigenous. This study explored patient experiences within the healthcare system and with the multi-disciplinary endocarditis clinical pathway (MENDO), which was introduced in September 2023. Data was collected via semi-structured interviews and the participant-as-observer method, and thematically analyzed through decolonial and social justice frameworks. The analysis highlighted three levels of influence: patient, provider, and hospital. Based on this categorization, this work has identified three main areas of support that are needed to improve patient health outcomes: patient understanding and education, access to safe and secure housing, and assistance for substance use disorder through harm reduction strategies. This work informed development of patient resources, and recommendations were proposed to address other gaps that were identified. Additional work to gather longitudinal data of patients who have completed treatment with support from MENDO is needed to determine impacts on long term outcomes.

Mignon Le Roux (Dr. Nazeem Muhajarine)

Trust Dynamics in Public Health During Health Emergencies: A Scoping Review

Trust in Public Health institutions is critical for the efficacy of public health interventions. However, trust at a population level is influenced by several factors including healthcare emergencies such as epidemics and pandemics, as well as the geopolitical landscape. Due to the shift from globalization to a multipolar geopolitical landscape in combination with multiple epidemics and pandemics, it is necessary to reassess the dynamics of trust in Public Health Institutions. The proposed scoping review assesses how has the trust in public health institutions in predominantly English-speaking OECD countries (i.e. Canada, the USA, the UK, New Zealand, and Australia), changed during health emergencies with a global dimension after January 1st, 2002 and how these changes were experienced by individuals during this period. The review protocol has been registered with Open Science Framework (DOI: https://doi.org/10.17605/OSF.IO/F97Q4) and the methodology is informed by the JBI Manual for Evidence Synthesis. The protocol, search, reference cleaning, and deduplication process has been completed, while the screening, data extraction, quality assessment, and analysis are the next steps. The results of the scoping review will provide context for the conclusions of a larger ongoing nationwide study called Trust Dynamics and Equity in Public Health: A Mixed-Methods Study on COVID-19.

Wardah Mahmood (Dr. Sarah Smith)

Assessing Contraception Access and Utilization Across Saskatchewan: A Comprehensive Survey and Analysis

Contraception, including medications, devices, and methods, can help prevent unintended pregnancies, manage medical conditions, and reduce reproductive cancers. However, there is limited data on contraception access and utilization in Saskatchewan, highlighting a need for more research to inform patient-centered policies and improve health outcomes. This study used an online survey through REDCap to gather data on sexual history, pregnancy, and contraception use among female residents of Saskatchewan aged 14-49. A total of 180 completed responses were obtained from May 27 to August 6, 2024. Data analysis included descriptive statistics, chi-square tests of independence, Fisher's exact test, and software analyses using R version 4.4.1. Findings indicated that participants who had greater education levels were more likely to choose a more effective form of contraception, while patients with lower income were more likely to view cost as a barrier to accessing their preferred form of contraception. These findings highlight the potential influence of education and income on contraceptive access and choice. Future research should aim to increase sample size and demographic diversity as well as include more qualitative data in the form of in-depth interviews or focus groups. This research is critical to better understand sexual health disparities and improve reproductive autonomy in Saskatchewan.

Bobbi Bedard (Dr. Nazeem Muhajarine)

Trust Dynamics: The Effects of COVID19 on Public Trust in Medical Care Providers

Prior to the COVID-19 pandemic, public trust in medical care providers had remained generally stable, with high levels of trust being reported.1,2 However, literature has demonstrated that major global crises can shape populations' views of health personnel, leading to changes in trust.3 Given the diversity of the Canadian population and the importance of trust for vaccine uptake, this study aimed to identify sociodemographic and vaccine-related factors that may be associated with changes in trust in medical care providers during the COVID19 pandemic, and compare the effects of these variables on trust levels (increased, decreased). Data was collected from 5609 randomly selected participant aged 18-65+ across Canada via a 70-question survey. Multivariate statistical analysis revealed age, ethnocultural identity, adherence to spiritual beliefs, and place of resident to be sociodemographic factors that are significantly associated with change in trust medical care providers. Vaccination status, trust level in vaccines, willingness to receive vaccines, and beliefs about the vaccination of family members are also associated with change in trust in medical care providers. These results can help inform health professionals about subpopulations that may be more likely to experience distrust and prompt engagement with these populations to improve provider-patient relations and health outcomes.

Muheeb Khan & Kyle Carriere (Dr. Jennifer O'Brien)

Anesthesia service provision in rural settings: a scoping review with findings mapped to the Core Outcome Measures for Perioperative and Anesthetic Care (COMPAC)

Background: Anesthesia provision in rural Canada faces challenges due to a shortage of qualified healthcare professionals, impacting patient safety and equity, with additional burdens on rural patients.

Objectives: This study aimed to identify anesthesia service models in rural areas and align these findings with a Core Outcome Set for anesthesia to identify knowledge gaps.
Design: We conducted a Scoping Review using a search developed in consultation with a Health Sciences librarian. We searched three databases, imported papers into Covidence, and two reviewers performed independent screening. Data on provider, staffing model, study design, and core outcomes were extracted and analyzed.

Results: Of 2870 studies screened, 80 were included, detailing seven anesthesia models: anesthesiologists, other specialists, CRNA, family physicians (FP), family physician anesthetists (FPA), non-physician providers, and multiple providers. 46.3% had positive assessments, 35% neutral, and 18.8% negative. No model was universally superior; effectiveness depended on local resources and infrastructure.

Conclusions: Multiple models for anesthesia in rural settings exist, but their effectiveness varies with local conditions. Communities should leverage available resources to develop tailored approaches that are most likely to work for them. Future research should focus on optimizing models and addressing resource and support gaps, with an emphasis on patient-centered outcomes.

Emergency Medicine

Renae Wenzel (Dr. Brittany Ellis)

Perspectives and Experiences of Older Adults in Royal University Hospital Emergency Department

The older adult population, 65 years and older, as of 2021 make up 19% of Canada's population and have a disproportionate high use of Emergency Departments (ED) than their younger counterparts. Despite older adults frequently using EDs, EDs are not tailored to accommodate their unique needs contributing to adverse outcomes such as functional decline, hospitalization, and unplanned ED return visits. We used an electronic survey composed of questions on wait times, comfort, communication, caregivers, and accessibility to identify patient perspectives and experiences. Previous research demonstrated the importance of sensory and mobility aids for older adults who use them to enhance their stay and decrease the risk of serious adverse events, including developing delirium. We found that while 81.67% of participants wear glasses,16.67% did not have them with them, 18.33% wear hearing aids but 19.09% did not have them, 42.02% regularly wear dentures but 9.82% did not have them, and 45.83% use a mobility aid such as a cane or walker but only 18.92% had one accessible to them for the duration of their stay. The results of the survey display unique challenges the older adult population faces, and highlights potential opportunities for patient centred care enhancement, and improved outcomes.

Amy Li (Dr. Andrea Lavoie)

Sex Differences in In-Hospital Management and Outcomes of Patients with Acute Heart Failure

Acute heart failure (AHF) patients have high morbidity and mortality, yet sex-specific differences remain poorly understood. We conducted a retrospective chart review to investigate sex-based differences in clinical presentations and outcomes in 384 patients with AHF admitted to Regina General Hospital (2018 – 2023).

Among the 384 patients, 168 (43.75%) were women. Mortality at 1 year post-hospitalization (38.54%) was significantly higher than in-hospital mortality (11.71%) or mortality at 30 days (19.53%), although no sex-based differences were noted. Women more often presented with heart failure with preserved ejection fraction (HFpEF; 52.97%), while men had heart failure with reduced ejection fraction (HFrEF; 57.40%). Men presented with higher incidences of previous myocardial infarction, diabetes mellitus, renal disease, atrial fibrillation, coronary artery disease and hyperlipidemia. Men were more likely to develop in-hospital acute kidney injury and received more medications based on their comorbidities. SGLT-2 inhibitors were prescribed significantly more to men (35.48%) than women (12.72%) for HFrEF, regardless of being cornerstone heart failure therapy for both.

Despite similar mortality rates between sexes, men had more comorbidities and received more medications. SGLT2-inhibitors were found to be under prescribed in women despite their proven benefits. Future AHF guidelines should consider sex-based discrepancies in their standards of care.

Travis Black (Dr. Brittany Ellis)

Does an age modifier enhance trauma triage for older people who suffer major trauma?

Older people face higher risks of complications and mortality following trauma and are overrepresented among major trauma victims. Historically, trauma criteria under-triaged older patients. From 2016 to 2023, the Trauma Team at Royal University Hospital used triage criteria allowing up-triage of people over 65 from Level 2 to Level 1. Only Level 1 Trauma leads to Trauma Team Activation.

This project aimed to determine if this age modifier improved the sensitivity and specificity of trauma triage criteria for older people with major trauma. Secondary objectives included evaluating injury severity, interventions, morbidity, and mortality of older versus younger trauma patients.

A retrospective chart review of all Level 1 and 2 trauma patients at RUH ED from January 1, 2016, to December 31, 2022, was conducted. The data is incomplete, but interim analysis shows older adults were often categorized as Level 1 trauma due to age rather than physiologic or mechanistic criteria. Despite this, they had increased complications, Alternate Level of Care designations, and mortality, despite similar initial injury severity scores. Some findings may be due to the increased complexity of older trauma patients.

Tanish Patel (Dr. Sachin Trivedi)

Every Second Counts: Quantifying how much time Emergency Physicians spend on electronic medical records

Introduction: The introduction of Electronic Medical Records (EMRs) revolutionized patient care. However, their efficiency is often questioned in high-volume environments like the emergency department (ED) due to the substantial time physicians must wait for systems to load. This impacts patient flow and increase wait times in the ED. With ED visits projected to increase by 40% in the next 30 years, optimizing EMR use is essential to keep up with demands.

Methods: A time-motion study was conducted in 3 Saskatoon EDs, observing 26 staff physicians and 7 residents over 150 hours. Physician and resident perceptions of the current IT infrastructure was assessed through a survey.

Results: Overall satisfaction with IT infrastructure was low. While perceived waiting times were higher than actual, delays increased significantly during IT issues. All respondents noted that technological difficulties negatively affected their ability to provide care and see more patients. Staff and residents could see 4.38 ± 2.10 and 3.26 ± 1.32 additional patients per shift, respectively, if these inefficiencies were resolved.

Discussion: Improving EMR systems could reduce wait times, enhance patient care, and increase patient flow. Addressing these inefficiencies would optimize ED workflow and support better emergency care delivery in high-demand settings.

Kate DeVito-Porter (Dr. Brady Bouchard)

A retrospective evaluation of phenobarbital versus benzodiazepine monotherapy for alcohol withdrawal syndrome in the emergency department (the PHENOBENZ-RETRO study)

Background: A single-site retrospective study conducted in North Battleford comparing benzodiazepine (BZD) and phenobarbital (PB) treatment in alcohol withdrawal syndrome (AWS) found that phenobarbital therapy performed better or equally as well as benzodiazepine therapy1. These findings led to the release of a new order set containing both PB and BZD treatment arms. The current study constitutes a multi-site expansion of the previous study.

Outcomes: Primary outcomes include establishing the non-inferiority of PB with regards to safety and determining whether the use of PB results in shorter admission times and lower admission rates when compared to BZD use. Secondary outcomes are gauging the uptake of the new provincial order set and analyzing site differences.

Methods: A review of charts containing a primary or secondary emergency department diagnosis related to AUD or AWS with ED presentations, conducted between the order set launch and chart review date (October 2023 to present) across six sites in Saskatchewan.

Methods, Results and Conclusions: Data collection is ongoing and primary outcomes and secondary outcomes cannot be determined. Based on initial analysis, adoption of the new order set and the PB treatment arm varies widely across the province, with greatest use in North Battleford.

Wilson Li (Dr. Helen Chang)

Primary Care, Second Language: Podcast Project Phase 2

Purpose: In 2021, 18.3% of Saskatchewan's population did not speak English as their mother tongue, creating potential communication barriers in healthcare settings. The "Primary Care, Second Language Podcast Project: Phase 2" evaluated a pilot project aimed at equipping healthcare professionals with a podcast resource to enhance care for marginalized populations. Interviews were conducted to explore podcast contributors' perspectives on its impact, creation process, challenges, and sustainability.

Methods: Ten contributors involved in the podcast's creation were interviewed via Zoom for 20-30 minutes. Interviews focused on the podcast's potential to improve communication between healthcare providers and patients, the creation process and its challenges, suggestions for improvement, and sustainability beyond the pilot phase.

Results: All participants agreed that podcasts are useful for teaching essential phrases in multiple languages, augmenting patient care and trust. Challenges included finding optimal translation phrases, funding, technical difficulties, and time constraints. Suggestions for sustainability included securing resources, adding subtitles, creating simplified audio formats, and engaging community organizations.

Conclusion: Our findings demonstrate that the podcast addresses important social determinants of health, such as education, literacy, and equitable healthcare access, by bridging communication gaps between healthcare professionals and patients. Feedback from contributors will guide future project development and potential expansion.

Noor Rehman (Dr. Bindu Nair)

Evaluation of Clinical Practice Guidelines for the Screening and Management of Glucocorticoid-Induced Osteoporosis

Background: Glucocorticoid-induced osteoporosis (GIOP) is a common condition in patients on long-term glucocorticoids. Clinical guidelines for management of GIOP vary widely across organizations, leading to differences in treatment. This review aims to compare these guidelines in terms of screening and management and evaluate their quality using the AGREE II instrument.

Methods: A scoping review was conducted on guidelines from 11 clinical organizations addressing GIOP. Data was extracted from these guidelines on certain variables, including prednisone use, risk assessment, treatment indications, and pharmacological/non-pharmacological treatments. The quality of the guidelines was assessed using the six domains of the AGREE II instrument.

Results: Significant variability was found across the guidelines, including prednisone dose thresholds and treatment indications. Bisphosphonates were the most recommended first-line pharmacologic therapy but monitoring and follow up differed. AGREE II scores varied from 13% to 90%, with stakeholder involvement, editorial independence and applicability showing the most inconsistencies. Categories with the most consistency included clarity of presentation as well as scope and purpose.

Conclusion: This review highlights the need for consistency in GIOP guidelines. Standardizing recommendations could improve guideline adherence and reduce treatment differences. Future research should focus on addressing gaps and developing unified guidelines to optimize care for patients at risk of GIOP.

Laraib Fatima (Dr. Seirin Goldade)

Follow-up among postpartum patients diagnosed with hypertensive disorders of pregnancy and gestational diabetes mellitus

Hypertensive disorders of pregnancy (HDP), including gestational hypertension, pre-eclampsia, and eclampsia, as well as gestational diabetes mellitus (GDM), are linked to a higher risk of maternal cardiovascular disease (CVD) later in life. Women with HDP have double the risk of developing essential hypertension, a leading cause of heart disease and stroke. Despite these associations, there is limited guidance on optimal screening for CVD risk, treatment initiation, and management in this population.

This quality improvement project evaluated follow-up rates for patients diagnosed with HDP and/or GDM at three key postpartum intervals: 4-8 weeks, 2-12 months, and after one year. A retrospective chart review was conducted for female patients whose family doctors were at Cornerstone Medical Clinic, Saskatoon, and who delivered between January 1 and December 31, 2022. Follow-up rates were 100%, 55%, and 22%, respectively, with a 20% follow-up rate for GDM at 6 weeks postpartum.

The findings highlight the importance of postpartum care for women with HDP and GDM, and the low follow-up rates align with existing literature. A key barrier is the lack of standardized postpartum care, emphasizing the need for consolidated recommendations to improve CVD risk management.

Valiyah Khurshid (Drs. Jon Witt & Segun Oyedokun)

Assessing Criteria for International Medical Graduate (IMG) Selection and Practice Readiness in Rural Saskatchewan: A Survey-Based Investigation of Faculty Assessors and Rural Physician Leaders

Background: International Medical Graduate (IMG) Family Physicians are essential to rural Saskatchewan's healthcare. To ensure preparedness, IMGs undergo a 12-week Clinical Field Assessment through the Saskatchewan International Physician Practice Assessment (SIPPA) program. However, there is limited research regarding criteria used to select IMG Family Physicians for Practice Ready Assessment (PRA) programs.

Methods: A cross-sectional survey targeted SIPPA assessors and Saskatchewan Health Authority (SHA) rural physician leaders to understand priorities regarding recent clinical practice in selecting IMG physicians for SIPPA.

Results: Of 104 physicians, 63 completed the survey (61% response rate). A longer duration of recent clinical practice was considered a key factor by most respondents. For IMGs out of practice for < 3 years, 45% viewed 3-6 months of recent practice as sufficient, while 48% considered 6-12 months necessary for those out of practice for 3-5 years. For IMGs out of practice > 5 years, 85% of SHA leaders supported 12-24 months of recent practice compared to 51.6% of SIPPA assessors ($p < 0.05$). The study also highlighted the value of other clinical experiences in maintaining practice currency, emphasizing these roles in the selection process.

Conclusion: The findings underscore the importance of recent and diverse clinical experiences in selecting IMG Family Physicians for SIPPA.

Medical Education

Brianna Andrews (Dr. Rahul Mainra)

Development of an Organ Donation and Transplantation Pathway of Excellence for Medical Students: Step 1, A Needs Assessment of Patients, Donors, and Families

Background: Organ donation and transplantation (ODT) is a lifesaving treatment where need exceeds supply. Barriers include limited ODT knowledge and comfort amongst physicians, and inadequate ODT education for medical students. Comprehensive curricular development beginning with a needs assessment of key stakeholders, including patients and donor families with lived experience, is crucial. This project aims to understand the needs of patients and donor families that will shape the development of an ODT 'Pathway of Excellence' for medical students.

Methods: Following Kern's curricular design step 1, 17 Saskatchewan Transplant donors, recipients, and donor families participated in semi-structured zoom interviews. Qualitative thematic analysis using NVivo software identified common interview themes.

Results: Qualitative interviews revealed that medical knowledge and understanding and patient-centered communication are essential topics in ODT medical education. Medical-focused-competencies include kidney diseases and transplantation, patient processes, post-surgery care, and logistical and financial challenges. Patient-focused-competencies involve empathy and compassion, personal connection, clear communication, and advocacy. Both require engagement in practical experiences. These competencies were developed from many themes and sub-themes revealed in the needs assessment.

Conclusion: Medical knowledge and understanding and patient-centered communication are key competencies required to be knowledgeable in ODT. These findings will subsequently inform a medical education 'Pathway of Excellence'.

Tauqeer Iftikhar (Dr. Scott Adams)

Evaluating the Quality of LLM-Generated Multiple-Choice Questions in Undergraduate Medical Education: A Comparative Study Across Five Language Models

Objective: To conduct a comparative analysis of five distinct large language models (LLMs) in terms of their ability to generate high-quality multiple-choice questions (MCQs) suitable for Undergraduate Medical Education (UGME) exams.

Methods: Five state-of-the-art LLMs were used to develop MCQs based on learning objectives from the Foundations in Clinical Medicine III course of the University of Saskatchewan's UGME Program. For the preliminary evaluation, three expert medical educators assessed a total of 15 MCQs using a standardized rubric. The rubric was developed using the Medical Council of Canada guidelines for developing MCQs. The rubric evaluated the stem, correct answers, distractors, overall quality, and technical quality across several categories, each rated on a Likert scale from 1 to 5.

Results: Llama 3.1 scored the highest in multiple domains, achieving the highest mean score of 4.91 (SD ±0.20; $p = 0.006$). While other models showed strengths in specific areas, such as Claude 3.0 Opus performing well in the domain of clear correct answer and GPT-4o and Mistral Large 2 performing well in the domain of homogeneity of distractors, the overall consistency of other models showed variability across generated MCQs.

Conclusion: The performance of advanced language models like Llama 3.1 highlights their significant potential to generate high quality MCQs for educational assessment. Further research is recommended to validate these findings and explore broader applications in medical education.

Rayan Shafi (Dr. Beverly Wudel)

Assessing the Impact of HIV Continuing Medical Education on Primary Care Clinical Practices in Saskatchewan

Background: Saskatchewan has the highest incidence of HIV diagnoses in Canada. HIV care has evolved and could be well-managed by Primary Care Providers (PCPs). HIV Continuing Medical Education (HIV CME) programming was created in Saskatchewan to empower PCPs to manage HIV and prescribe antiretroviral therapy (ART).

Methods: We assessed how HIV CME impacted PCPs' clinical practices in Saskatchewan and their motivations and experiences. In Phase I, 5 HIV CME educator interviews were thematically analyzed to develop interview questions for Phase II. In Phase II, 10 HIV CME alumni were interviewed to understand motivations, outcomes, facilitators, barriers, and future education needs.

Results: Motivations included improving access to care and expanding scope of practice. Learner-reported outcomes included increased confidence in providing primary care, prescribing ART, and improved access to care for people living with HIV (PLWH). Facilitators included virtual delivery, preceptorship and mentorship. Barriers to changing clinical practice included a need for additional HIV CME, and scarcity of clinical resources. Ongoing education, quick reference materials, and HIV clinician networking opportunities were suggestions for future CME programming.

Conclusions: The PCPs reported increased confidence and improved access when providing primary care to PLWH and prescribing ART in the context of external clinical barriers to providing care.

Jade Ong-Tone & Sibtain Ali (Dr. Henry Bi)

The Misunderstood Anesthesiologist: A Prospective Cohort Study Comparing the Effectiveness of Educational Media in Preoperative Assessment Clinics

Patients often lack understanding and insight into the anesthesiologist's role on their healthcare team. This can lead to negative consequences such as poor patient experience and lack of engagement in healthcare decisions. Additionally, there is a shortage of accessible, and up-to-date educational material dedicated for patients. This study evaluated the effectiveness of different educational materials in improving patients' knowledge about anesthesiologists. A prospective cohort study was undertaken and recruited over 200 patients from the preoperative assessment clinic (PAC) at Saskatoon City Hospital over a 10-week period. Patients received one of three educational resources—physical pamphlet, video, or website—after their PAC visit. Their knowledge was then assessed using surveys at three time periods: before PAC consult (Survey 1), after PAC consult (Survey 2), and post-op (Survey 3). Early data analysis from survey responses suggests that physical media - the pamphlet – was the most effective resource for educating patients. Ultimately, all educational materials seem to enhance knowledge retention immediately after their PAC consult compared to the control. Furthermore, positive feedback on all educational materials highlights their value in patient education. Future research could explore the effect of educational material on long term retention.

Iqbal Azhar (Dr. Anurag Saxena)

Evaluation of the Quality Referral and Consultation Education (QRCE) Curriculum at the University of Saskatchewan

Introduction: The Quality Referral and Consultation Education (QRCE) course was designed to improve interprofessional communication during patient care transitions between generalist and specialist care. This study evaluates learning outcomes based on Kirkpatrick's levels 3 and 4, focusing on residents' application of referral and consultation resources and the impact of their consultation in real-world practices.

Methods: Ten residents participated in semi-structured virtual interviews. Questions revolved around experiences, impacts, challenges, and improvements. Transcripts were analyzed using thematic analysis.

Results: The QRCE curriculum helped residents develop a structured approach to consultations. Templates, checklists, and anticipation of consultant needs were highlighted as valuable tools. While participants noted an increase in efficiency and confidence, some challenges remain, including systemic barriers such as variability in expectations across specialty services as well as a lack of practice cases in the course itself. Overall, the improvements in consultation processes were recognized as potentially beneficial, but their direct impact on patient outcomes remains difficult to quantify.

Conclusions: The findings support the QRCE curriculum's positive influence on improving communication and enhancing the quality of patient care transitions. Ongoing training, including refresher courses for senior residents and better alignment of referral expectations across specialties has been recommended.

Zili Zhou (Dr. Scott Adams)

Identifying Educational Competencies for Artificial Intelligence in Radiology

Objective: The integration of artificial intelligence (AI) in radiology may necessitate a fundamental shift in the competencies expected of radiologists. There is currently a lack of understanding on what AI-related competencies radiology residency programs should incorporate. This study aimed to identify what knowledge, skills, and attitudes are important for radiologists to use AI safely and effectively in clinical practice.

Methods: Following Arksey and O'Malley's methodology, a scoping review was conducted by searching PubMed, Embase, Scopus, and ERIC for articles published between 2010 and 2024. Two reviewers independently screened articles based on title and abstract, and full text review. Data was extracted using a standardized form to identify the knowledge, skills, and attitudes that may be important for the safe and effective use of AI.

Results: Of 8,945 articles screened, 47 articles were included. Core competencies were related to AI model development, evaluation, clinical implementation, algorithm bias and handling discrepancies, regulation, ethics, medicolegal issues, and economics of AI.

Conclusion: Current AI educational programming in radiology demonstrates substantial heterogeneity. Further research is needed to develop consensus on the core AI-related competencies for radiologists, to support integration of AI training and assessment into radiology residency programs.

Kailee Skinner (Dr. Niels Koehncke)

Ergonomic Risk of Abdominal Ultrasonography in Veterinary Radiology Workers

Musculoskeletal symptoms related to work activities are reported by 65-91% of human patient medical sonographers performing ultrasounds. Data on the injury risk of veterinary ultrasound only exists in the form of self-reported questionnaires; there is no observational data to support perceived ergonomic risk. This observational study is designed to investigate the level of ergonomic risk associated with veterinary ultrasound by generating ergonomic risk scores using AI-powered commercial software (Tumeke Ergonomics). An action level based on a RULA (rapid upper limb assessment) score, and a safety rating based on the RHSI (revised hand strain index) score were generated from 95 videos of a convenience sample of veterinary sonographers. Risk factors for musculoskeletal injury risk were examined by evaluating individual scores for the 7 main organs scanned during abdominal ultrasound sessions. Risk of long-term musculoskeletal symptoms were identified for all ultrasounds; 41% required possible changes to practice, 55% required change soon, and 4% required change immediately. Unsafe hand strain indices were identified for 19% of ultrasounds and were significantly associated with scanning of the right adrenal gland of the patient (57% of right adrenal gland scans, $p<0.001$).Our findings suggest that veterinary ultra-sonographers face significant musculoskeletal injury risk related to their work.

Hasan Jamil (Dr. David Leswick)

Climate-Conscious Radiology: A Mixed-Methods Saskatchewan Study

Radiology contributes to the climate crisis, generating up to 1% of global greenhouse gas (GHG) emissions. Knowledge of medical imaging's carbon footprint is a precursor to effective action. Patient commute is often overlooked yet is a significant source of emissions. This was a two-part study. The first was assessing radiologists' and radiology residents' knowledge and attitudes on radiology's environmental impact. The second analyzed GHG emissions saved by patients attending rural ultrasound clinics. A survey was distributed via SurveyMonkey to all Saskatoon radiologists and radiology residents which evaluated knowledge and attitudes regarding climate change. A separate survey was distributed to the patients of two rural Saskatchewan ultrasound clinics to assess commute. Radiology staff and residents displayed moderate understanding of radiology's and healthcare's contribution to climate change. 87% agreed slowing climate change should be a top priority, whereas only 47% agreed it is currently a top priority for society. Younger respondents rated current societal priority of climate change lower than their older colleagues. Through rural ultrasound clinics, the average traveler saved 184 km and almost 2 hours of time. Extrapolated to every clinic visit over a year, the total travel saved would be 1.9 million km or 384 tons of CO2.

Ismail Kamel (Dr. Steven Machtaler)

Imaging Cisplatin-Induced Acute Kidney Injury Using Ultrasound Molecular Imaging

Cisplatin is a commonly used chemotherapeutic for the treatment of cancers of the bladder, ovaries, and testes. Nephrotoxicity is the major dose limiting side effect from cisplatin usage and manifests in the form of Acute Kidney Injury (AKI) in patients. AKI affects about 30% of patients undergoing treatment under cisplatin. The goal of this project was to develop a model tracking the development cisplatin-induced AKI in FVB mouse using three different doses of 7mg/kg, 10mg/kg, 15mg/kg. Each mice group was given one weekly intraperitoneal injection over the course of four weeks and monitored daily to track their weight progression and condition. Masson's Trichrome and H&E staining was performed on histological samples from harvested kidneys to be imaged and analyzed later for inflammation and fibrosis from tubular damage. The histological samples indicate a progression in AKI with the increased dosage as expected. Following this model, later experimentation for the future can test to see if utilization of ultrasound molecular imaging and kidney-safe contrast agent microbubble could potentially detect the damage before normally used clinical tests such as GFR measurements.

Sierra Leonard (Dr. Scott Adams)

Comparing Artificial Intelligence and Traditional Regression Models in Lung Cancer Risk Prediction

Purpose: To compare the performance of traditional regression models and artificial intelligence (AI)-based models in predicting future lung cancer risk.

Methods: A systematic review and meta-analysis were conducted with reporting according to PRISMA guidelines. We searched MEDLINE, Embase, Scopus, and CINAHL databases for studies reporting the performance of AI or traditional regression models for predicting lung cancer risk. Two researchers screened the articles and a third researcher resolved any conflicts. Model characteristics and predictive performance metrics were extracted. The quality of studies was assessed using the PROBAST tool. A meta-analysis was conducted to assess the discrimination performance of AI and traditional regression models, based on area under the receiver operating characteristic curve (AUC).

Results: One-hundred-forty studies met the inclusion criteria including 185 traditional regression and 64 AI-based models. The pooled AUC of external validations of AI models was 0.82 (95% confidence interval [CI], 0.80-0.85), while the pooled AUC for traditional regression models was 0.73 (95% CI, 0.72-0.74). In a subgroup analysis, AI models which included low-dose CT had a pooled AUC of 0.85 (95% CI, 0.82-0.88). Overall risk of bias was high for both AI and traditional models.

Conclusion: AI-based models, particularly those using imaging data, show promise for improving lung cancer risk prediction over traditional regression models, although the latter remain more extensively validated. Future research should focus on multi-center prospective validation of AI models and direct comparisons with traditional methods in diverse populations.

Rowen Greene (Dr. Dean Chamberlain)

Tumoroid model undergoes developmental reprogramming that drives chemotherapeutic resistance

The tumor microenvironment (TME) consists of a unique biochemical signature that plays a significant role in cell proliferation, invasion, and metastasis in solid tumors. The development of hypoxia is a common phenomenon within the TME, that shapes the metabolic and signaling landscape of solid tumors. The work presented here utilizes a novel three-dimensional tumour model known as tumoroids, which are small, 2mm-long units of collagen containing a cancer cell line. Hypoxia has previously been shown to develop naturally in the model due to condensation caused by rapid proliferation within days of fabrication. By embedding triple negative breast cancer cells in the model, this project aimed to determine how drug resistance could be linked to the development of hypoxia within tumoroids as they condensed. Through the use of confocal imaging, hypoxic changes were tracked and aligned with protein level changes detected through western blot. This foundational work demonstrated that gene expression is consistently altered throughout the course of tumoroid development, indicating that the model has promising applications for studying TME dynamics in future projects.

Harmony Grainger (Dr. Franco Vizeacoumar)

Validation of genetic vulnerabilities of telomerase-overexpressing ovarian cancers

Ovarian clear cell carcinoma (OCCC) is a subtype of ovarian cancer, representing 10-13% of cases. It commonly involves activating mutations in the telomerase reverse transcriptase (hTERT) promoter, leading to its overexpression, aiding tumorigenesis (1). hTERT overexpression is common in 85-90% of cancers, making this a promising therapeutic target (2-9). This project uses a genetic approach called synthetic dosage lethality (SDL) to indirectly target hTERT overexpression. Specifically, where secondary gene inactivation becomes lethal to cancer cells only when hTERT is overexpressed. The hypothesis is that genes whose loss-of-function causes lethality, only when hTERT is overexpressed, represent targetable vulnerabilities in OCCC tumors. Using CRISPR/Cas9 and shRNA screens, the entire genome was screened to identify SDL targets specific to telomerase-overexpressing cells (11-14). Seven target genes identified in the previous screen were individually knocked down in four hTERT-overexpressing cancer cell lines and four control cancer cell lines (using alternative lengthening of telomere mechanism). Clonogenic assays were performed to assess cell growth, viability, and clonogenicity. Among the identified genes, three (ENO2, PACSIN1 and AK7) showed selectivity for impairing cancer growth in hTERT-overexpressing cell lines. This study provides new insights into potential therapeutic targets for OCCC and for the development of novel cancer therapies.

Omar Hafez (Dr. Osama Souied)

Retrospective Analysis of Metastatic EGFR Mutant Lung Cancer Patient Outcomes in the Province of Saskatchewan

Lung cancers continue to be one of the most prevailing and deadly forms of cancer worldwide. This retrospective study intends to investigate the outcomes of lung adenocarcinoma patients in the province of Saskatchewan, with a focus on epidermal growth factor receptor (EGFR) mutated lung adenocarcinomas, specifically within the population of Canada from 2015 to 2023.

Our objective is to study real-world outcomes of lung adenocarcinomas with EGFR mutations and determine their overall survival. Furthermore, different factors affecting prognosis such as age at diagnosis, presence of brain metastasis, smoking history, type of treatment, and Osimertinib use were reviewed. We hypothesize that Saskatchewan has less incidence and prevalence of EGFR mutated lung cancer as EGFR mutant lung cancer is more common in Asian populations.

315 patient charts were reviewed in the study, excluding patients treated with Osimertinib as an adjuvant therapy or patients with abnormal EGFR modifications outside Exon 21 point mutations (L858R) or Exon 19 deletions. The statistical analysis includes chi-squared tests, Cox regression, and Kaplan-Meier methods to evaluate the correlations between the overall survival of the patient and treatment variables. The findings from the investigation will yield a valuable understanding of the clinical course of EGFR mutant NSCLS in Saskatchewan.

Brooke Heinbigner (Dr. Marilyn Kinloch)

Defining the Grey Zone in Homologous Recombinant Testing in Ovarian Cancer – Using Bioinformatics to Determine Response to Precision Medicine

High-grade serous carcinoma (HGSC) patients that test positive for homologous recombinant deficiency (HRD), defined as those who have a Genomic Instability Score (GIS) of ≥ 42, are eligible for PARP-inhibitor (PARPi) therapy. These patients have longer average progression-free survival (PFS), but little is known about patients who have a GIS in this 'grey zone', defined as within 1-2 integers of the arbitrary 42 cut-off. In this project, patients with and HRD score within the grey zone had their GIS repeated multiple times to determine the test reproducibility. Three patients were identified with HRD of 42 or 44. The data demonstrated variability within patient testing. In one patient, all 10 runs showed reproducible results while in another patient, with an initial HRD of 44, the NGS showed an HRD range between 38-45 from 9 runs even though the sample was taken from same tissue block and library preparation. Tumour content was not shown to be an independent factor. It is important to consider patient range for retesting. The data suggests a patient with a HRD score as low as 38 to as high as 45 could be considered for reassessment to ensure only patients that will see benefit receive a PARPi.

Ali Khan (Dr. Ibraheem Othman)

Presentation and clinical outcomes in AL amyloidosis patients diagnosed in Saskatchewan: A population-based cohort study

Introduction: Approximately 7.5% of heart failure patients pass away within 30 days post-transplant, with the mortality rate reaching 17.5% among those with congenital heart disease (CHD). Survival rates for those awaiting transplants increased from 34.1% in 1980 to 67.8% in 2010. This study evaluated the mortality rates of patients requiring heart transplantation from Southern Saskatchewan.

Methods: We conducted a retrospective review of patients referred for heart transplantation from the Heart Function Clinic between 2007 and 2023. Kaplan-Meir curves and log rank tests were calculated to assess survival rates.

Results: From 62 patients, 7 had CHD, 17 underwent heart transplantation (1 with CHD), and 45 are awaiting transplantation or have passed away. Patients who passed away had higher prevalence of chronic kidney disease ($p=0.010$), were less likely to have transplant ($p=0.003$), and had lower diastolic pressure ($p=0.049$). Log rank test showed differences in survival distribution ($p=0.003$) for those who had a transplant compared to those who did not.

Conclusion: Timely heart transplant reduces the likelihood of mortality in these patients. Future research will build on these findings by using a patient-centered approach and increasing collaboration with the transplant centers.

Sonya Mannala (Dr. Shahid Ahmed)

Role of Individualized Intervention(s) on Quality of Life and Adherence to Adjuvant Endocrine Therapy in Premenopausal Women with Early-Stage Breast Cancer: MyChoice Study

Breast cancer is one of the most prevalent cancers among women, with approximately 25,000 new cases diagnosed each year in Canada. For premenopausal women with high-risk, hormone receptor-positive early-stage breast cancer, five years of ovarian suppression combined with an aromatase inhibitor (AI) or tamoxifen significantly reduces the risk of recurrence. However, combination endocrine therapy often leads to severe side effects that diminish quality of life (QOL) and reduce adherence to therapy. The MyChoice trial, a prospective phase II study, was designed to assess the impact of individualized, behavioral and complementary interventions on improving QOL and adherence to adjuvant endocrine therapy in premenopausal women with early-stage breast cancer. Primary outcomes focused on changes in QOL and cognitive function, while secondary outcomes explored treatment discontinuation rates and the socio-demographic and clinical factors that affect QOL and adherence. Preliminary findings show high adherence to treatment, with over 90% of participants engaging in at least one behavioral or complementary intervention. Early results suggest promising trends in maintaining QOL and cognitive function with initial QOL scores indicating potential stabilization or improvement in symptom burden. Final results will elucidate the impact of individualized interventions on the treatment experience for premenopausal women undergoing endocrine therapy.

Nima Toussi (Dr. Mita Manna)

Epidemiology and Outcomes Triple Negative Breast Cancer Patients in Saskatchewan - A Retrospective, Multi-center Cohort Study

Breast cancer is the leading cause of new cancer cases in women, with one in four cancer diagnosis being breast cancer in 2022. A subset of patients that are at higher risk of relapse and recurrent disease include those with triple-negative breast cancer (TNBC), representing about 15% of all breast cancers. The introduction of immunotherapy, imaging modalities and protocol, and demographic progression have altered the epidemiology of TNBC. This retrospective cohort study provides a comprehensive database of all TNBC cases in Saskatchewan from 2017 to 2023.

A preliminary analysis of 234 patients has shown an elevated mean (29.07) and median (27.99) BMI. There is a significant relationship between BMI and Death from TNBC ($p < 0.001$; $Z = 18.13$) and BMI and failure of neoadjuvant chemo- or immunotherapy as assessed by residual disease post-surgery ($p < 0.001$; $Z = 9.99$). There is a positive correlation between the presence of tumor necrosis and pre-systemic therapy peritumoral edema on MRI ($p < 0.001$; $\Phi = 0.399$), and rim enhancement on MRI ($p < 0.001$; $\Phi = 0.234$), as well as Stage T3 or greater disease and peritumoral edema ($p < 0.001$; $\Phi = 0.438$) or rim enhancement ($p < 0.001$; $\Phi = 0.398$).

Amina Alvi (Dr. Franco Vizeacoumar)

Validation of genetic vulnerabilities of telomerase-overexpressing prostate cancers

TERT, the gene encoding telomerase, is overexpressed in 85-90% of cancers, allowing these cancers to regenerate their telomeres and achieve cell immortality. TERT has been shown to be upregulated in prostate cancer, a prevalent malignancy worldwide, providing a model and reason for this research. Attempts have been made to target TERT directly to inhibit cancer cell growth, however they have not performed well in clinical trials. Synthetic dosage lethality (SDL) is a concept in which simultaneous overexpression of one gene with the inhibition of another partner gene results in cell death only when both conditions are met. Given that telomerase is overexpressed in many cancers, it is a promising target for SDL therapy.

Previous screens in the Vizeacoumar lab identified genes NDAP1, GPBP1, IFPB1, TMNA2, HDCS3, PM5SS, and DPA2S as potential SDL partners for TERT. The goal of this project was to identify the most promising gene candidates for further investigation Clonogenic assays with knockdowns of these genes using lentiviral shRNA were performed in TERT overexpressing and non-TERT overexpressing cell lines, with shRFP controls. Results of these assays have identified NDAP1 and GPBP1 to be the most effective SDL partners with TERT, showing selective lethality in TERT-overexpressing cell lines.

Pediatrics

Sarah-Marie Durr (Dr. Susan Petryk)

Asking the Parents: Implementing a Pediatric Patient feedback form in Medical Student's Clinical Sessions

Our previous research project identified the most important areas of feedback that parents of pediatric patients and simulated patients (SPs) would want to comment on, as well as the areas medical students and residents would want to hear about from patients. We have developed short, easy-to-use parent and SP feedback forms for medical learners.

Our objective is to evaluate the feedback forms during pediatric clinical sessions of medical students and family medicine or pediatric residents, as well as clinical sessions with SPs for year 1 and 2 medical students. We will determine if the developed feedback forms can provide medical learners with meaningful feedback regarding their patient-centered skills, as well as allow parents and patients to shape the medical education of future physicians.

We plan to collect 100 parent and 50 SP feedback forms during the academic year. We will then interview 20 medical learners on the usefulness of the feedback they received, as well as 20 parents and SPs on the ease of use of the form. De-identified survey data will be aggregated and shared with learners and clinical preceptors. Categorical variables will be summarized in counts and percentages. We will perform qualitative analyses of the interviews.

Tapanga Brooks (Dr. Andrea Tang)

Challenges and barriers faced by caregivers involved in pediatric medication management

Background: Medication use in children has many complicating factors. The healthcare system, alongside non-professional caregivers (NPCs), must learn to navigate these complexities and barriers to provide adequate medication management care for their children.

Objective: The larger qualitative health research study aims to identify and describe the challenges and barriers of NPCs in Saskatchewan related to pediatric medication management. The objective of this pilot study was to gain experience using the interview guide and make any revisions that may be needed for richer responses.

Methods: This is a qualitative health research study that will utilize the interpretative description design utilizing semi-structured interviews. In this pilot study, we conducted one interview with a participant that met our inclusion criteria. We have also consulted with a pharmacist and with pediatricians to improve the interview guide. We will then inductively code each barrier identified by participants using NVivo, and we will group these each into the major themes found.

Results: We have piloted our interview with one NPC. From this interview, we found the main themes to be consistent with those found in a previously conducted scoping review. We also amended the interview guide to better reflect the flow of conversation that will help us capture detailed descriptions of caregivers' experiences.

Samantha Bundus (Dr. Susan Petryk)

Comparing the diagnostic profile of Fetal Alcohol Spectrum Disorder in southern Saskatchewan with other prairie provinces using our CanFASD national database

Fetal Alcohol Spectrum Disorder (FASD) is a complex brain condition associated with prenatal alcohol exposure (PAE) affecting cognitive, neurological, social and interpersonal functions leading to lifelong disability. FASD is estimated to affect up to 4% of the Canadian population. The CanFASD database compiles data from multiple Canadian diagnostic centres and thus provides the most comprehensive profiles on individuals assessed for FASD in Canada. The present study compared the CanFASD demographic and assessment data for FASD in children ages of 6 to 18 years amongst the three Prairie Provinces, Saskatchewan (SK), Alberta (AB), and Manitoba (MB).

Results: This study found some similarities but several important differences amongst Canadian Prairie Provinces diagnosing FASD. There was a higher likelihood (p-value<0.05) of receiving an FASD diagnosis in AB than in SK and MB. AB had the highest rate of individuals with all three sentinel facial features (SFF) and highest rates of neurodevelopmental impairment amongst the provinces. There are numerous challenges and nuances around diagnosing FASD, making it difficult to pinpoint the reasons for differences across the three provinces. The results may indicate differing referral patterns, intake criteria, definition of PAE, age at assessment and diagnostic team composition.

Lorynn Labbie (Dr. Tim Bradley)

Comparing Sex Differences in Aortic Root to Somatic Growth in Children with Marfan Syndrome in Saskatchewan

Background: Marfan syndrome (MFS) is the most common heritable thoracic aortic disease and can progress to life-threatening aortic dissection without effective management. MFS males have more rapid somatic growth and are more likely to meet surgical indications based on aortic root dimension (AoRD) growth sooner. The aim of this study was to compare sex differences in AoRD to somatic growth in children with MFS in Saskatchewan.

Methods: We conducted a retrospective chart review collecting serial data on height, weight, BMI and AoRD and compared MFS males and females with normative data.

Results: Of 18 MFS patients (14 males), height in MFS tended to be taller compared with normative data for all ages, with males taller than females. Weight and BMI in MFS tended to be similar compared with normative data and with no sex differences. AoRD in MFS tended to be larger compared with normative data and with no sex differences. AoRD for height increased in both male and female MFS patients.

Conclusions: This pilot project is to be expanded within the Canadian Aortopathy and Connective Tissues Disorder (CAN-ACT) Registry, which will include ~600 MFS, to determine whether AoRD for height is a better sex-dependent determinant of AoRD growth.

Muaaz Asghar (Dr. Lalenthra Naidoo)

The Rate of Pediatric Stridor in the Emergency Department

Objective: Stridor is a clinical manifestation that arises from the narrowing of the airway. Recent research has demonstrated that COVID 19 infection, especially with the Omicron variant, can lead to more severe presentations of stridor such as severe croup. Furthermore, croup and recurrent croup have been associated with asthma. The purpose of this study is to assess the effect of COVID-19 and the pandemic on stridor related presentation and development of asthma/RAD.

Methods: This study employed a retrospective chart review of Jim Pattison Children Hospital and Royal University Hospital emergency department visits (ED) during the period of March 2018 to March 2022. March 2018 - March 2020 would be considered pre-pandemic and onwards will be considered post-pandemic. Stridor related presentations to ED visits were assessed for rates of stridor visits, severity and current or later asthma diagnosis.

Results/Conclusion: The COVID-19 pandemic caused a decrease in stridor-related presentations due to masking protocols causing decreased spread of respiratory viruses. Stridor related presentation during the first year of the pandemic or the delta wave was associated with higher risk of current or later asthma/RAD diagnosis. There were no differences in severity measures (admission, inhaled bronchodilator use, and CTAS). COVID-19 related croup only and rarely occurred in the Omicron wave.

Mahrukh Masood (Dr. Polya Ninova)

Health Outcomes in Young Children Born to Antenatal COVID-19 Positive Mothers

The SARS-CoV-2 pandemic has had a profound impact on global health, with emerging evidence suggesting negative effects on children born to mothers who contracted COVID-19 during pregnancy. This study investigates the health outcomes of these children by focusing on emergency room (ER) visits and hospitalizations as early indicators of potential long-term health challenges. Data from children under two years old were analyzed to assess ER visit frequency, hospitalization rates, and reasons for medical consultations.

Results indicated that 63% of children born to mothers infected in the third trimester visited the ER, compared to 36% from the first and second trimesters. Although not statistically significant, this trend suggests that maternal infection during the third trimester may have a more pronounced impact on children's health, particularly with respiratory issues, which accounted for 71% of ER visits. Hospitalization rates were highest in children born to mothers infected in the third trimester, with average length of stay highest in the third trimester as well. These findings emphasize the importance of further research on trimester-specific impacts of maternal COVID-19 infection to guide healthcare strategies and interventions for affected children.

Syed Subhan (Dr. Susan Petryk)

Feeding difficulties in children with Autism Spectrum Disorder

Introduction: Children with Autism Spectrum Disorder (ASD) experience significantly more feeding related problems than their neurotypical peers. Children with ASD may consume less protein, calcium, vitamin D, Vitamin B12, etc. The severity of Vitamin D deficiencies correlates with ASD severity. Blood tests and diet history may be required to assess nutritional deficiencies and to identify individuals at risk of serious complications from these deficiencies.

Methods: A retrospective chart review was conducted on 130 children with ASD (3-18 years) who attended an appointment at Child and Youth Services, Regina, SK between April 2020 – March 2024 focusing on mentions of feeding concerns. Data was collected on ASD severity, sensory issues, comorbidities and medication. Statistical analysis was performed using R software, version 4.4.0.

Results: Results showed no association between feeding issues and comorbidities, ASD severity ($p=0.798$), BMI ($p= 0.418$), sensory sensitivities ($p=0.127$). Comparisons between BMI and different medications also showed no association. Vitamin D lab work was only ordered in 7.7% of patients.

Conclusion: In this cohort, 32% of children with ASD had feeding issues significant enough to be mentioned in the medical record. This indicates this group with ASD may not experience more feeding difficulties than their peers (reported incidence of 4.8%).

Annaka Chorneyko (Dr. Angelica Lang)

Assessment of upper limb kinematics and function in patients with rheumatoid arthritis

Rheumatoid arthritis (RA) is an inflammatory joint disorder that causes pain and disability. The shoulder joint in particular is important for the maintenance of functional abilities, including work-related function. Biomechanics, or movement, of the shoulder joint are an important consideration for function. Compensatory movement patterns may lead to disease progression and increased disability. The objective of this study was to assess shoulder biomechanics in people with RA during a functional task protocol. Upper limb motion was tracked using optical motion capture during simulated activities of daily living. Paired t-tests were used to compare more affected and less affected shoulders. The primary finding was higher scapular internal rotation in the more affected limb in several tasks, which has also previously been connected to shoulder instability and negatively altered glenoid shape in osteoarthritic shoulders. In addition, the more affected limb demonstrated less upward rotation, less humeral elevation, and less humeral axial rotation during an overhead reaching task, suggesting that other movement compensations are occurring on the affected side that could have implications for overall abilities. Given the preliminary nature of this work, future research will deepen our understanding of the connection between RA and shoulder function.

Maya Berscheid (Dr. Sarah Donkers)

Rehabilitation Interventions to Support Fatigue Management in Multiple Sclerosis

Background: Fatigue is a prevalent and debilitating symptom of MS that significantly impacts quality of life. Despite growing evidence to support rehabilitation interventions for MS fatigue management, no comprehensive guideline exists to bridge the gap between research and clinical practice. To address this, MSBEST, in partnership with MS Canada and the Canadian Network of MS Clinics, is developing the first comprehensive MS Rehab Best Practice Guideline. This work pertains to the chapter on fatigue management. As an initial step, an umbrella review was conducted to identify and critically appraise existing systematic reviews and meta-analyses regarding rehabilitation interventions for MS fatigue.

Methods: Multiple databases were searched to identify relevant articles. Citations were imported into Covidence and independantly reviewed for inclusion by two assessors. Data extraction and quality assessment was also carried out by two independant reviewers. At every step, a third member was involved to resolve disagreements.

Results: 111 studies were included for data extraction. Data extraction is complete; however, analysis is currently ongoing. Existing literature primarily covers exercise and psychological/cognitive interventions, with significantly variability intervention types, dosage, timing, and delivery methods.

Conclusion: The results from this umbrella review will inform future guideline development.

Saidee Fooks (Dr. Janine Eckstein)

The Impact of Cardiac Rehabilitation on Quality of Life in Transcatheter Aortic Valve Implant (TAVI) Patients

Background: Transcatheter aortic valve implantation (TAVI) offers a valve replacement option for patients ineligible, or at elevated risk, for surgical aortic valve replacement (SAVR)1. Cardiac rehabilitation (CR) has proven benefits in coronary artery disease, but its' impact on quality of life (QoL) in TAVI patients is not well-studied2,3,4. This review aims to evaluate how CR affects QoL outcomes in TAVI patients.

Methods: Participants included in this study, permitting availability of adequate QoL data, were categorized according to CR attendance. A two-sample t-test was used to compare QoL scores between the CR and no CR (NCR) groups at 1-year post-TAVI. Paired t-tests were then used to analyze changes in QoL scores from pre-TAVI to one-month and one-year post-TAVI.

Results: Of 31 TAVI patients, 9 attended CR. At 1-year post-TAVI, these CR participants exhibited a significantly higher average QoL value index when compared to their NCR counterparts ($p = 0.0490$). While both groups experienced short-term improvements, only CR participants maintained improved QoL scores, as NCR participants experienced a significant decline over one year ($p = 0.0136$).

Conclusion: CR significantly improves and maintains QoL post-TAVI, suggesting its crucial role in long-term patient recovery. Without CR, patients showed a decline in QoL, highlighting the importance of structured rehabilitation programs.

Hannah Verity (Dr. Angelica Lang)

Shoulder kinematics change over time in the presence of rotator cuff disorders: a preliminary analysis of longitudinal data

Background: Shoulder pain, often caused by rotator cuff injuries, is the third most common consultation in primary care. Recent cross-sectional research has confirmed a potential relationship between shoulder biomechanics and duration of rotator cuff injury, but true longitudinal data are needed.

Purpose: To determine if shoulder biomechanics change over time in people with rotator cuff disorders.

Hypothesis: Shoulder kinematics will change over time and changes will be influenced by individual characteristics.

Methods: Scapular and humeral motion of participants with shoulder pain was assessed during seven functional tasks in two sessions: baseline and 6-months. Two-way repeated measures ANOVA analyses were used to assess the interaction of time and individual characteristics (residence, age, sex) on six month change in humeral and scapular angles.

Results: Scapular movement and humeral rotation changed between sessions. More harmful adaptations were associated with the older category (over 35), being male, or residing in a rural center.

Conclusions: These results suggest that kinematics change over time in a group with shoulder pain in a manner that could contribute to lasting injuries. These findings highlight the importance of longitudinal measurements and the need to include time as a factor in assessments of rotator cuff disorders.

Quality Improvement

1

Andy Luu (Dr. Erin Yakiwchuk)

Drug Therapy Problems in Older Adults Referred for Geriatric Assessment

The Geriatric Evaluation and Management Day Hospital Program (GEM) is an 8-week multidisciplinary outpatient program that assesses and manages complex cognitive, medical, functional, and psychosocial issues in older adults. Older adults are more likely to live with multiple medical comorbidities and take many chronic medications. Combined with the physiological changes associated with aging, older adults are more susceptible to Drug Therapy Problems (DTPs). The purpose of this project was to determine which DTPs are commonly identified in patients referred to the GEM program. This project was approved by the University of Saskatchewan Biomedical Research Ethics Board. De-identified data was obtained from the charts of patients enrolled in the GEM Day Hospital between January 1, 2023, and June 30, 2024. Descriptive analysis was performed to determine the most common DTP categories, implicated medications and medical conditions in this patient population. The most common DTP category identified by this review was "Additional Drug Required", most often due to lack of osteoporosis medication and inadequate pain control. "Adverse Drug Reactions" was the second most prominent DTP category; the most common culprit was orthostatic hypotension from antihypertensives. This study highlights potential areas of improvement when caring for older adults in the community.

1

Elizabeth Pywell (Dr. Eric Sy)

Palliative Care Utilization Near the End of Life in Critically Ill Patients

Palliative interventions can improve outcomes in the ICU; however, they are often underutilized. This study evaluates palliative care utilization in the ICU at Regina General Hospital to inform improvements in end-of-life care. A retrospective chart review included patients who died during their ICU admission or within 7 days and examined the use of palliative or comfort care order sets before end-of-life. Secondary outcomes included life support therapies and palliative care interventions provided, palliative care consultation, and documented end-of-life and prognosis conversations. The sample consisted of 200 patients with ICU admission dates between February 2 and December 10, 2022, with a mean age of 62, a slight male predominance (54.8%), and a mean SOFA score of 11.7 at admission. The results demonstrate that 68% of patients had a palliative or comfort care order set ordered before death, which was associated with increased utilization of palliative interventions, an increased likelihood of having a documented end-of-life or prognosis conversation, and decreased CPR and vasopressor use. Palliative care consultations occurred in only 11 (5.5%) of cases. These findings highlight the potential of palliative or comfort care order sets to improve end-of-life care and emphasize the need for improved palliative care integration in the ICU.

Kyle Luo (Dr. Steven Machtaler)

Evaluating the incidence and severity of nephrotoxicity associated with platinum-based chemotherapy in cancer patients treated in Saskatchewan

Cisplatin is a platinum based antineoplastic drug that is commonly used to treat advanced ovarian, testicular, bladder, and head and neck cancers. Nephrotoxicity in the form of acute kidney injury(AKI) is the most clinically significant toxic effect of cisplatin. Mechanism of cisplatin induced AKI includes inflammation, oxidative stress, renal vasoconstriction, and direct renal cytotoxicity. The present study hypothesizes that the incidence of cisplatin induced AKI is significant and influenced by various factors, and the purpose of this study is to evaluate the incidence and severity of cisplatin induced AKI in Saskatchewan cancer patients through a retrospective chart review. Data was collected including demographic information, diagnosis and treatment, and relevant diagnostic test information and analyzed using two tail t-test and 2-population z-test. Factors explored include dose response, treatment protocol, comorbidities, concurrent medications, and more. In conclusion, we present evidence for the incidence and severity of cisplatin induced AKI in Saskatchewan cancer patients and its association with various factors explored.

1

Indiana Best (Dr. Peter Hedlin)

Night-time noise levels and patients' sleep experiences on ward units throughout Royal University Hospital, Saskatoon, SK

Approximately 30-60% of patients experience sleep disturbances while hospitalized. These disturbances can increase risk of delirium, which affects one-third of general medical patients over the age of 70. Current literature emphasizes the importance of sleep enhancement interventions to prevent and mitigate delirium. This prospective observational study aimed to identify night-time noise levels and patient sleep experiences in various hospital rooms. Audits were conducted of the general surgery, orthopedic, and internal medicine wards. Forty participants across private, semi-private, and observational hospital rooms were consented and monitored for up to 4 days. Demographic data and baseline sleep history were collected. Dosimeters recorded noise levels in each hospital room during hospital quiet hours (8pm-8am). Each morning, patients completed questionnaires evaluating their sleep quality in hospital versus at home and identifying factors contributing to sleep disruption. Future analysis will use generalized linear mixed models to assess whether different types of hospital rooms and wards have significant differences in mean noise levels. Correlation analysis will be used to: 1) explore sleep scale factors and noise-related variables, such as general noise, number of nursing interventions, and frequency of overhead announcements, and 2) examine relationship between pain ratings with sleep quality and overall sleep scores.

1

Meet Patel (Dr. Scott Adams)

Recommendations Regarding the Use of Virtual Mental Healthcare: A Systematic Review

Technological advancements and increased patient and provider acceptance has accelerated the adoption of virtual mental healthcare (VMH). With a broader array of options for VMH interactions, clinicians must now assess which method of interaction is most appropriate for a given patient and episode of care to ensure patient safety and quality care. Our study aimed to identify recommendations for determining when virtual or in-person care is more appropriate for mental healthcare and, from these recommendations, develop an intake questionnaire to help providers determine the most appropriate care modality. We conducted a systematic review with reporting based on PRISMA guidelines. From the systematic review, the recommendations indicated that VMH is considered appropriate for underserved populations, individuals with mild to moderate mental health conditions, and in situations where language or cultural matching are important. VMH was less appropriate for patients with severe mental disorders, conditions requiring precise assessments (e.g., autism, developmental disabilities), and in cases such as domestic violence where finding a safe space for virtual care may be challenging. Based on these recommendations, we developed the Virtual or In-Person Care Assessment Tool (VIP-CAT) questionnaire to aid providers in determining the appropriateness of VMH for specific clinical encounters. Findings and recommendations from this study will provide clinicians and policy makers with solid evidence to guide clinical decision making and clinical policy surrounding VMH.

2

Alexandre Belisle (Dr. Susan Petryk)

Optimizing E-Prescribing in Saskatchewan: An Analysis and Improvement Initiative

Introduction: Saskatchewan's Pharmaceutical Information Program (PIP) is a digital platform that allows healthcare professionals secure access to patients' medication records. Furthermore, prescriptions can be made directly through PIP. While pharmacists in Saskatchewan routinely use PIP, there scant data on the usage of PIP by physicians and nurse practitioners. Therefore, the purpose of this quality improvement project is to investigate (1) knowledge, (2) usage, (3) advantages, and (4) barriers of E-prescribing through PIP.

Methods: We employed a mixed-methods study design which consisted of a REDCap survey (n = 48) and a semi-structured interview (n = 4). Statistical and Thematic analysis was performed using R-software and NVivo, respectively.

Results: (1) Only 47.9% (n = 23) of participants surveyed were aware that PIP could be used to E-prescribe medications. (2) Of these 23 participants, 56.5% (n = 13) had previously used PIP to E-prescribe medications. (3) 69.2% (n = 9) participants appreciated that E-prescribing through PIP does not require knowing where to send the prescription. (4) 53.8% (n = 7) participants reported issues with pharmacy staff accessing prescriptions made through PIP.

Conclusion: This research reveals the need to raise awareness of PIP's prescribing functions and brings forward barriers that should be addressed.

2

Muhammad Abdullah Shakeel (Dr. Ziaur Rehman)

Quality of Care assessments of patients with intracerebral hemorrhage presenting to the stroke unit

Background: Intracerebral hemorrhage (ICH) has a mortality rate of 40% at 30-days. Mortality at 30 days is used as a standard outcome of ICH diagnosis. Blood pressure control is considered most effective modifiable risk for acute management of ICH and functional improvement. This study investigated clinical outcomes of patients admitted to the stroke ward with ICH at the Regina General Hospital (RGH).

Method: A retrospective chart review of patients admitted to the stroke unit with ICH between January 2020 to Dec 2023. A general linear model was used to identify parameters which are associated with mortality.

Results: Of 24 patients (n=11 female), 4 patients passed away. Patients who passed away were older ($p<0.05$) than those who did not. All 4 patients who passed away presented with hypertension compared to 75% of patients who did not pass away. Age was significantly positive association with mortality (OR=1.15; 95% CI: 1.03-1.39, p=0.04), including when adjusting for gender (OR=1.16; 95% CI: 1.04-1.31, p=0.03). This significance was attenuated when adjusting for mean arterial blood pressure.

Discussion: Age is critical to consider when treating patients presenting with ICH. Attenuation of the significance of age when controlling for blood pressure further suggests blood pressure to be a modifiable risk factor. Future research should include reproducibility across multiple centers, and a clinical trial to identify if regulating blood pressure improves patient outcomes.

Sabahat Saeed (Dr. David Sauder)

Cost Improvement and environmental protection related to outpatient department surgery vs. operating room surgery

Introduction: The Canadian healthcare sector is responsible for 4.5% of the national total greenhouse gas emissions (3). Operating rooms (ORs) generate about 30% of a hospitals' solid waste and are three to six-times more energy intensive than the rest of the hospital (4, 5). One method of reducing the carbon footprint of ORs is to move simple operative procedures (SOPs) from ORs to outpatient procedure rooms.

Hypothesis: We hypothesize that SOPs performed in the OPD will be more cost effective and environmentally more sustainable than SOPs performed in the OR.

Methods: We took an observational approach to data collection by observing several OPD and OR SOPs from the time patients registered at the hospital to when they were discharged. We collected data from managers of OPD Surgery, OR, PACU/Recovery, Day Surgery, housekeeping, central processing, and facilities/utilities. We then determined the cost difference and the kilograms of carbon dioxide emitted (kgCO2e).

Results and Conclusion: Data collection is not complete. Currently, OR procedures are 2.5x more costly, produce 18x more surgical waste, and they have about a 9x greater carbon footprint than OPD procedures.

2

Shawn Silver (Drs. Sabira Valiani & Colin Gebhardt)

Critical Care Medicine Quality Improvement - Asking Questions that Inform Practice

Implementing Quality Improvement (QI) in Intensive Care Units (ICUs) is essential for improving patient care and outcomes. In Saskatoon's ICUs, the absence of standardized data collection tools and processes has been a hurdle in effective benchmarking and targeted improvement efforts. To address this gap, a user-friendly, adaptable QI data collection tool was developed and implemented for use by the entire ICU team.

Through consultation with key stakeholders and obtaining necessary approvals, a REDCap-based tool was created. This tool focused on capturing vital patient information related to nursing, respiratory therapy, physiotherapy, social work, and physician care, with a particular emphasis on conditions like ARDS, delirium, and acuity levels.

Over a 10-week period, data was collected on 164 patients, resulting in a total of 1,312 records, despite encountering challenges related to data collection tool modifications and time constraints. This dataset allows for comparisons between different ICUs in Saskatoon and facilitates benchmarking against national critical care standards. The project highlights the transformative potential of a collaborative, data-driven approach to QI in critical care settings. It aims to promote continuous improvement and optimal resource allocation to enhance the quality of care for critically ill patients in Saskatoon.

2

Kishore Hari (Drs. Jon Witt and Segun Oyedokun)

Assessing International Medical Graduate (IMG) Proficiency in Procedural Skills During a 12-Week Clinical Field Assessment

Assessment and training of procedural skills are critical components of medical education; however, there is limited research pertaining to International Medical Graduates (IMGs). This study aims to quantify IMG physicians' exposure to and competency in procedural skills during a 12-week clinical field assessment (CFA) in the Saskatchewan International Physicians Practice Assessment (SIPPA) program. We analyzed data from skill evaluation forms completed by SIPPA preceptors of IMGs enrolled between 2017 and 2023. Descriptive statistics were calculated to assess exposure and competency across 66 procedures. Data from 299 participants were reviewed. Procedural competencies were categorized by exposure level as: high (80-100%), moderate (40-79%), low (20-39%), and very low (<19%). High-exposure procedures included injections, EKG interpretation, cerumen removal, and laceration repair. Moderately exposed procedures included lumbar puncture, central line insertion, and slit lamp examination. Low- to very-low-exposure procedures included thoracentesis, phlebotomy, and intraosseous needle insertion. Procedural exposures for all 66 items were generally consistent across 2017-2023, with minor variations observed. Our study identified areas where IMGs demonstrate higher exposure and competency, especially in common procedures, highlighting the need to focus on specialized procedures with lower exposure. The variability in procedural exposure suggests the need for standardized training protocols to ensure comprehensive skill development.

Abd Alfatah Alras (Dr. Scott Adams)

Recommendations Regarding the Appropriateness of Virtual Care

Introduction: The COVID-19 pandemic accelerated virtual care adoption, improving patient care quality and efficiency. However, determining when virtual care is appropriate remains challenging, as varying access to technology and differing healthcare needs complicate the decision-making process. This highlights the importance of analyzing factors influencing the suitability of virtual versus in-person care.

Methods: Four databases (MEDLINE, CINAHL, Embase, APA PsychInfo) and Google Scholar were searched for studies and guidelines on virtual care appropriateness from January 2014 to January 2024. Two researchers independently screened 5136 articles, with 75 included after review. Eight additional articles were identified through reference lists, totaling 83. Data extraction was supported by the Elicit platform.

Results: Six primary concepts (patient characteristics, clinical presentation, care process timepoint, burden of care, provider factors, and technology platform) and 22 sub-concepts influencing virtual care appropriateness were identified. A decision tree incorporating these concepts was developed to guide clinical practice.

Conclusion: Determining virtual care appropriateness can be complex. This review provides a decision-making framework that can aid clinicians, with future research needed to refine virtual care guidelines and explore hybrid care models for optimal healthcare delivery.

Michelle Desjarlais (Dr. Sarah Smith)

Comparing surgical time amongst different salpingectomy techniques at cesarean delivery

Permanent contraception techniques including tubal ligation and salpingectomy are effective methods commonly performed at the time of caesarean section. While traditional salpingectomy can decrease ovarian cancer risk, it is associated with increased surgical time. Advanced bipolar energy devices offer a promising time saving alternative but the data comparing the techniques is limited. The primary outcome was to determine if implementation of the bipolar energy device for complete salpingectomy at the Regina General Hospital (RGH) can reduce surgical time and improve outcomes (reduced blood loss and complication rate) for patients. A retrospective chart review of 232 cases was conducted using records from May 2022 to March 2024 to compare tubal ligation, traditional salpingectomy, and bipolar salpingectomy. Results showed that bipolar salpingectomy significantly reduced operating time. The duration for bipolar salpingectomy, salpingectomy without electrosurgery, and tubal ligation were found to be 54.8 ± 1.01; 60.5 ± 1.01; 71.0 ± 4.37 minutes, respectively. Although bipolar salpingectomy was associated with slightly more cases of increased blood loss, the overall complication rate remained low. These findings support the use of advanced bipolar energy devices for salpingectomy as a safe and efficient alternative during caesarean sections, offering reduced procedure time and potential improvements in surgical outcomes.

Natisha Thakkar (Dr. Sarah Smith)

Cost-effectiveness analysis of salpingectomy during cesarean delivery

Background: Female sterilization is often performed opportunistically at cesarean section (CS). At our institution, salpingectomy at CS is performed by "traditional" salpingectomy (TS) using clamps and sutures, or "bipolar" salpingectomy (BS) using the advanced electrocautery device. BS at CS offers a shorter operative time than TS, but may have increased cost. Cost-effectiveness analyses and incremental cost-effectiveness ratios (ICERs) compare interventions based on their resource expenditure and perceived benefit. This study aims to compare the surgical duration and cost of TS and BS at CS.

Methods: A retrospective chart review was conducted on 226 patients who underwent salpingectomy at CS between May 2022-March 2024. The associated costs of BS and TS at CS were tabulated. The ICER was calculated by dividing the total cost difference of each procedure by the difference in surgical duration.

Results: BS at CS had a 5.65-minute shorter operative time compared to TS. While BS had a higher cost per minute of operative time, the total costs were similar. The ICER indicated an additional cost of $21.78 for every minute saved with BS.

Conclusion: BS and TS at CS were comparably cost-effective, with the shorter surgical duration of BS not justifying the increased cost.

Jess Klaassen-Wright (Dr. Gaurav Jain)

The Perioperative Experiences of Patients Undergoing Gender Affirmation Surgery in Saskatchewan

Transgender and gender-diverse individuals (TGDI) may undergo surgical procedures to align their physical attributes and gender identity. This group continues to be marginalized in healthcare spaces and experiences high rates of psychiatric diagnoses and suicide. While gender affirmation surgery (GAS) can reduce gender dysphoria and improve psychological stress, TGDI have poor experiences in the healthcare system and face barriers to accessing equitable care. Literature on the experiences of patients undergoing GAS is sparse, and this study aims to fill this gap to understand the needs of TGDI and improve the process in future. Eight participants completed semi-structured interviews (n=5) or online questionnaires (n=3) about their surgical experiences in Saskatchewan. Data was analyzed with qualitative thematic analysis. Participants discussed barriers, including lack of trans competency in healthcare providers (HCPs) and long wait times. They also discussed support systems like community organizations and family, as well as emotions like fear, excitement, and love for self. These preliminary themes connect to initiatives that could be implemented in Saskatchewan to improve the perioperative experience for TGDI, including increasing the number of trans competent HCPs, streamlining the referral process, increasing support for community organizations, developing post-operative supports, and reducing travel and surgical costs.

M. Abdullah Shafiq (Dr. Payam Dehghani)

Mortality in Patients Requiring a Heart Transplant

Introduction: Approximately 7.5% of heart failure patients pass away within 30 days post-transplant, with the mortality rate reaching 17.5% among those with congenital heart disease (CHD). The mortality rate for those awaiting transplants is high, as the 1-year survival rate is currently 68%. This study evaluated the mortality rates of patients requiring heart transplantation from Southern Saskatchewan.

Methods: We conducted a retrospective review of patients referred for heart transplantation from the Heart Function Clinic between 2007 and 2023. Kaplan-Meir curves and log rank tests were calculated to assess survival rates.

Results: From 62 patients, 7 had CHD, 17 underwent heart transplantation (1 with CHD), and 45 are awaiting transplantation or have passed away. Patients who passed away had higher prevalence of chronic kidney disease ($p=0.010$), were less likely to have transplant ($p=0.003$), and had lower diastolic pressure ($p=0.049$). Log rank test showed differences in survival distribution ($p=0.003$) for those who had a transplant compared to those who did not.

Conclusion: Timely heart transplant reduces the likelihood of mortality in these patients. Future research will build on these findings by using a patient-centered approach and increasing collaboration with the transplant centers.

Michael Thorpe (Dr. David Kopriva)

Do Gait Changes from Vascular Claudication Revert to Normal after Endovascular or Open Revascularization of the Lower Extremities?

Despite optimal medical treatment and improved lifestyle factors, patients with intermittent claudication (IC) continue to demonstrate altered gait patterns1,2, limiting their functional capacity. This study aimed to assess the efficacy of surgical interventions for IC in improving gait parameters in IC patients compared to IC patients with non-surgical interventions. Participants from Saskatchewan were retrospectively recruited based on having IC symptoms and no gait-altering conditions (non-surgical) or receiving surgery to treat IC and having no gait-altering conditions (surgical). Lower limb blood flow was assessed using ankle-brachial index. Height, weight and BMI were measured. Gait characteristics such as step time, symmetry and regularity were measured using a triaxial accelerometer attached to participants at the posterior waist while walking on a 200-meter track as previously described3. Results indicated a near-significant ($p = 0.055$) improvement in step regularity in the X-axis in the surgical group compared to the non-surgical group, and significant ($p < 0.01$) improvements in ABI values were found in the surgical group consistent surgical interventions. Despite these findings, the low sample size limits conclusions regarding the efficacy of surgical intervention on normalizing gait patterns. Further studies should focus on improving recruitment and controlling for confounders related to patient self-reporting.

Zili Zhou & Vrinda Anand (Drs. Dexter James & Allan T. Dolovich)

Force Analysis for Surgical Instruments: Assessing Tissue Damage Risk from Incremental Clicks on Tissue Mimics

Background: Surgical instruments are used to grasp, manipulate, or remove tissues. Excessive tool-tissue interaction forces can result in tissue damage and complications. We aim to study short and long Allis, Babcock and Kocher, and quantify the forces encountered by their end effectors.

Methods: 3D-printed TPE and silicone were used as tissue mimics. A load cell and height gauge were used to measure the force subjected to, and displacement of, the mimics with subsequent clicks on each instrument.

Results: For silicone, forces encountered at end effectors of surgical instruments are higher in the short than long Babcock; higher in the long than short Kocher; higher in the short than long Allis. TPE was different in that the force measured was higher in the long than short Allis.

Conclusion: While shape of the stress-strain curve for the 3D-printed mimic closely resembled the curve of body tissues, force magnitudes in the silicon sample more accurately reflected stress-strain characteristics of body tissues. Local distribution of forces at the tips might differ by material, thereby affecting the stress field and force-displacement. We plan to model forces encountered by the mimics using analysis with ANSYS to eliminate the effect of the shape of the instrument tip.

Abby Jia (Dr. Bonnie Richardson)

Subtotal vs. total parathyroidectomy in end stage renal disease: evaluation of outcomes

Secondary hyperparathyroidism is a common complication in patients with end-stage renal disease with long term sequalae including renal osteodystrophy and vascular calcification. Parathyroidectomy surgeries are the only definitive treatment and are offered to patients that are refractory to medical management. Currently, there is a lack of consensus around which type of surgery yields better patient outcomes, warranting the need for thorough systematic review. In this study, we selected and reviewed 22 articles from PubMed on subtotal parathyroidectomy, total parathyroidectomy and total parathyroidectomy with auto transplantation. We assessed for primary (serum PTH, calcium, phosphorus) and secondary outcomes (complication rate, 30-day mortality, hypocalcemia, recurrence). We found no significant differences in post-operative biomedical markers including PTH, calcium and phosphorus levels. Studies showed that subtotal parathyroidectomy had a lower rate of hypocalcemia and fewer extended hospital stays, while total parathyroidectomy with auto-transplantation had a lower rate of recurrence and persistence. Future research should be conducted to assess for treatment response to different types of surgeries in specific target patient populations.

Rishi Vakulabharanam (Dr. Peter Hedlin)

Effects of Position and Sensory Deprivation on BiSpectral Index Data

Many have demonstrated that pre-operative bispectral index (BIS) values may have a link to incidence of post-operative outcomes such as delirium and cognitive decline. To better understand how pre-operative BIS values vary, we investigated the effects of age, position, and sensory deprivation on BIS values among healthy participants (n=24). In this study, participants were recorded in these positions: supine with headphones/blindfold, supine with blindfold, upright with headphones/blindfold, upright with blindfold, upright with headphones, upright without restrictions. These participants were divided by age into three categories: 18-39, 40-64, >65 years old. BIS readings were not significantly different between age groups, including parameters for median frequency, spectral edge frequency, and signal quality index. However, BIS readings varied significantly between all 6 positions. Compared to the first position (emulation of surgical environment) other positions showed significant differences in median frequency, spectral edge frequency, and signal quality index. Along with this, all 6 positions demonstrated an acclimation period of 30 seconds. This indicates that while age may not be an important consideration in using BIS pre-operatively, standardizing the position in which data is collected, along with allowing for an acclimation period, is critical to obtaining consistent BIS readings in future extra-operative usage of BIS.

Zili Zhou (Dr. Michael A. J. Moser)

Irreversible Electroporation in Unresectable and Borderline Resectable Liver Tumors

Introduction: While over 80% of colorectal liver metastases are currently resectable with technical advances, some patients still have liver cancers that are unresectable due to their proximity to anatomically sensitive structures. Irreversible electroporation (IRE), a non-thermal ablation technique, offers an option for these patients.

Methods: We recorded the survival and complications of 19 patients undergoing 22 IRE procedures for unresectable liver cancers between July 2015 and February 2024. All cases were deemed unresectable by a multidisciplinary tumor board due to abutment of hepatic veins or IVC (n=10), recurrence near the hilum after lobectomy (n=4), involvement of the portal vein bifurcation (n=3), and cirrhosis contraindicating resection (n=3).

Results: Patients had a median overall survival of 1103 days from the time of the procedure, while patients with colorectal liver metastases had a median survival of 1470 days. Local recurrence occurred in 7 of 22 (32%) cases, with a median recurrence-free survival of 818 days. Complications were infrequent; 3 patients reporting pain beyond 24 hours, but all settled without the need for any intervention.

Discussion: Our medium-sized center achieved outcomes comparable to those reported in much larger centers, further supporting the use of IRE in managing unresectable liver tumors in anatomically sensitive locations.

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