UNIVERSITY OF SASKATCHEWAN

Program and Abstracts

Department of Medicine

Research Day

May 2, 2025

10am-1pm

University Club, USask

LEARNING OBJECTIVES

At the end of this research day participants will be able to

- Develop an understanding about the quality and scope of research (from biomedical to clinical to population-based research) being conducted in our department
- Develop an understanding about the various research methodologies used
- Understand and discuss results of research presented in a way to help inform their practice and future research
- Get together and discuss current and novel research with researchers from across the department to increase research connections and collaborations

PROGRAM

10:00-10:05
Opening comments
Dr. Josh Lawson

10:05-10:30
Keynote address:
Dr. Darryl Davis

Dr. Davis is a clinician-scientist and cardiac electrophysiologist in the Division of Cardiology at the University of Ottawa Heart Institute. He directs the Cardiac Translational Research Laboratory. He is a professor in the Division of Cardiology in the Department of Medicine at the University of Ottawa where he is cross appointed to the Department of Cellular and Molecular Medicine.

Faculty Session

10:31-10:42
Shavadia, Tomilin, Chumala, Mangipudi, Udell, Haddad, and Katselis. *Sodium Glucose Cotransporter 2 inhibitors Preceding ST-elevation Myocardial Infarction: Global Proteomics and Pathobiological Insights*

10:43-10:54
Ness and **Gordon**. *Development of cyclosporin-induced human regulatory dendritic cells for atopic asthma immunotherapy*

10:55-11:06
Ishaque, Lamb, and Hunter. *Ticagrelor As an Add-on Antiplatelet Therapy for Secondary Stroke Prevention In Patients with Cerebrovascular Disorders: Indications and Outcomes*

11:07-11:18
Hansen, Shaw, Bolt, Verity, Nataraj, and **Schellenberg**. *Electric Impedance Tomography Detects Lung Volume Changes in Amyotrophic Lateral Sclerosis*

11:19-11:30
Shahab, Le, Poliakov, and Knox. *Health related quality of life in people with Multiple Sclerosis in Saskatchewan*

11:31-11:42
Prasad, Soliman, Garg, Schott, Connaughton, Lanktree. *A Comparative Whole Exome Analysis in Patients with Loin Pain Hematuria Syndrome and Isolated Hematuria*

11:43-11:54

Ravindran, Shah, Noyes, Zherebitski, **Rajput**, Farrer, and Rajput. *Dopa-Responsive Parkinsonism Secondary to Tauopathy: Clinical, Pathological, and Genetic Study*

11:55-12:06

Kosteniuk, Morgan, O'Connell, Cameron, Elliot, and Karunanayake. *Service needs and self-efficacy of care partners attending rural primary care memory clinics*

12:07-12:18

Skinner, Williamson, **Rampersad**, Reed, Spence, Rourke, and MacLennan, Galli. *Implementation of a Community Driven Point-of-Care Test and Treat Approach to HIV and Syphilis across 28 Diverse Saskatchewan Sites*

12:19-12:30

Lang, Fitzgerald, Bath, Carr, Kim, Loewen Walker, Ray Peters, and McKnight. *Exploring upper limb musculoskeletal symptoms after gender-affirming top surgery*

12:30-12:32
Closing comments
Dr. Josh Lawson

12:33-1:00
Lunch and Discussion

ABSTRACTS

Sodium Glucose Cotransporter 2 inhibitors Preceding ST-elevation Myocardial Infarction: Global Proteomics and Pathobiological Insights

Jay S. Shavadia, MD, Megan Tomilin, MSc, Paulos Chumala, PhD, Rama Mangipudi, MSc, Jacob Udell, MD, Haissam Haddad, MD, George S. Katselis, PhD

This work was supported by Royal University Hospital (RUH) Foundation, R210202 grant, Saskatoon, Saskatchewan, Canada, and by Department of Medicine, internal grant, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada. All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Background: While sodium-glucose cotransport 2 inhibitors (SGLT2i) improve post infarction cardiovascular outcomes, limited understanding exists on how these agents influence pathophysiology preceding myocardial infarction.

Objectives: The objective of this study was to explore how proteins are differentially regulated in patients on and not on an SGLT2i preceding ST-segment elevation myocardial infarction (STEMI).

Methods: Between Jun-2021 and Oct-2023, blood was collected at the time of arterial sheath insertion from consecutive STEMI patients. We then identified patients with diabetes and created propensity matched pairs of patients on and not on SGLT2i prior to STEMI (SGLT2i+ and SGLT2i-). Serum was separated, and following immunodepletion and enzymatic digestion, liquid chromatography-tandem mass spectrometry was performed to identify differentially regulated proteins between the two SGLT2i groups.

Results: Of the 560 STEMI patients, 149 eligible patients had diabetes distributed by pre-existing SGLT2i use as: SGLT2i+ n=35, SGLT2i- n=114. Both SGLT2i groups were comparable in their presenting demographics and reperfusion strategies, except for higher proportion of insulin use in SGLT2i+ patients. 33 SGLT2i+/SGLT2i- propensity matched pairs were created from which 21 differentially expressed proteins were identified; dominantly noted was upregulation of proteins involved in heme-scavenging and nitric oxide transport in patients on SGLT2i+ compared with SGLT2i preceding STEMI.

Conclusions: SGLT2i appears to predominantly associate with upregulation of heme-scavenging and nitric oxide, and plausibly through a related reduction in infarct size also associates with the observed related improvement in post infarction heart failure.

Development of cyclosporin-induced human regulatory dendritic cells for atopic asthma immunotherapy.

Sara Ness, PhD and John R Gordon, PhD

Over half of asthmatic disease falls within the atopic asthma subtype, in which allergen-specific type II T helper (Th2) cells are pivotal players. Dendritic cells (DC) normally activate these Th2 responses but under some conditions DC can instead develop into anti- inflammatory cells called 'regulatory DC (DCreg) which can induce antigen-specific T cell tolerance and regulatory T cell (Treg) differentiation. Herein we have developed a novel cyclosporine A-differentiated DCreg (DCCsA) and examined its tolerogenic potential *ex vivo* in the context of human atopic asthma. We generated DCCsA from blood monocytes of asthmatic donors and characterized their cell surface markers and secreted mediators, transcriptomic profile and abilities to suppress T cell responses *in vitro*.

We found that DCCsA secreted more than 500-fold more IL-10 than comparator stimulatory DC populations (DCstim). Cell surface marker analysis of DCCsA by FACS and CyTOF revealed reduced expression of stimulatory markers relative to DCstim. Transcriptomic analysis via RNA sequencing identified transcripts for more than 13,000 differentially regulated genes between DCCsA and DCstim, 59 of which we focused on herein. DCCsA expressed increased levels of IL-10, IL-6, ALDH1A2 and C1Q, various T cell chemoattractants, chemokine receptors (i.e., CCR5 and CXCR1), and other tolerance-associated markers (eg, stabilin-1).

Co-culture experiments with allergen-presenting DCCsA and autologous Th2 cells demonstrated that DCCsA suppress activation of allergen-specific Th2 cell responses. Moreover, they induced activated Th2 cells to become functional Treg, which also suppress down-stream Th2 cell activation. When purified DCCsA-induced Treg were introduced into cultures of allergen-activated Th2 cells we observed a 4.8-fold increase in the induction of Treg. That is, both our DCCsA and DCCsA-induced Treg were each able to independently convert Th2 cells into Treg, a critical feature of the feedback loop known as 'infectious tolerance' that drives successful outcomes in DCreg immunotherapy.

Ticagrelor As An Add-on Antiplatelet Therapy For Secondary Stroke Prevention In Patients With Cerebrovascular Disorders: Indications and Outcomes

Noman Ishaque[1], Darcy Lamb[2], Gary R Hunter[1]

[1] Division of Neurology, Department of Medicine, USask; [2] Saskatchewan Health Authority

Introduction: Dual antiplatelet therapy is shown to be effective for secondary stroke prevention. In patients with CYP2C19 loss of function alleles, the combination of Aspirin and Ticagrelor modestly reduced risk of recurrent stroke but was associated with higher total number of bleeding events. In this retrospective study, we assessed the use of Ticagrelor in addition to Aspirin for prevention of ischemic stroke in patients with cerebrovascular disorders.

Methods: All the patients who were treated with Ticagrelor on Neuroscience unit of the Royal University hospital between March 2023 and January 2025 were included in this study. Results are descriptive.

Results: A total of 33 patients were treated with Ticagrelor, 17 had neurologic indication and 16 had neurosurgical indication. The median age of patients was 61 years (IQR, 54-71 years), and 19 (57.5%) were female. The most common diagnosis was MCA stroke in neurologic patients (9/17, 53%) and unruptured ICA aneurysm in neurosurgical patients (8/16, 50%). ASPECT score for patients with anterior circulation stroke was 9 (IQR,8-10), and that in patients with posterior circulation stroke was 9 (IQR,8-9). Main indication for Ticagrelor in stroke patients was Clopidogrel failure (13/17, 76.4%), confirmed by platelet assay in 8/13 patients (61.5%). Mild hemorrhagic transformation was noted on baseline scan of 2/17 (11.7%) ischemic stroke patients, one of those patients developed fatal hemorrhagic transformation while on Ticagrelor. Also, 3/16 (18.7%) patients had subarachnoid hemorrhage from aneurysmal rupture, none of those patients developed worsening of subarachnoid hemorrhage on Ticagrelor. One of neurosurgical patients developed fatal traumatic subdural hemorrhage while on Ticagrelor. None of the patients experienced recurrence of ischemic stroke.

Conclusion: Ticagrelor use as add-on antiplatelet therapy prevents recurrence of ischemic stroke in cases of Clopidogrel failure, but caution should be used in patients with hemorrhagic transformation on baseline scan.

Electric Impedance Tomography Detects Lung Volume Changes in Amyotrophic Lateral Sclerosis

Hansen G, Shaw A, Bolt K, Verity R, Nataraj R, Schellenberg KL.

Introduction/Aims: Spirometry is the conventional means to measure lung function in amyotrophic lateral sclerosis (ALS), but is dependent on patient effort and bulbar strength. We aimed to use electric impedance tomography (EIT), an emerging non-invasive imaging modality, to measure dynamic lung volume changes.

Methods: Twenty-one patients with ALS underwent sitting and supine spirometry for forced vital capacity (FVC), and sitting and supine EIT. There were 13 patients in the high FVC group (FVC ≥80% predicted) and 8 in the low FVC group (FVC <80% predicted). Additional demographic and clinical data were collected from clinical records.

Results: Only the low FVC group had significant loss of lung volumes in the supine position (R^2 = 0.89 and $p < 0.001$). The supine volume loss measurement at 10 minutes correlated with sitting (r^2 = 0.47) and supine FVC (r^2 = 0.36), maximum inspiratory (r^2 = -0.44) and expiratory pressures (r^2 = 0.36) (MIP, MEP), and the ALS Functional Rating Scale-Revised (ALSFRS-R) dyspnea subscore (r^2 = 0.36).

Discussion: EIT is an emerging alternative to existing measures of lung function in ALS, but without need for patient effort or bulbar strength. Significant losses in lung volume are seen on supine compared to upright position in patients with respiratory dysfunction. Further study is needed to determine relationships to existing clinical measures.

Health related quality of life in people with Multiple Sclerosis in Saskatchewan

Izn Shahab[1], Thuy Le[2], Ilia Poliakov[1], Katherine Knox[3]

[1]Department of Medicine, USask; [2]The Clinical Research Support Unit, Department of Community Health and Epidemiology, USask; [3]Physical Medicine And Rehabilitation

For people living with multiple sclerosis (MS), health related quality of life is an important aspect of their lived experience and is correlated with disease severity. People with MS referred to Saskatchewan MS Drugs Program were provided with a survey which measured health related quality of life (using the Health Utilities Index Mark 3 [HUI3]) and physical activity (using the Godin Leisure-Time Exercise Questionnaire). 613 people (of 1312) responded to the survey in the period between September 1st, 2014 and August 20, 2024. Scatter plots with fitted linear regression found no significant change in overall HUI3 quality of life score over time. However, a considerable decrease was seen in the emotion score component of the HUI3 (0.008 units for every calendar year of data collection ($p=0.002$); beyond the limit of what is considered clinically meaningful). Univariate, followed by multivariable linear regression analyses examined the associations between independent variables. A significant association was found between measures of physical activity (health contribution score) and the HUI3 multi-attribute utility function score. The HUI3 score on average increased 0.004 unit for every unit increase in the health contribution score ($p<0.001$). Our results indicate that emotional wellbeing may be falling over time in people with MS in Saskatchewan (when they first contact the provincial drug program) and that health-related quality of life is associated with increasing levels of physical activity.

A Comparative Whole Exome Analysis in Patients with Loin Pain Hematuria Syndrome and Isolated Hematuria

Bhanu Prasad (1), Ahmed M. Soliman (2), Aarti Garg (3), Clara Schott (4), Dervla Connaughton (4), Matthew B. Lanktree (5)

(1) Section of Nephrology, Department of Medicine, (2) Department of Chemistry and Biochemistry, University of Regina, (3) Department of Biology, University of Regina, (4) Department of Biochemistry, Schulich School of Medicine and Dentistry, Western University, (5) Departments of Medicine and Health Research Methodology, Evidence, and Impact, McMaster University

Background: Loin pain hematuria syndrome (LPHS) is an ultrarare disease characterized by unexplained chronic loin pain and hematuria, with no identifiable urological causes.

Objectives: To investigate the genetic factors contributing to hematuria and pain in patients with LPHS and isolated hematuria (IH) using whole exome sequencing (WES).

Methods: In this single-center study, 17 consecutive patients with LPHS and 10 with IH underwent WES from January 2022 to January 2023. Bioinformatically created hematuria (n = 130) and pain (n = 577) gene panels were evaluated. Variant annotation, interpretation, and prioritization were performed using the Franklin platform. American College of Medical Genetics and Genomics (ACMG) guidelines were followed for interpreting the identified variants.

Results: A total of 44 variants were identified in 35 hematuria genes. 17 and 27 variants were found in 8 IH patients and 16 LPHS patients, respectively. In three LPHS patients, we detected 3 pathogenic/likely pathogenic (P/LP) missense variants in *COL4A4* (c.G3044A:p.Gly1015Glu), *ABCA1* (c.2861C>T: p.Ser954Leu) exacerbating glomerular endothelial cell injury by promoting cholesterol accumulation and *CXCR4* (c.373C>G: p.Leu125Val) inducing podocyte injury. In another two IH patients, we found a missense variant in *COL4A5* (c.T4561A:p.Cys1521Ser) and a frameshift deletion in *COL4A3* (c.4329_4330del:p.Gly1445Lfs*64). *COL4A3/4/5* genes encode collagen IV, a structural component of the glomerular basement membrane (GBM). A total of 34 variants of uncertain significance (VUS), including genes affecting podocytes (*FAT1*, *ITGB3, ITGB4*, *COQ2*, *APOA1,* and *GAPVD1*), GBM (*GPC5*, *COL4A5*), and endothelial cells (*CFH*, *PLG*) were also identified. A total of 18 rare variants were found in 17 pain genes unique to LPHS patients. None of these pain variants were P/LP.

Conclusions: The etiology of LPHS might be polygenic with a diverse array of hematuria genes affecting the glomerular filtration barrier. Variants in *COL4A3/4/5* were P/LP and identified in IH and LPHS patients. To our knowledge, this is the first WES report on LPHS patients globally.

Dopa-Responsive Parkinsonism Secondary to Tauopathy: Clinical, Pathological, and Genetic Study

S Giri Ravindran[1], B Daud Shah[2], E. Noyes[3], V Zherebitski[4], A. Rajput[5], M. Farrer[6], A. Rajput[7]

Saskatchewan Movement Disorder Program, University of Saskatchewan[1,2,3,5,7], Pathology Department, RUH, University of Saskatchewan[4], Laboratory of Neuroscience and Neurogenetics, University of Florida[6]

Objective: To report on the clinical, pathological, and genetic findings of four cases of levodopa-responsive parkinsonism with long survival and tauopathy.

Background: The most common form of parkinsonism (PS) is Lewy body disease (PD). The second most common degenerative cause of PS is progressive supranuclear palsy (PSP), where abnormally phosphorylated tau inclusions characterize the pathology. A relatively uncommon tauopathy with features of PS is corticobasal degeneration (CBD). Prognosis in PSP and CBD is less favorable than PD. We report four cases of dopa-responsive PS tauopathy with unusually long survival.

Methods: Saskatchewan Movement Disorder Program (SMDP) has operated uninterrupted since 1968. Videos are made on all consenting individuals. Autopsy studies are offered to patients to establish a definitive diagnosis. Canadian certified neuropathologists performed pathology studies at no cost to the family.

Results: Four patients (3 males, 1 female) with clinical diagnosis of Parkinsonism are included. Median onset age was 28 years (range: 13-53 years) and median survival after onset was 52 years (range: 25-61 years). One patient with a heterozygous LRRK2 Gly2019Ser mutation showed substantia nigra degeneration tau inclusions involving multiple brain regions. Another case with a homozygous DNAJC12 p.K63* mutation exhibited mild tauopathy predominantly in the brainstem and deep grey structures. Third case with PARKIN mutation displayed mild tauopathy with tau inclusions in the midbrain, hippocampal formation, and cingulate gyrus. The fourth case, without genetic study, had pathology consistent with PS-neurofibrillary tangles. Notably, all cases were levodopa-responsive. Tau distribution patterns in these cases differed from typical PSP and CBD, suggesting a distinct form of tauopathy-associated parkinsonism.

Conclusion: We show another mostly genetic form of tauopathy associated parkinsonism, distinct from PSP and CBD. These findings suggest that there are several different metabolic pathways for tau inclusion formation with widely varying outcomes. Further studies are needed to determine the pathophysiology of tau protein formation.

Service needs and self-efficacy of care partners attending rural primary care memory clinics

Julie Kosteniuk, Debra Morgan, Megan E. O'Connell, Chelsie Cameron, Valerie Elliot, Chandima Karunanayake

Background: Rural primary care memory clinics have been adapted and implemented by primary health care teams in southern Saskatchewan in collaboration with the Rural Dementia Action Research (RaDAR) team at the University of Saskatchewan. The memory clinics situated in rural communities aim to improve accessibility of dementia diagnosis and management, and timely connections to services and supports.

Objective: The objectives were to compare the service/support needs and self-efficacy of care partners at the time of initial assessment in a memory clinic and 1-month post-assessment, and to examine care partner perceptions about the adequacy of information received at initial assessment.

Methods: At initial assessment and 1-month post, from November 2019 to March 2024, semi-structured interviews were conducted with 38 care partners. The interview at both timepoints included an open-ended question about potentially beneficial services/supports not yet received, and the 4-item Care Ecosystem Caregiver Self-Efficacy Scale (score 5-20). In the 1-month interview, care partners were asked if they had received adequate information about 12 specific topics and services at the initial assessment. Paired samples proportion tests and t-tests were used to compare initial assessment and post-assessment measures.

Results: Between initial assessment and 1-month post, the proportion of care partners who identified potentially beneficial services/supports decreased significantly from 45.7% to 31.4% (p=0.048), and the mean caregiver self-efficacy score increased significantly from 14.3 to 16.2 (p=<0.001, Cohen's d=0.70). The proportion of care partners who reported receiving adequate information about 12 particular topics/services ranged from 43.3% to 90.6%.

Conclusion: This study suggests that rural primary care memory clinics in local communities may facilitate connections to beneficial services/supports and promote caregiving self-efficacy. These findings are consistent with an expanding evidence base demonstrating the benefits of primary care-based models of dementia care.

Implementation of a Community Driven Point-of-Care Test and Treat Approach to HIV and Syphilis across 28 Diverse Saskatchewan Sites

Skinner S[1,2], Williamson N[1,2], Rampersad V[3], Reed N[1], Spence C[1], Rourke S[4], MacLennan K[4], Galli R[4]

[1]University of Saskatchewan, Saskatoon, Saskatchewan; [2]Wellness Wheel Medical Clinic, Regina, Saskatchewan; [3]Indigenous Services Canada – Saskatchewan Region, Regina, Saskatchewan; [4]MAP Centre for Urban Health Solutions, St. Michael's Hospital (Unity Health Toronto), Toronto, Ontario

Background: Rural, street-involved, and underserved populations are at the highest risk for sexually transmitted infections (STIs), including HIV and syphilis, due to significant barriers in accessing care, leading to delays in diagnosis and treatment. In 2023, Saskatchewan reported 19.4 new HIV diagnoses per 100,000 people—nearly three times the national rate. Similarly, the 2023 rate of new syphilis diagnoses was 159.3 per 100,000 in Saskatchewan, reflecting a 1,213% increase since 2018. In response, Wellness Wheel Medical Clinic and REACH Nexus employed a point-of-care testing (POCT) and treatment model for HIV and syphilis.

Methods: A community-level strategy was developed with input from Indigenous peoples, healthcare providers and community leaders to ensure alignment with cultural practices and values. Sites were mobile and adaptive, leveraging local community-based partnerships to utilize trusted spaces. Sites were staffed by a diverse team of health providers, outreach workers, and peer support workers. Participants were offered POCT for HIV and/or syphilis, along with serological testing. Participants with positive POCT results for syphilis were immediately provided treatment when deemed appropriate, while positive POCT results for HIV triggered rapid linkage to care.

Results: The study recruited 1,797 participants from 28 sites throughout Saskatchewan, including First Nations communities (14), community-based organizations (5), healthcare clinics/facilities (4), rural towns (3), pharmacies (1), and correctional facilities (1). The results are presented in Table 1.0.

Conclusion: The approach, grounded in collaboration, cultural safety, and resource integration, was effective in reaching high-risk populations. The straightforward design and emphasis on partnerships facilitated rapid implementation. The strength-based approach involved numerous First Nations communities and community-based organizations along with other diverse sites across Saskatchewan. By utilizing trusted local spaces, this model provides a reproducible and scalable solution for addressing similar STIs and health challenges in Saskatchewan and for First Nation communities across Canada.

Exploring upper limb musculoskeletal symptoms after gender-affirming top surgery

Angelica E. Lang, Sarah Fitzgerald, Brenna Bath, Tracey Carr, Soo Kim, Rachel Loewen Walker, Meaghan Ray Peters, & Liz McKnight

Introduction: Transgender and gender diverse (TGD) people are important members of our diverse society with distinct health care experiences and needs. An estimated one in 300 people in Canada over the age of 15 are transgender. Many TGD individuals choose to have gender-affirming surgery, such as top surgery, to modify their bodies to better conform to their gender identity and expression. Gender-affirming surgery is often medically necessary to alleviate gender dysphoria. These procedures may also have physical side effects for patients that are not well understood. The purpose of this study was to define the scope and scale of potential postsurgical upper limb musculoskeletal symptoms in TGD individuals in Canada.

Methods: Adults living in Canada who had undergone gender-affirming top surgery (either masculinizing or feminizing) were recruited to complete an online survey with closed- and open-ended questions about postsurgical musculoskeletal experiences.

Results: The majority of respondents (77 out of 78) underwent masculinizing surgery. All but two participants indicated the presence of at least mild effects of at least one symptom. Symptom reports ranged from 19% to 83%, with changes in front of chest sensation being the most common symptom (83%), followed by chest tightness (71%). Front chest sensation changes were severe or limiting for 33% of participants. Additionally, only 28% of participants felt their musculoskeletal symptoms were fully resolved, and 29% sought postsurgical musculoskeletal rehabilitation.

Discussion: These findings indicate there is a need for improved access to safe care for TGD individuals after surgery. Bearing in mind that gender-affirming surgery is medically necessary and leads to enhanced happiness and mental health for patients, awareness of the potential musculoskeletal symptoms, combined with enhanced trans-specific resources and care pathways, would help to maintain high quality of life.