PATHOLOGY AND LABORATORY MEDICINE

# RESEARCH DAY 2023

# PROGRAM GUIDE

Schulich MEDICINE & DENTISTRY

London Health Sciences Centre

Western

Welcome to one of our department's most important academic events of the year. Our Pathology and Laboratory Medicine Research Day showcases our research accomplishments, celebrates our people, and gives us a glimpse into an exciting future for both our department, as well as for our School and University.

This year, we have a record number of 121 research presentations, given by an array of researchers that displays the breadth of our department's research. These presenters include undergraduate students, graduate students, postdoctoral fellows and scholars, research scientists and residents. The research being presented spans all of our department's research themes, including amongst others, cancer biology, cardiovascular, respiratory and metabolic diseases, infection, immunity and inflammation, and bioinformatics and data science.

This year, we welcome Dr. Anne Martel as our Keynote Speaker. Dr. Martel is a Professor in Medical Biophysics at the University of Toronto and a Senior Scientist at Sunnybrook Research Institute. Her research is focused on advanced machine learning methods for segmentation and classification, digital pathology and personalized medicine. In 2006, Dr. Martel co-founded Pathcore, a digital pathology software company. She is also a board member and fellow of the Medical Image Computing and Computer Assisted Interventions Society, and a member of the advisory board for the Imaging Data Commons – part of the NIH-NCI Cancer Research Data Commons.

The organizing committee and many members of our department have dedicated considerable time to ensure that this day is a rewarding experience for our department members and for our wider community. I would like to thank the Research Day Committee as well as the members of our university department staff for their tremendous work in putting this day together, and my thanks to all of the judges for their invaluable service. My heartfelt congratulations to all of the presenters for the work that you have done on your research and for representing the Department of Pathology and Laboratory Medicine. And finally,

I would like to thank all of you for attending and supporting our department. I hope that you enjoy our multi-disciplinary approach to studying health and disease, as you listen to the platform presentations and view the posters.

David Driman, MBChB, FRCPC
Chair, Department of Pathology and Laboratory Medicine,
Schulich Medicine & Dentistry, Western University
Chief, Department of Pathology and Laboratory Medicine,
London Health Science Centre and St. Joseph's Health Care





# Dr. Anne Martel

Senior Scientist,
Sunnybrook Research Institute
Professor, Medical Biophysics
Faculty of Medicine, University of Toronto

## 9:15 am - 10:15 am

## *"AI in digital pathology: opportunities and challenges"*

Dr. Martel is a Professor in Medical Biophysics at the University of Toronto, and a Senior Scientist at Sunnybrook Research Institute. Her research program is focused on medical image and digital pathology analysis, with particular focus on applications of machine learning for segmentation, diagnosis, and prediction/prognosis. Dr. Martel has co-founded Pathcore, a complete workflow solution for digital pathology.

| | |
|---|---|
| 9:00 – 9:15 am | **Welcome and Opening Remarks**<br>**Dr. David Driman**<br>Chair/Chief, Pathology and Laboratory Medicine, Schulich Medicine & Dentistry, Western University and London Health Science Centre |
| 9:15 – 10:15 am | **Keynote**<br>**Dr. Anne Martel**<br>Senior Scientist, Sunnybrook Research Institute<br>Professor, Medical Biophysics<br>Faculty of Medicine, University of Toronto |
| 10:15 – 10:30 am | Nutritional Break |
| 10:30 – 11:00 am | **Oral Presentations – Session A** |
| 11:00 – 11:15 am | Group Photo |
| 11:15 – 12:45 pm | **Poster Presentations – Session A** |
| 12:45 – 1:45 pm | Lunch |
| 2:00 – 3:00 pm | **Oral Presentations – Session B** |
| 3:00 – 4:30 pm | **Poster Presentations – Session B** |
| 5:00 – 7:00 pm | **Award Ceremony** |





## **Oral Presentations – Session A** (Morning)

| Time | First Name | Last Name | Title |
|---|---|---|---|
| 10:30 am | Tommaso | Romagnoli | Comparison of BRAF V600E immunohistochemistry of corresponding biopsy and resection specimens of colorectal adenocarcinomas |
| 10:45 am | Erin | Brintnell | HUNePi: A rapid method for estimating the lineage-specific number of infections from SARS-CoV-2 phylogenies |

## **Oral Presentations – Session B** (Afternoon)

| Time | First Name | Last Name | Title |
|---|---|---|---|
| 2:00 pm | Shervin | Pejhan | Clinical relevance, and prognostic significance of isolated angiitis of the vasa vasorum in temporal artery biopsies |
| 2:15 pm | Katherina | Baranova | A landscape of composite lymphomas associated with Hodgkin lymphoma |
| 2:30 pm | Frederikke | Larsen | DNA hypomethylation inhibits colitis-associated cancer |
| 2:45 pm | Michael | Roes | HOXA9 promotes enzalutamide resistance in RB-p53 deficient prostate cancer |

**Presenter's Name:** Romagnoli, Tommaso

**Additional Author(s):** Keow K, Wehrli B

**Abstract Title:** Comparison of BRAF V600E immunohistochemistry of corresponding biopsy and resection specimens of colorectal adenocarcinomas

**Abstract:**
**Introduction:** BRAF is a proto-oncogene involved in MAPK/ERK signal transduction pathway. In colorectal adenocarcinoma, mutations in this gene are associated with oncogenesis and have important implications for hereditary cancer syndromes such as Lynch syndrome and prognostic value. The most common activating mutation is a V600E point mutation, however, its identification is limited to Next Generation DNA sequencing (NGS), a costly technique with a relatively long turnaround time. The anti-BRAF V600E antibody was previously applied to melanoma, hairy cell leukemia and colon adenocarcinoma. However, the results using colon resection specimens (38 total cases) was variable (sensitivity 77-100% and specificity 64-96%). In this study we aim to optimize the use of this antibody for application in colorectal cancer using biopsy specimens to minimize pre-analytical variables such as ischemic and fixation times.

**Methods:** Seventeen colonic biopsy cases with corresponding resections and a diagnosis of invasive colorectal adenocarcinoma were identified (7 with BRAF V600E mutation, 10 without). Cases with superficial sampling or ones performed at different institutions were excluded. Next generation sequencing was previously performed on the corresponding resection case. BRAF V600E immunohistochemistry (clone VE1, Abcam, 1:100) was performed on tissue sections from each case on a Dako OMNIS platform (Agilent, Santa Clara). BRAF stained slides were reviewed by a pathologist, and scored according to cytoplasmic staining intensity.

**Results:** There was strong staining in 6 of 7 colon adenocarcinoma cases with a BRAF V600E mutation. One case with a BRAF V600E mutation had no staining. There was no staining in 9 of 10 cases without a BRAF V600E mutation and one had equivocal staining. In comparison, 3 resection cases without a BRAF V600E mutation and previous equivocal BRAF staining were negative on the corresponding biopsies. A false positive resection case was equivocal on the biopsy.

**Discussion:** The sensitivity and specificity of a BRAF V600E immunohistochemical antibody using biopsies (86-100% and 90%, respectively) was improved relative to resections (77-100% and 64-96%, respectively). This may be attributed to minimizing pre-analytical variables such as ischemic and fixation times. We conclude that molecular NGS testing should be performed on any negative or indeterminate cases. Overall we demonstrate a viable assay for expediting Lynch Syndrome screening.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Brintnell, Erin

**Additional Author(s):** Gugan G, Poon A

**Abstract Title:** HUNePi: A rapid method for estimating the lineage-specific number of infections from SARS-CoV-2 phylogenies

**Abstract:**
Throughout the SARS-CoV-2 pandemic, tracking and dynamic modeling of circulating infections has been instrumental in guiding public health decision making. However, it is difficult to accurately estimate the number of infections from confirmed cases, for example due to variation in testing rates. We, therefore, aimed to develop new estimators of the number of infections (I) based on features of virus phylogenies.
We simulated 1,000 replicate phylogenies under a susceptible-exposed-infected-recovered (SEIR) model using the R package TiPS. We then simulated sequences from the phylogenies using INDELible v.1.03, and reconstructed neighbor-joining phylogenetic trees from the resulting data using the method implemented in CoVizu, a real-time tracking and visualization system for SARS-CoV-2 lineages. For each simulated tree, we extracted the Shannon Index (H), the number of unsampled internal nodes (U), the λ-skyline effective population size (Ne) and the nucleotide diversity (π, thus "HUNePi").

All statistics were significantly associated with I, however when infections were decreasing this association was less powerful. Consequently, we trained logistic regression classifiers to predict if I was increasing or decreasing. We then individually trained Gamma regression models to estimate I for each of increasing and decreasing infections. For each model we assessed whether selecting all or some of the summary statistics increased model accuracy. We determined that the models containing all summary statistics performed the best, likely due to each summary statistic representing different population dynamics. Finally, we applied HUNePIE to actual sequence data for recent SARS-CoV-2 lineages sampled predominantly in the USA and Denmark, e.g., BA.1.17, BA.1.23, BA.2.2. The ratio of predicted I to sample sizes were generally consistent with known differences in sequencing between countries.

Once applied to SARS-CoV-2 phylogenies, our models could predict which SARS-CoV-2 variants are being significantly under sampled. Coupled with data on the epidemiological effects of certain SARS-CoV-2 mutations, this information could alert public health officials to future variants of concern.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Pejhan, Shervin

**Additional Author(s):** Barra L, Basharat P, Allen LH, Bursztyn LL, Proulx AA, Chen RY, Smith M, Hackett MJ, Hammond RR

**Abstract Title:** Clinical relevance, and prognostic significance of isolated angiitis of the vasa vasorum in temporal artery biopsies.

**Abstract:**
**Introduction:** Temporal arteritis (TA) is a well-known clinical-pathological entity. Untreated, many patients will suffer vision loss and/or stroke. Angiitis of vasa vasorum (AVV) and small vessel vasculitis of the periadventitia (SVV), whose significance is uncertain, may also be present in isolation or in combination with TA.

**Methods:** We investigated the relevance of small vessel inflammation in temporal artery biopsies. Our dataset consists of 72 consecutive temporal artery biopsies (TAB) and matching retrospective clinical data. Scoring of inflammation on TAB was designed to include vasa vasorum and periadventitial small vessels. Specimens were categorized into 3 subgroups: TA, Isolated AVV (IAVV), and Isolated SVV (ISVV). Follow-up was 1 year post-biopsy.

**Results:** Microscopy revealed TA in 25% of cases, IAVV in 21% and ISVV in 7%, while 47% were negative. All TA cases had accompanying small vessel inflammation (AVV in 78%, SVV in 5%, and AVV+SVV in 17%). Demographics were similar across the groups. Diplopia and jaw claudication were more common in TA than IAVV/ISVV. ESR and C-reactive protein were higher in TA as well. In patients with IAVV/ISVV, 44% had a moderate to high clinical probability of TA at presentation and 28% acquired a diagnosis of TA during follow-up versus 14% with a negative TAB. The interval between initiation of corticosteroids and biopsy was longer in IAVV/ISVV than in TA.

**Discussion:** The significance of small vessel inflammation in temporal artery specimens has been debated. In our study, TA and AVV frequently co-exist, reinforcing their association. Patients with IAVV/ISVV had longer corticosteroid exposure, which may have impacted TAB findings. These patients were also twice as likely to receive a clinical diagnosis of TA in follow-up compared to those with no inflammation on TAB. The effects of corticosteroids, and the segmental nature of vascular involvement in TA should be considered in assessing inflammation, and planning treatment.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** Infection, Immunity, and Inflammation
**Research theme 3:** Pathobiology of Neurologic Diseases





**Presenter's Name:** Baranova, Katherina

**Additional Author(s):** Howlett C, Sangle N, Tran C

**Abstract Title:** A landscape of composite lymphomas associated with Hodgkin lymphoma

**Abstract:**
Composite lymphoma is diagnosed when there is synchronous presence of two distinct varieties of lymphoma in one patient, with 1-4% of lymphomas being composite lymphomas. Classic Hodgkin lymphoma can rarely co-exist with B-cell non-Hodgkin lymphoma with only a few hundred cases reported in the literature, limited to case reports and small series. Here we present seven composite lymphomas with classic Hodgkin lymphoma (CHL). The majority of cases (five; 71%) were composite chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) with CHL. The remaining two cases were composite marginal zone lymphoma (MZL) and composite follicle centre cell lymphoma with CHL. Interestingly, in two of the composite CLL/SLL cases, previous biopsies showed Reed-Sternberg-like cells without a conclusive diagnosis of CHL, possibly indicative of either precursor lesions or sampling issues. For one case, a subsequent biopsy several months later was diagnostic of composite CLL/SLL and mixed cellularity classic Hodgkin lymphoma. The second case was re-biopsied several times, with one lymph node showing a diagnosis of CHL with no CLL/SLL component. PCR-based testing for clonal immunoglobulin heavy chain (IgH) and light chain (IgK) rearrangements may shed light on the potential genesis of select composite lymphomas. Simultaneous involvement of a lymph node with two separate lymphomas is quite rare. In this case series, we review the pathogenesis of composite lymphomas associated with CHL, diagnosis, histopathology, and molecular mechanisms with a review of the literature. Our case series suggests re-biopsy is potentially warranted for cases which show Hodgkin/Reed-Sternberg-like cells, but do not meet diagnostic criteria for composite lymphoma.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Larsen, Frederikke

**Additional Author(s):** Good HJ, Shin AE, Derouet MF, Zhang L, Castellani C, Asfaha S

**Abstract Title:** DNA hypomethylation inhibits colitis-associated cancer

**Abstract:**
**Introduction:** Colorectal cancer is the second leading cause of cancer death globally. A major risk factor is chronic inflammation leading to colitis-associated cancer (CAC). We previously described a CAC mouse model in which tumors arise from DCLK1+ cells following loss of the tumor suppressor adenomatous polyposis coli (APC) and induction of colitis. Interestingly, both colitis and CAC display epigenetic changes that modulate gene expression. However, the impact of DNA methylation on colonic tumorigenesis is unknown. Thus, we hypothesize that inhibition of DNA methylation reduces colonic tumorigenesis. We investigated this by inhibiting DNA methylation by genetic and pharmacologic means.

**Methods:** Using a publicly available dataset (GSE75214) of gene expression data analyzed by microarray from colonic biopsies of patients with active ulcerative colitis and Crohn's disease, we examined the expression of DNA methyltransferases (DNMTs). Expression of DNMTs in mice with colitis was examined by RT-qPCR. In separate experiments, Dclk1/Apcf/f mice were crossed to Dnmt1f/f mice to knock-out the DNA methyltransferase DNMT1 in DCLK1+ cells. Dclk1/Apcf/f and Dclk1/Apcf/f/Dnmt1f/f mice were administered three doses of tamoxifen followed by 2.5% dextran sodium sulfate (DSS) for five days to induce colitis. Fourteen weeks later, we assessed colonic tumor number. In a separate cohort of Dclk1/Apcf/f mice, we induced colitis and treated the mice with six doses of the DNA de-methylating drug 5-AZA-2'-deoxycytidine (AZA) or vehicle, and assessed colonic tumor number. To examine DNA methylation changes, we treated WT mice with AZA and DSS and isolated colonic epithelial cells. DNA was then isolated and run on the Infinium Mouse Methylation BeadChip Array.

**Results:** Patients with IBD were found to have increased expression of DNMT1 compared to healthy controls. Similarly, mice treated with DSS had increased DNMT1 expression. Deletion of DNMT1 in DCLK1+ cells significantly inhibited the number and size of colonic tumors. Treatment of mice with AZA decreased global and gene specific DNA methylation levels, and significantly reduced both the number of mice with tumors, colonic tumor number, and size.

**Discussion:** Our findings demonstrate that colitis in both patients and mice is associated with DNA methylation. Furthermore, DNA hypomethylation by AZA treatment or DNMT1 loss reduces CAC formation suggesting that DNA methylation plays a critical role in colonic tumorigenesis.

**Research theme 1:** Cancer Biology
**Research theme 2:** Epigenetics
**Research theme 3:**





**Presenter's Name:** Roes, Michael

**Additional Author(s):** Dick F

**Abstract Title:** HOXA9 promotes enzalutamide resistance in RB-p53 deficient prostate cancer.

**Abstract:**
Castration resistant prostate cancer (CRPC) cells can acquire resistance to the androgen receptor (AR) inhibitor enzalutamide (EZ). These cells can switch lineages from an adenocarcinoma to a neuroendocrine (NE) cell type that proliferate independently of AR signaling. Studies have shown that RB1 and TP53 co-deletion can promote the acquisition of EZ resistance and NE features. However, RB and p53 are tumour suppressors and are difficult to target therapeutically. This study aims to identify an actionable molecular factor downstream of RB and p53 that drives EZ resistance in CRPC. To characterize the features of RB and p53 loss, we generated double knockout (DKO) LNCaP prostate cancer cells. Compared with LNCaP wild type (WT) cells, only DKOs formed colonies over a 4-week colony forming assay under EZ treatment. RNA sequencing and gene ontology (GO) analysis of DKO and WT cells revealed NE and stemness genes, including HOXA9, were significantly upregulated in DKOs. To categorize gene loss events in EZ-treated LNCaP cells, a genome-wide CRISPR knockout (KO) screen was performed. Pools of KO cells were treated with EZ or DMSO and analyzed by next generation sequencing to identify gene KOs that confer increased sensitivity to EZ. GO analysis of de-enriched genes following EZ treatment identified stemness genes, including HOXA9, highlighting the importance of a stem-like phenotype for acquiring EZ resistance. To investigate the significance of HOXA9 we analyzed EZ-resistant prostate tumour data. HOXA9 is amplified or overexpressed in 10% of cases and is associated with poorer prognosis. HOXA9 expression is also positively correlated with NE features and negatively correlated with RB1 expression. LNCaP WT and DKO cells engineered to overexpress HOXA9 displayed increased IC50 values following a 6-day EZ treatment, compared with parental lines. DKO cells overexpressing HOXA9 also formed significantly more drug resistant colonies than parentals. In contrast, shRNA knockdown of HOXA9 drove a reduction in IC50 values and formed fewer colonies compared with control cells. Finally, DKO and WT cells were co-treated with the HOXA9 inhibitor DB818 and EZ. Compared with WT cells, DKOs were more sensitive to DB818 alone and showed higher synergy to reduce cell viability, when co-treated with EZ. Overall, these results suggest that HOXA9 regulates EZ resistance in prostate cancer. Furthermore, HOXA9 inhibition may provide therapeutic benefit for treating EZ-resistant CRPC.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**

# Poster Presentations
# Session A
# 11:15 am - 12:45 pm



| # | First Name | Last Name | Title |
|---|---|---|---|
| 1 | Ronan | Anderson | Synovial Pathophysiology Across a Spectrum of Hip Disorders: From Pre- to End-Stage Hip Arthritis |
| 2 | Maria Paula | Arias Rodriguez | A Case of Pediatric Arrhythmogenic Right Ventricular Cardiomyopathy |
| 3 | Maria Paula | Arias Rodriguez | Examining the Variability in Number of Lymph Nodes Based on Colorectal Specimen Size. |
| 4 | Reza | Asakereh | An Automated Scoring Method to Determine the Infiltrative Pattern of Lung Cancer Brain Metastasis |
| 5 | Ela | Bandari | Undergraduate Classroom Crowdsourcing of Cell Height-to-Width Ratio in Papillary Thyroid Carcinoma: Implications for Diagnosis and Progression-Free Survival |
| 6 | Helen | Boles | Understanding Circular RNA Back-splicing Regulation and Efficiency |
| 7 | Tony | Chen | Investigating the Effects of Timing, Accelerometry, and Temperature of Pneumatic Tube Systems on Blood Samples |
| 8 | Farhan | Choudhary | Using the One Health Approach to Investigate the Extent of Human Health Impacts due to Climate Change on Walpole Island First Nations and the Broader Southwestern Community |

| # | First Name | Last Name | Title |
|---|---|---|---|
| 9 | Joni | Cogghe | AIM2 as an Endogenous DNA Sensor and a Potential Player in Post-Heart Transplantation Organ Viability |
| 10 | Gabriela | Dabrowski | Evaluation of the Roche Cobas® Pulse Glucose Monitoring System |
| 11 | Chen Jun | Gao | Upstream Regulators of YAP/TAZ in Non-alcoholic Fatty Liver Disease |
| 12 | Laura | Gendron | A One Health Approach to Examining Potential Reprogramming Events Causing Neoplastic Change in Oviductal Cells |
| 13 | Hasti | Gholami | Analyzing the Immunomodulatory Effects of Immunotherapy Responsive Neuroblastoma Tumours with Induced DNA Mismatch Repair Deficiency and their Gut Microbial Features |
| 14 | Madison | Gray | Immune checkpoint inhibitor myositis: a rare complication of an important therapeutic intervention |
| 15 | Adam | Greasley | Generation of Hypoxic Real-time Cell Monitoring Model for Cardiac Ischemia and Ischemia Reperfusion Injury |
| 16 | Natalie | Grindrod | Digital assessment of TILs as a biomarker in breast cancer |
| 17 | Moheem | Halari | A Postmortem Study of Injury Patterns in Pedestrian and Cyclist Fatalities in Ontario |





| # | First Name | Last Name | Title |
|---|---|---|---|
| 18 | Ji Hyun | Han | Osteomyelitis of the jaw: An investigational study of the clinicopathological features and pathogenesis of refractory vs non refractory osteomyelitis |
| 19 | Natasha | Holder | Glandular Odontogenic Cyst: Molecular Analysis using Targeted Next-Generation Sequencing |
| 20 | Aansah | Imran | Islet Hormone Regulation of Glucagon Secretion Occurs Through Increased Trafficking to the Endolysosomal System Mediated by STMN2 |
| 21 | Matthew | Jackson | Use of a VHH-IgA Fc fusion protein targeting surface protein Intimin to block E. coli O157:H7 colonization in GI tract of mice |
| 22 | Christian | James-McDonald | Investigation of the Effects of DNA Demethylating Drugs on DCLK1+ Cell Derived Tumor Organoids |
| 23 | Helen | Ji | Simulated biopsy cores in lung cancer resections to understand cellularity distribution across tumours and adequacy for molecular testing |
| 24 | Bernie | Jin | Comparing Intrinsic Disorder of Core and Accessory Viral Proteins |
| 25 | Victor | Lam | Digital Quantification of Tumor Density in Relation to Human Papillomavirus status in Head and Neck Squamous Cell Carcinoma |

| # | First Name | Last Name | Title |
|---|---|---|---|
| 26 | Michael | Levy | Quantification of DNA methylation episignatures for the diagnosis of Mendelian neurodevelopmental disorders |
| 27 | Amanda | Liddy | Bacterial-Based Therapy with Akkermansia muciniphila to Modulate Tumour and Gut Microbiome and Activate T-Cells in Pancreatic Cancer |
| 28 | Sherman | Lin | 1000 Mitoses Project: An International Consensus on Mitotic Figures |
| 29 | Amber | Liu | Benchmarking BABEL Deep Learning Method Against Various Cell Types in Humans and Mice |
| 30 | Laura | Lockau | The use of fiducial markers to improve orientation and facilitate preparation of cell block specimens in cytopathology |
| 31 | Bonnie | Lu | Bayesian analysis of generative models of sequence insertion events in HIV-1 envelope glycoproteins |
| 32 | James | MacDonald | Netrin signaling mediates survival of dormant epithelial ovarian cancer cells |
| 33 | Allison | McLoughlin | CircHUWE-1 as a Regulator of Prostate Cancer Growth |
| 34 | Anushga | Muralitharan | Reflexive ABPAS Staining of Esophageal Biopsies is Not Cost-Effective |





| # | First Name | Last Name | Title |
|---|---|---|---|
| 35 | Prey | Parikh | The Characterization of a 'Scar Tissue' Phenotype of Fibrous Proliferations of the Oral Mucosa and Gingiva |
| 36 | Milica | Pavlovic | Diabetes and the Relationship Between Post-Stroke Cognitive Impairment and Falls |
| 37 | Raissa | Relator | Methylation status of imprinted regions in neurodevelopment disorders |
| 38 | Julie | Richmond | Correlation between Gross and Radiologic Size of Lung Cancers |
| 39 | Ananilia | Silva | DNA methylation episignature for Neurodevelopmental Disorder with Hypotonia, Stereotypic Hand Movements, and Impaired Language, NEDHSIL, syndrome |
| 40 | Brandon | Tapp | Questionnaire Design for the Identification of Oral Health Status and Oral Health Service Utilization Among Rwandan Pregnant Women |
| 41 | Michael | Tran | Candescence 2.0, developing an accessible deep learning approach to identifying Candida albicans morphology |
| 42 | Erik | Trautrim | Anxiety in the workplace: handling abnormal prions and common infectious agents |
| 43 | Venkat | Vaibhav | The role of 5-lipoxygenase (5-LO) expressing cells in colitis-associated colorectal cancer |

| # | First Name | Last Name | Title |
|---|---|---|---|
| 44 | Meggie | Vo | Doxorubicin induces SerpinA3 expression in cardiomyocytes |
| 45 | Sachee | Vora | Applying a One Health Approach to Investigating Refugee Health Models and Evaluating the Efficacy of the Newcomer Clinic and Integration Program |
| 46 | Kevin | Vytlingam | Determining the interaction between junctophilin-2 and junctin by the bimolecular fluorescence complementation (BiFC) assay |
| 47 | Eric | Wang | miR-9 regulates endothelial-to-mesenchymal transition in diabetic complications |
| 48 | Sumaiyah | Wasif | Investigating the Role of Netrin Signalling in High-Grade Serous Ovarian Cancer Spheroid Survival and Chemotherapy Resistance |
| 49 | Isabel | Wang | What We Can Learn From the Victorians: A Comparison of Modern and Victorian Epidemic Response and Prevention |
| 50 | Shirley | Wang | Unlocking cellular potency in human cells through chemical reprogramming |
| 51 | Honglin | Wang | CircRNA_012164 interacts with microRNA-9-5p to mediate diabetic cardiac fibrosis |
| 52 | Phyo | Win | The role of mitochondrial DNA modifying agents on the nuclear epigenome and transcriptome |





| # | First Name | Last Name | Title |
|---|---|---|---|
| 53 | Elissa | Woo | Use of flexible transparent film as a novel physical support for histologic slides to facilitate next generation slide scanning |
| 54 | Ha Ryun | Yang | Anemia associated with Decreased Plasma Zinc Levels is Likely Secondary to Acute Inflammation |
| 55 | Manus | Yu | IL-21 and TGFβ Influence Glucocorticoid Insensitivity in Th2-Th17 double-positive cells. |
| 56 | Danish | Zahid | Assessing the Robustness of Episignature-Based Disease Prediction Methodology to Random Variation: A Feasibility Study on Artificially Forging an Episignature in the Absence of Disease |
| 57 | Angela | Zemingui | Characterizing the Impacts of Lifelong Western Diet Exposure on Maternal and Fetal Renal Tissues |

**Presenter's Name:** Anderson, Ronan

**Additional Author(s)**: Lanting B, Appleton CT, Degen RM, Brackstone M

**Abstract Title:** Synovial Pathophysiology Across a Spectrum of Hip Disorders: From Pre- to End-Stage Hip Arthritis

**Abstract:**
**Introduction:** Femoroacetabular impingement (FAI) and hip osteoarthritis (HOA) are two pathologies affecting vastly different populations, with FAI affecting young adults and HOA associated with the elderly. FAI is considered pre-arthritic, yet little research has addressed pathophysiology of the disorder in relation to HOA. Synovium's role in joint homeostasis makes the focus on synovial pathophysiology important to improving understanding of early processes involved in OA onset. Microvascular dysfunction (MVD) in OA synovium is an important pathogenic change associated with pain, inflammation, and aberrant gait biomechanics in knees. The present study seeks to understand pathophysiological changes in synovium that may occur in young FAI patients and may mark the earliest beginnings of changes leading to HOA.

**Methods:** Synovium and fat pad were collected from hips of patients undergoing surgery to treat FAI and/or HOA. Patients completed clinical outcomes assessing pain, function, and QoL. Synovium and fat pad tissues were graded using a 7-item synovitis scoring system, including 3 parameters measuring MVD. Synovial microvessel stability was assessed using immunofluorescence, reported as mature versus immature microvessel density. Increased immature microvessel density was considered an indicator of neovascularization.

**Results:** Participants were stratified into one of three cohorts based on radiographic findings: (1) FAI, (2) early HOA, (3) advanced HOA. Clinical outcomes, histopathological grading, and microvessel stability will be reported. Correlations between individual parameters of synovitis and patient-reported pain will be tested. Histopathology will be compared between subsets of HOA patients with concurrent FAI versus those without FAI.

**Discussion:** The connection between FAI and HOA remains unknown. Although research has evaluated the presence of inflammation and fibrosis in OA, most of these studies are focused on knee OA rather than HOA. Furthermore, there is limited inquiry into pathophysiological features across the disease spectrum of OA, from pre-arthritic FAI to early OA, to end-stage OA. This work aims to improve the understanding of FAI and HOA pathophysiology and seeks to understand whether synovium is involved in changes occurring between FAI development and OA onset. This is the first study to address pathophysiology of synovium in FAI, and the first to investigate synovial MVD in this young, pre-arthritic hip population.

**Research theme 1:** Infection, Immunity, and Inflammation
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Arias Rodriguez, Maria Paula

**Additional Author(s):** Glembocki A, Krutikov K, Chiasson D

**Abstract Title:** A Case of Pediatric Arrhythmogenic Right Ventricular Cardiomyopathy

**Abstract:**
**Introduction:** Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inheritable progressive cardiac disease that affects the myocardium. ARVC is characterized by the fibrofatty replacement of the right ventricular free wall, this can cause arrhythmias, heart failure and sudden death. The prevalence of ARVC in adults is estimated to be 1:5000, however the prevalence in pediatric patients is not know because ARVC is rarely diagnosed during childhood. Pediatric ARVC is difficult to diagnose as patients do not often present with any symptoms until the disease has progressed too far.

**Case:** The patient is a 14-year-old that presented with new onset severe biventricular dysfunction, a thrombus in the left ventricle, abdominal distension, and bilateral leg edema. The patient had no history of cardiomyopathy. The echocardiogram showed the thrombus, no outflow obstruction, severe tricuspid valve regurgitation and severe biventricular dysfunction. The patient was able to undergo a heart transplant, but the underlying cause of heart failure was unknown.

**Discussion:** A gross examination of the explanted heart was conducted and revealed cardiomegaly, moderate biventricular chamber dilation and most notably that the right ventricular myocardium was extensively infiltrated by fat. Sections revealed abundant epicardial adipose tissue, with patchy surface fibrosis and chronic reactive changes. Extensive fatty infiltration of the right ventricular wall including inflow, apex, outflow tract and anterior free wall regions was also observed. The left ventricle showed interstitial patchy, multifocal fibrosis with myocyte atrophy, with relative sparing of the subendocardial zone. Overall, pediatric ARVC remains difficult to diagnose unless symptoms are exhibited by the patient. Current diagnostic criteria for the pediatric population are not validated and there is a need for ARVC family screening at a younger age for earlier diagnosis to be made, before the disease progresses to a stage that is not manageable.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Arias Rodriguez, Maria Paula

**Additional Author(s):** Biswas S, Pasman E, Wilsdon D, Cecchini MJ

**Abstract Title:** Examining the Variability in Number of Lymph Nodes Based on Colorectal Specimen Size.

**Abstract:**
**Introduction:** Colorectal cancer (CRC) is the third most common cancer in Canada. Over the years mortality rates have declined significantly, this is a combination of a decrease in incidence and improved treatments. To appropriately treat CRC an accurate stage must be determined, hence identification of all lymph nodes (LNs) is critical. Studies show that the number of LNs identified is directly correlated with survival rates. Current guidelines suggest that a minimum of 12 LNs are assessed. Sampling less than 12 LNs is a high-risk feature and in some patients may result in increased treatment. However, CRC specimens have a variable amount of mesentery and in some smaller cases, finding 12 LNs can be challenging. In this project we sought to measure the number of LNs as a function of the weight of mesenteric tissue to understand how the number of expected LNs may vary based on specimen size.

**Methods:** To find all LNs we utilized a combination of ultrasound device to highlight the LNs and manual assessment. Tissue from non-neoplastic colonic resections was utilized. A 5 x 5 cm sample of tissue was utilized and weighed then scanned using the ultrasound sound device to localize potential LNs. The LNs were then dissected by a pathologists' assistant or pathologists' assistant student.

**Results:** Overall, ten independent experiments were conducted, and 26 samples were dissected. The mean weight of the 5 x 5 cm specimen was 43 g. The mean #LNs/100 g was 28. The median #LNs/100 g was 25. The maximum number of LNs was 34 and the minimum number of LNs was 2.

**Discussion:** In this study we identified that with extensive search on average 28 LNs are identified per 100 g of tissue. However, there was a range with some samples having less LNs. Further expanded studies may allow for better understanding on the variability. Given the variable size of colonic resections it may be more accurate to use a cutoff that is normalized by the amount of tissue available for assessment.

**Research theme 1:** Interdisciplinary Research in Health and Education
**Research theme 2:** Test Utilization, Optimization and Quality Assurance
**Research theme 3:**





**Presenter's Name:** Asakereh, Reza

**Additional Author(s):** Zhang Q, Shooshtari P

**Abstract Title:** An Automated Scoring Method to Determine the Infiltrative Pattern of Lung Cancer Brain Metastasis

**Abstract:**
**Introduction:** Residual lung cancer brain metastatic cells are a major contributor to post-treatment relapse and poor overall survival. Characterizing the invasion patterns of these cells is important in predicting the chance of relapse. However, manual characterisation of invasion patterns is a tedious and error-prone task.

**Methods:** We have defined a new scoring system to quantify the infiltrative patterns of lung cancer brain metastatic cells. This system addresses the heterogeneity in invasion patterns. We developed an automated algorithm that can calculate this score for any slide with GFAP + CK immunohistochemistry staining. Our algorithm detects the tumor regions and the surrounding brain tissue using a color deconvolution based segmentation method. It then extracts 33 features that describe morphological characteristics of the boundary between tumor and surrounding brain tissue (8 features), the intensity of invasion (15 features), and the integrity of the brain tissue (10 features). Finally, a random forest classifier is fitted on the extracted features to provide us with the inferred score for each patient.

**Results:** We manually labeled 829 images and found that the automated method could predict the labels with 60% balanced accuracy in a supervised setting. Furthermore, we conducted analysis on the extracted morphological features and identified a subset of features that were significantly correlated with the patient's overall survival ($p < 0.01$). These correlative features include eccentricity of tumor-brain boundary and high co-occurrence of brain and tumor cells. This finding suggests that our computational image analysis method can be used for the characterization of the invasiveness of lung cancer brain metastasis cells, and also has potential clinical utility in predicting patient outcomes.

**Conclusion:** Our automated scoring system is a promising approach for determining the invasiveness of lung cancer brain metastasis cells. It is objective and is a faster and more accurate alternative to manual characterization of invasion patterns. It also provides a set of morphological markers that are potentially predictive for patients' prognosis.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:** Cancer Biology
**Research theme 3:** Digital Pathology

**Presenter's Name:** Bandari, Ela

**Additional Author(s):** Keow S*, Kukkadi R, Wu D, Lombo L, Choudhary F, Subramaniam M, Kuczek J, Jeong J, Boles H, Wang S, Lorimer L, Dan A, Raina N, Ramnarine J, Patel A, Korzen A, Bhatia GK, Cecchini M

**Abstract Title:** Undergraduate Classroom Crowdsourcing of Cell Height-to-Width Ratio in Papillary Thyroid Carcinoma: Implications for Diagnosis and Progression-Free Survival

**Abstract:**
**Introduction:** Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer, and its tall cell (TC) variant is characterized by cells that are at least twice as tall as they are wide. Patients with the TC variant have worse disease outcomes and require more aggressive treatments. However, there is controversy surrounding the cut-off point for the cell height-to-width ratio, which is used as one of the criteria for diagnosing the TC variant with some studies suggesting a ratio of > 2 and others a ratio > 3. Measuring cell ratios can be time-consuming, and in this study, we sought to develop a novel approach to measure it using participatory student research.

**Methods:** We conducted a retrospective cohort study of patients with PTC using data from The Cancer Genome Atlas (TCGA) database. Undergraduate students enrolled in PATH 4200 were trained to identify and measure tumour cells on digital pathology slides. The students were provided with rulers to measure the tumour cell ratios of 10 cells per patient and to document this ratio in a shared database. An average ratio was used to compare the cell ratios of patients with disease progression to those without.

**Results:** Our study included 491 patients with PTC. The average cell height-to-width ratio for all patients was 2.27. Patients with disease progression (PFS event) had an average cell ratio of 3.32, while patients without disease progression (censored) had an average cell ratio of 2.10. The difference in ratios between the two groups was statistically significant ($p < 0.01$). Using a Cox proportional hazards regression model, we analyzed the association between ratios of > 2 and > 3 and PFS. The hazard ratio for cell ratio > 2 was 0.88 (95% CI: 0.48-1.59), with no statistical significance ($p = 0.66$). The hazard ratio for cell ratio > 3 was 1.57 (95% CI: 0.59-4.14) with no statistical significance ($p = 0.37$).

**Conclusion:** This study demonstrates the potential of undergraduate classroom crowdsourcing as a feasible and valuable tool for medical research. Although our study did not show a statistically significant association between cell height-to-width ratios > 2 or > 3 and PFS, patients with disease progression had a higher proportion of cell ratio >3 compared to patients without disease progression. This supports the need for further research to validate and explore the potential clinical implications of using different cell ratios in the diagnosis and management of TC variant PTC.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:** Digital Pathology
**Research theme 3:** Interdisciplinary Research in Health and Education





**Presenter's Name:** Boles, Helen

**Additional Author(s):** Greasley A, Zheng X

**Abstract Title:** Understanding Circular RNA Back-splicing Regulation and Efficiency

**Abstract:**
**Background:** Circular RNA (circRNA) is created endogenously and has a variety of functions within our cells. However, differential expression of circRNA from its linear home gene is not well understood. Previously, our lab showed that cell injury during ischemia reperfusion, can differentially express circHIPK3 from its linear counterpart, HIPK3. Thus, I hypothesize that injurious stimuli, such as LPS, H2O2, and CoCl2, can regulate circRNA back-splicing within a cell and stimulate circRNA biogenesis.

**Methods:** Naïve HL-1 murine cardiomyocytes were treated with LPS, H2O2, and CoCl2 and circHIPK3 and HIPK3 expression was quantified using qPCR. To test whether LPS can further promote back-splicing, circHIPK3 expression was measured in HL-1 cells that were transfected with a plasmid encoding circHIPK3 and treated with LPS 24 h post transfection. To identify which RNA binding proteins (RBPs) are upregulated because of treatment, whole cell proteomics will be conducted using mass spectrometry following LPS stimulation. The upregulated proteins will be used in an immunoprecipitation assay to determine which proteins interact with HIPK3 pre-mRNA and promote formation of circHIPK3.

**Results:** H2O2, treatment shows no significant increase in circHIPK3 ($p>0.05$). However, CoCl2 treatment show an increase in both circHIPK3 and linear HIPK3 ($p<0.05$). Plasmid encoding circHIPK3 is able to increase circHIPK3 expression compared to control cells or empty vector. Our data also shows that circHIPK3 expression through plasmid can be further up-regulated following LPS treatment 24 h post-transfection when compared to the empty vector treated with LPS ($p<0.05$). RBPs binding to HIPK3 pre-mRNA will be identified.

**Conclusions:** In conclusion, this study will identify novel regulation of circRNA differential expression, in hopes to develop targets of circRNA regulation for treatment and inhibition in disease.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Chen, Tony

**Additional Author(s):** Stevic I, Knauer M

**Abstract Title:** Investigating the Effects of Timing, Accelerometry, and Temperature of Pneumatic Tube Systems on Blood Samples

**Abstract:**
**Introduction:** Pneumatic tube systems (PTS) are often used to transport blood and other samples throughout the hospital without a porter using compressed air. However, the effect that the acceleration and g-forces created by the PTS may have on the sample itself is poorly understood. Previous research suggests that transport through PTS or excessive vibration may cause hemolysis in blood samples, but there is little research which seeks to assess the actual level of g-forces experienced by blood samples in PTS.

**Methods:** To examine the effect of g-forces experienced in PTS on blood samples, we collected human blood samples and transported them throughout the hospital on various PTS routes. We used an accelerometer, timer, and temperature probe in order to directly measure the parameters experienced by those blood samples while being transported via PTS. We then measured the level of certain hemolytic markers to evaluate the degree of hemolysis, and compared these values to the g-forces experienced to establish a correlation.

**Results:** We expect to find that although transportation by PTS does not cause gross hemolysis, there is still some significant effect that increased g-forces can have on blood samples.

**Discussion:** The results of our study can elucidate the relationship between the level of g-forces applied to blood samples by PTS and hemolysis. These findings could be used to develop a method to test the efficacy of PTS using accelerometry without the need for fresh blood samples.

**Research theme 1:** Test Utilization, Optimization and Quality Assurance
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Choudhary, Farhan

**Additional Author(s):** McKinley GP

**Abstract Title:** Using the One Health Approach to Investigate the Extent of Human Health Impacts due to Climate Change on Walpole Island First Nations and the Broader Southwestern Community

**Abstract:**
Climate change poses a serious threat to human health, with its effects expected to worsen in the future. The One Health approach offers a comprehensive framework to analyze the interconnected nature of human, animal, and environmental health. Consequently, by the use of this approach, it is possible to explore the intricate association between climate change and human health. Many of these connections remain largely unexplored for the Walpole Island First Nations (WIFN) and the broader Southwestern community. In order to gain a better understanding of these relationships, a scoping review was conducted. We searched four databases - PubMed, EMBASE, Web of Science, and CINAHL - using relevant search phrases and a temporally and geospatially restrictive inclusion criterion. We broadly defined health to include emotional, physical, occupational, social, spiritual, intellectual, environmental, and financial aspects. We organized articles linking climate change and human health into broad clusters. Suggested pathways were critically appraised against available literature to establish general Impact Pathways (IPs). Our review suggested various One Health-based interventions, in combination with Traditional Indigenous Epistemologies, to mitigate the detrimental effects of climate change on human health while preserving values of key local and regional stakeholders. Our findings emphasize the need for continued research into the relationships between climate change and human health and underscore the importance of interdisciplinary and collaborative approaches, including One Health framework and Traditional Indigenous Epistemologies, to mitigate the negative impacts of climate change on human health.

**Research theme 1:** One Health
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Cogghe, Joni

**Additional Author(s):** Zhang ZX

**Abstract Title:** AIM2 as an Endogenous DNA Sensor and a Potential Player in Post-Heart Transplantation Organ Viability

**Abstract:**
**Introduction:** The recognition of damage-associated molecular patterns (DAMPs) by pattern recognition receptors (PRRs), leads to cellular dysfunction and death. These DAMPs include components like DNA that is recognized by endogenous sensors like AIM2, which recruits caspase-1 in the formation of the inflammasome, leading to cell death. The IRF transcription factors relay PRR signals to regulate the type I interferon response. We hypothesize that DAMP-induced AIM2 activity triggers IRF3-mediated signaling to cause necroptotic cell death in mouse cardiac tissue.

**Methods:** Mouse endothelial cells will be treated with a synthetic dsDNA sequence and analyzed for the presence of IRF3 via immunoblotting. Cells will be treated with the synthetic dsDNA and investigated via immunoblotting for the presence of caspase-1 to determine whether AIM2 was activated. Finally, cells will be subjected to a cell death assay with a caspase inhibitor and analyzed for the uptake of SYTOX green to quantify cell death. The cell lysates will be immunoblotted for the presence of caspase-1 and phosphorylated MLKL (pMLKL) in order to determine if the cell death produced in response to the dsDNA was necroptotic.

**Results:** It is expected that the dsDNA will result in IRF3 activation and caspase-1 presence, indicating the initiation and activity of the AIM2 inflammasome and the downstream involvement of IRF3. Following the cell death assay it is expected that an increased uptake of SYTOX green will indicate that cell death was induced, and that immunoblotting will reveal the presence of caspase-1 and pMLKL, indicating the initiation and activity of the AIM2 inflammasome, and that the cell death was necroptotic.

**Discussion:** The findings of this study will help to better understand the cellular mechanisms underlying ischemia-reperfusion injury and necroptosis, allowing for future studies to develop therapies to limit the injury by fine-tuning the involved inflammation and cell death pathways. Such therapies have the potential to attenuate the deleterious inflammation in cardiac tissue induced by DAMPs, allowing for donor organs to be utilized effectively without the fear of graft dysfunction or failure.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** Infection, Immunity, and Inflammation
**Research theme 3:**





**Presenter's Name:** Dabrowski, Gabriela

**Additional Author(s):** Knauer MJ, Richardson K

**Abstract Title:** Evaluation of the Roche Cobas® Pulse Glucose Monitoring System

**Abstract:**
Glucose monitoring continues to be a very important aspect of patient care, particularly when treating or monitoring patients who are experiencing or risk experiencing hypo- or hyperglycemia. Roche has recently developed a new point-of-care testing (POCT) device to measure blood glucose: the cobas® pulse system. This study will focus on testing the cobas® pulse system to determine if the new glucose monitoring system is suitable for clinical use within London Health Sciences Centre (LHSC). The glucose meter will first undergo quantitative evaluation, comprised of the following tests: precision assessment, method comparison, linearity assessment, and interference testing. The results of these tests will be compared to POCT guidelines set by the Clinical and Laboratory Standards Institute (CLSI) as well as to the current glucose meter used at LHSC, the Accu-Chek® Inform II system. A survey will then be completed by members of the POCT team to qualitatively evaluate the cobas® pulse system. The glucose monitoring system is expected to meet all CLSI guidelines for POCT devices, meaning that adequate precision and linearity are expected, the meter is expected to be comparative to other glucose monitoring instruments, and finally, no interfering substances are anticipated. If the cobas® pulse system is deemed fit for use within LHSC, Roche may use the data collected in this study in their application for approval from Health Canada. With this approval, the new glucose meter will be made available in clinical settings nationwide, allowing for enhanced glucose monitoring in Canada.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** Test Utilization, Optimization and Quality Assurance
**Research theme 3:**

**Presenter's Name:** Gao, Chen Jun

**Additional Author(s):** Ramachandran R, Zhao L

**Abstract Title:** Upstream Regulators of YAP/TAZ in Non-alcoholic Fatty Liver Disease

**Abstract:**
**Introduction:** Non-alcoholic fatty liver disease (NAFLD) affects 25% of the world population underpinning the urgent need to understand molecular pathways and develop effective therapeutic interventions. Recently, yes-associated protein (YAP) and transcriptional coactivator with PDZ-binding motif (TAZ) have emerged as two important transcriptional regulators implicated in liver fibrosis and injury. Despite the growing recognition of YAP/TAZ in several liver diseases, YAP/TAZ expression has not been extensively characterized in hepatic cells, and the upstream regulators of this pathway in the setting of liver injury remain poorly understood. Here, we examined the expression pattern of YAP/TAZ in NAFLD patient samples and demonstrated that PAR receptors could be regulators of the YAP/TAZ pathway.

**Methods:** Archival human liver sections of normal and NAFLD including cases of simple steatosis, steatohepatitis, various stages of fibrosis and cirrhosis were analyzed using immunostaining and the activation status of YAP/TAZ and PAR receptors was monitored through subcellular localization. The expression pattern of YAP in various hepatic cell types was characterized by colocalization with clinically validated markers. An in-vitro reporter assay was used to directly assess YAP/TAZ activation by PAR1 and PAR2 agonists.

**Results:** Confocal imaging combined with semi-supervised automated image analysis revealed increased nuclear YAP expression in Kupffer cells, myofibroblasts and cholangiocytes as NAFLD progresses from steatosis to fibrosis and cirrhosis. PAR receptors showed different expression patterns in diseased livers indicative of the receptor upregulation and activation. In complimentary in-vitro studies, specific PAR1 and PAR2 agonists increased YAP/TAZ nuclear activity providing further evidence that PAR receptors can directly regulate this pathway.

**Discussion:** Immunostaining of liver biopsy samples revealed that the progression of NAFLD is associated with nuclear translocation of YAP/TAZ in specific hepatic cell types. These two transcription factors could drive inflammation in myofibroblasts and Kupffer cells, and promote bile duct regeneration in cholangiocytes. Immunostaining analysis and in-vitro assays indicated that PARs are disease relevant regulators of YAP/TAZ in the liver and may be targeted to modulate YAP/TAZ activation. Take together, our findings can help guide the development of novel therapeutic agents for treating NAFLD.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** Infection, Immunity, and Inflammation
**Research theme 3:**





**Presenter's Name:** Gendron, Laura

**Additional Author(s):** Haagsma J, Shepherd T

**Abstract Title:** A One Health Approach to Examining Potential Reprogramming Events Causing Neoplastic Change in Oviductal Cells

**Abstract:**
**Introduction:** Epithelial ovarian cancer (EOC) is the most lethal gynecological malignancy in developed countries, with a 5-year survival rate of only 30 percent. A contemporary lack of early detection strategies results in frequent late stage diagnoses due to the generic symptoms associated with ovarian cancer, making self diagnosis difficult. The most common and lethal form of EOC is high-grade serous carcinoma (HGSC), which is linked to mutations of the Trp53 gene, encoding the tumor suppressor protein p53. There is also evidence linking personal and environmental factors, such as carcinogen exposure or birth control, to EOC. Animal models have been successful at modelling human EOC and are crucial tools for better understanding HGSC progression. Using animal models, it is hypothesized that the exposure of oviductal epithelial (OVE) cells to the ovarian microenvironment causes transformational changes to promote their progression towards HGSC.

**Methods:** This hypothesis was assessed by examining phenotypic differences between an engineered HGSC precursor cell line, OVE4p53R175H, and a cell line derived from ascites fluid after interaction with the ovarian microenvironment in an in vivo mouse model. The proteins and genetic sequences responsible were identified using Western Blotting and PCR. Trypan Blue Exclusion, Caspase-Glo, and Cell Titer Glo assays were utilized to quantify proteins, assess cellular viability, and evaluate apoptotic regulation. A soft agar growth assay was used to assess anchorage-independent growth capabilities.

**Expected Results:** The two cell lines are expected to appear morphologically distinct and exhibit differences in behaviour. The ascites-derived cells are predicted to have a faster growth rate, increased viability, and form more robust spheroids compared to the OVE4p53R175H cells.

**Discussion:** Understanding of the changes resulting in invasive HGSC and uncovering biomarkers for future therapeutics is vital for advancing early diagnosis strategies, thereby improving the prognoses for women worldwide. This may be accomplished by engaging stakeholders, like pharmaceutical companies and research agencies, in a collective effort to mitigate the impact on at-risk women. The abundance of factors influencing patient outcomes, including genetics and environment, makes EOC a multi-dimensional disease. Thus, using the one health approach is crucial to gain a holistic understanding of challenges faced by patients and improve health.

**Research theme 1:** Cancer Biology
**Research theme 2:** One Health
**Research theme 3:**

**Presenter's Name:** Gholami, Hasti

**Additional Author(s):** Maleki Vareki S, Burton JP

**Abstract Title:** Analyzing the Immunomodulatory Effects of Immunotherapy Responsive Neuroblastoma Tumours with Induced DNA Mismatch Repair Deficiency and their Gut Microbial Features

**Abstract:**
A growing line of evidence suggests a role for the gut microbiota as a modulator in anti-tumour immunity and improving the efficacy of immunotherapy treatments. Recent clinical trials have shown that transferring the microbiome of an immunotherapy responder via fecal microbiota transplant (FMT) to another patient with immunotherapy-refractory melanoma can sensitize 30% of those patients' tumours to anti-PD1 therapy. However, the microbial features that are responsible for the therapeutic effects of microbiome transplants from responders to a new host remain elusive. Our lab has previously shown that 70% of induced mismatch repair deficient (idMMR) neuroblastoma tumour-bearing mice were cured when treated with anti-CTLA-4 therapy. Therefore, this study aims to provide mechanistic insight into the specific bacterial species in the gut of immunotherapy-responsive animals that can transform the immune phenotype of tumours in new hosts and sensitize them to immunotherapy.

Flow cytometry was used to assess the immunomodulatory effects of FMT from anti-CTLA4-responsive- and isotype control-treated idMMR neuro-2a (neuroblastoma) primed mice on the immune phenotype of tumours in new hosts. To better understand the gut microbial composition of immunotherapy responders, DNA was extracted from the stool of anti-CTLA-4-responsive- and isotype control-treated idMMR neuro-2a primed mice and region V4 the 16S rRNA gene was PCR amplified. Amplicon libraries were sequenced on the MiSeq paired-end Illumina platform and downstream analyses on the sequences will be completed to infer the microbial profiles of the animals. To determine the effect of bacteria in the stool of anti-CTLA-4-responders on the maturation of dendritic cells (DCs), the most predominant culturable bacterial strains of responders will be grown on selective bacteriological media and will be co-cultured with bone marrow-derived DCs. The upregulation of DC maturation markers will be assessed by flow cytometry.

Preliminary data suggests that the neuroblastoma tumours of mice that received an FMT from anti-CTLA-4-responsive mice had lower levels of overall tumour-infiltrating lymphocytes (TILs), however, these TILs had a higher level of tumour-specificity and activation, marked by an increase in CD39 and CD38 expression, respectively. Results from this study will provide mechanistic insights into the bacterial species that possess immunomodulatory properties in immunotherapy responders.

**Research theme 1:** Cancer Biology
**Research theme 2:** Infection, Immunity, and Inflammation
**Research theme 3:** Regenerative and Transplantation Medicine





**Presenter's Name:** Gray, Madison

**Additional Author(s):** Ang LC

**Abstract Title:** Immune checkpoint inhibitor myositis: a rare complication of an important therapeutic intervention

**Abstract:**
**Introduction:** Immune checkpoint inhibitors (ICI) are a recent development in cancer therapeutics. These therapies, targeted to endogenous antigens, can result in serious auto-immune adverse events.

**Case:** The patient, a 55-year-old man, was first diagnosed with melanoma in 2019 with nodal involvement at presentation progressing to distant muscle, lung, and breast metastases in late 2022. He began combined Nivolumab/Ipilimumab immunotherapy in December 2022. Days after his second course of immunotherapy, he began to suffer myalgias, progressive proximal muscle weakness and dysphagia. Exam revealed proximal MRC grade 4/5 weakness with preserved strength distally and normal sensation and deep tendon reflexes. CK reached a peak of 4823 (units/L). Creatine was mildly elevated at 201 (µmol/L). EMG showed fibrillation potentials and positive sharp waves in both biceps. A nerve conduction study was normal. An auto-immune myositis antibody panel was negative.

Roughly two weeks from the onset of weakness, a muscle biopsy was performed. This demonstrated widespread myofiber necrosis and myophagocytosis together with non-granulomatous lymphohistocytic inflammation of the endomysium. Lymphocytes stained for CD4 and CD8 in roughly equal proportions. An anti-PD-L1 antibody stained histiocytes in the endomysium and within muscle fibres as well as the sarcoplasm of rare necrotic myofibres. Ultrastructural examination was most significant for subsarcolemmal accumulation of mitochondria and numerous paracrystalline inclusions. With the history of recent combination ICI therapy and demonstration of a severe immune-mediated necrotising myositis, the diagnosis of ICI myositis was made.

**Discussion:** An adverse response to cancer immunotherapy, while rare, can result in dire consequences — both inflammatory and oncological. In addition to skeletal muscle, ICI myositis can also involve the heart resulting in severe and sometimes fatal myocarditis. While many ICI-related adverse events can be treated rapidly with immunosuppressive drugs, immunotherapy must often be suspended or even terminating, removing an important therapeutic avenue. To date, there are no specific histological findings for ICI-related adverse events and no tissue markers are known to predict adverse responses to immunotherapy.

**Research theme 1:** Cancer Biology
**Research theme 2:** Infection, Immunity, and Inflammation
**Research theme 3:** Pathobiology of Neurologic Diseases

**Presenter's Name:** Greasley, Adam

**Additional Author(s):** Peng T, Zheng X.

**Abstract Title:** Generation of Hypoxic Real-time Cell Monitoring Model for Cardiac Ischemia and Ischemia Reperfusion Injury

**Abstract:**
**Introduction:** Ischemia and ischemia-reperfusion injury (IRI) remain leading complications in many conditions of the heart such as, ischemia heart disease or myocardial infarction, and in treatments involving cardiac by-pass or heart transplantation. Although IRI research has been present for over 30 years across multiple organs, there remains a lack of standardized in vitro modelling for cardiac ischemia or IRI. The hypoxic conditions, storage solutions and incubation times, all of which effect cellular preservation and response following reperfusion, varies by research group and often lacks validation with hypoxic monitoring. Therefore, a standardized model for cardiac ischemia or IRI is needed, which can validate cell response to different hypoxic conditions and solutions is needed.

**Methods:** To study the effects of hypoxia on cell survival and response, AC16 cardiomyocytes are monitored using an cytation-5 coupled with a bio-spa under different hypoxic conditions (O2 level, temperature, time). High-contrast brightfield is used to monitor cellular size, circularity and number, while necrotic cell death is monitored using propidium iodide. To assess the effects of immediate vs gradual hypoxia were determined by using nitrogen bubbled and non-bubbled solutions are time of experimental start. Furthermore, cells are incubated clinically relevant solutions to determine if the hypoxic model can mimic clinical representation.

**Results:** Our preliminary results suggest that AC16 cells incubated with HTK or Cardioplegia show hypoxic induced injury following 1% O2 at 32°C characterized by increase circularity, loss of morphology and some necrotic cell death. In addition, time to first injury is reduced in N2 bubbled solutions from 8 h to 2 h.

**Conclusion:** So far, my findings indicate that real-time monitoring of hypoxia combined with N2 bubbled solution will allow us to mimic and validate clinical cell injury and representation using a standardized in vitro model.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Grindrod, Natalie

**Additional Author(s):** Brackstone M, Cecchini M.

**Abstract Title:** Digital assessment of TILs as a biomarker in breast cancer

**Abstract:**
While originally thought to be devoid of immune cells, it is now known that breast cancer (BC) can have tumour infiltrating lymphocytes (TILs). What is known about TILs in BC is that it is a prognostic and predictive biomarker, which can help to establish the best course of treatments. Previous research shows that chemotherapy with high TILs shows good prognostic information. BC can be treated by more than just chemotherapy, which makes researching TILs in BC a necessity. Assessing this includes quantifying TILs in slides, which can be a difficult and time consuming task. Using digital pathology, allowing image analysis and machine learning workflows would be much more efficient. For this study we are using the local study SIGNAL slides previously collected, that include a variety of BC types. Patients underwent neoadjuvant chemo-radiation or chemotherapy alone. We aim to quantify TILs in each case, assess how certain disease parameters may affect TILs, assess treatments affect on TILs, and assess if there is any TILs clustering and how that may impact outcomes. Our hypothesis is that spatial mapping of the lymphocyte distribution within the tumour will then provide more robust and accurate predictions of response to neoadjuvant therapy and BC. First we digitized slides, then performed image analysis, we performed analysis using QuPath, an open source software. This included doing cell detections on each slide. Then annotating and giving this information to train the object classifier which identifies between stroma, tumour, and lymphocytes. This classifier was made for one slide, and currently has been able to be applied to other slides. Density maps will be applied to slides to assess areas high in TILs. Delaunay Triangulation will be used to assess clustering between cell types. Our results show the ability to use QuPath's object classifier to identify lymphocytes accurately and efficiently. Initial findings show from using Delaunay Triangulation that there are many TILs clusters that can be found in slides. Further analysis and results are to be done and collected. These findings still do show promise in the digital assessment of TILs in BC as a biomarker. Further work is to be completed but may show correlations between TILs quantity and outcomes, as well as the clustering of TILs may impact outcomes.

**Research theme 1:** Cancer Biology
**Research theme 2:** Digital Pathology
**Research theme 3:**

**Presenter's Name:** Halari, Moheem

**Additional Author(s):** Charyk Stewart T, McClafferty K, Pellar A, Pickup M, Shkrum M

**Abstract Title:** A Postmortem Study of Injury Patterns in Pedestrian and Cyclist Fatalities in Ontario

**Abstract:**
**Introduction:** The United Nations reports that annually 1.35 million fatalities occur worldwide due to motor vehicle collisions (MVCs), more than half of which involve pedestrians, cyclists, and motorcyclists. In Ontario, coroners' investigations of pedestrian and cyclist fatalities from MVCs include post-mortem examinations by pathologists who document injuries to determine a cause of death and mechanisms of injury. The purpose of this study is to understand these mechanisms by correlation of trauma patterns sustained by fatally injured pedestrians and cyclists with MVC findings.

**Methods:** An Injury Data Collection Form (IDCF) was used to extract motor vehicle, MVC, pedestrian demographic and injury information from the Office of the Chief Coroner for Ontario database using autopsy data from cases done between 2013 – 2019. Injuries were coded using the Abbreviated Injury Scale (AIS) 2015 revision and classified using the maximum AIS by body region (MAISBR). Because AIS 1 (minor) and 2 (moderate) injuries are least likely to cause death, the study focused on serious (MAISBR ≥ 3) injuries.

**Results:** The literature described injuries in both fatal and non-fatal cases and showed varying injury patterns between children, youth, adults, and the elderly. The most frequent vehicle type and impact zone described in the literature were cars and frontal impacts, respectively.

The IDCF was used to extract data from 766 post-mortems (670 pedestrians and 96 cyclists) from 2013 – 2019. These included 26 children, 88 youth, 318 adult and 238 elderly pedestrians and 5 children, 14 youth, 66 adult and 11 elderly cyclists. The following overall injury patterns based on MAISBR ≥ 3 emerged: pedestrians [children (0-10): head, neck and thorax; children (11-14): head, neck, thorax and abdomen; youth (15-24): head and thorax; adults (24-64): head, neck, thorax, abdomen and pelvis; elderly (≥ 65): head, thorax and pelvis] and cyclists [children and youth: head and thorax, adults: head, neck thorax, abdomen and pelvis, elderly: head, thorax, abdomen and pelvis].

**Discussion:** The injury patterns emerging from the literature review differed from the present study. This could arise from the differences between older vehicles and the current more diverse motor vehicle fleet.

**Research theme 1:** Digital Pathology
**Research theme 2:** Forensic Pathology
**Research theme 3:** Pathobiology of Neurologic Diseases





**Presenter's Name:** Han, Ji Hyun

**Additional Author(s):** Sabharwal A, Armstrong J, Khan Z, McCord C.

**Abstract Title:** Osteomyelitis of the jaw: An investigational study of the clinicopathological features and pathogenesis of refractory vs non refractory osteomyelitis

**Abstract:**
**Introduction:** The term Osteomyelitis (OM) means inflammation/infection of the bone marrow. The initial source of infection can be caused by a multitude of different factors; however, this process continues to propagate until the source of infection has been removed. In recent years, there has been an increase in subset of patients, who present with clinically aggressive disease. Based on the classifications present in literature, we have classified the groups into refractory vs non refractory cases, with refractory patients requiring more than 1 surgical procedure after adequate initial management. We hypothesize that refractory OM patients are associated with specific bacteria/inflammatory markers that make them more clinically aggressive, associated with poor clinical outcomes, and demonstrate distinguishing clinicopathologic features. The objectives are to examine the clinical and histological characteristics of OM to determine if differences exist between the two groups.

**Methods:** A retrospective chart review of the records of patients diagnosed with OM in the OMFS/dental departments of LHSC from January 1, 2002 until January 31, 2021 will be completed. Cases grouped according to their outcome; refractory vs non refractory. Initial confirmation of RNA isolation from formalin-fixed paraffin embedded tissues (FFPE) completed. Following this, FFPE obtained from patients found during the retrospective chart review will be used to complete Immunohistochemistry for TLR signaling, qPCR to assess for specific inflammatory factors, and potentially preliminary bacterial identification to characterize the microbial groups responsible for the difference seen in these two groups. Results: The retrospective chart review included a total of 87 patients; 45 females and 42 males. Out of the 87 patients, 56 samples were determined to be OM. 8 Refractory groups and 8 non-refractory OM groups chosen for experimental portion. Initial RNA retrieval from FFPE soft tissue and bone samples was successful. Further results are to be determined.

**Discussion:** Currently in the literature, very few studies examine the features of refractory OM compared to those with non-refractory OM. It is expected that a difference in microorganisms, inflammatory markers, as well as other environmental/personal risk factors of individuals will be seen in the refractory OM subset. The data from this study will help guide future clinical decision making in the treatment of refractory OM of the jaw.

**Research theme 1:** Infection, Immunity, and Inflammation
**Research theme 2:** Oral Biology and Medicine
**Research theme 3:**

**Presenter's Name:** Holder, Natasha

**Additional Author(s):** Shimizu M, Cecchini M, Howlett C, McCord C.

**Abstract Title:** Glandular Odontogenic Cyst: Molecular Analysis using Targeted Next-Generation Sequencing

**Abstract:**
**Introduction:** Glandular odontogenic cyst (GOC) is an uncommon, developmental cyst of the jaws making up less than 0.5% of odontogenic cysts. GOC is unique to most cysts found in the jaws in that it can have variation in clinical presentation and may behave aggressively. Although benign, aggressive lesions can cause local bony destruction and have a high rate of recurrence, demonstrating some similarity to neoplastic lesions. The molecular pathogenesis of GOC has rarely been investigated and remains unclear. This study aims to use targeted next-generation sequencing techniques to identify potentially pathogenic nucleotide variations in GOC, which may help in understanding the biologic behaviour of these lesions. Due to the rare nature of these lesions, this study also aims to contribute histopathologic and clinical data of GOC found within our archives to the literature. We hypothesize that glandular odontogenic cyst shows distinct pathogenic nucleotide variations at both the DNA and RNA level.

**Methods:** All samples of GOC and odontogenic cysts with features of GOC from 2003-2020 were retrieved from the archives. Clinicopathologic data was gathered from the pathology reports and summarized. Histopathologic features were identified and frequency of known microscopic criteria were recorded and summarized. Targeted next-generation sequencing was used to interrogate a panel of a 161 cancer-associated genes in GOC.

**Results:** A total of 84 specimens were identified from the Western University and LHSC archives. The mean age was 50 years old with a male predilection. The majority of lesions were found in the mandible with a tendency for the posterior region. Histopathologic features most commonly identified were clear cells, variable thickness in the epithelial lining, and eosinophilic cuboidal cells. Tier I and II variants in the NRAS, TP53 and NF1 genes were found at frequencies greater than 10%.

**Discussion:** Diagnosis of GOC is based on microscopic features of the lesion and these diagnostic criteria are based on the limited cases reported in the literature. In our samples, we found a frequency of histopathologic features that differs from those found in the literature. Contribution of this data could influence diagnostic decision making in the future. Our study is also the first to identify these genetic variants at such frequencies in GOC, which may provide insight into the molecular pathogenesis of these lesions.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Imran, Aansah

**Additional Author(s):** Chang N, Dhanvantari S

**Abstract Title:** Islet Hormone Regulation of Glucagon Secretion Occurs Through Increased Trafficking to the Endolysosomal System Mediated by STMN2

**Abstract:**
**Introduction:** Patients with diabetes mellitus present with both hyperglycemia caused by disturbances in glucose homeostasis, and hyperglucagonemia resulting from dysregulated glucagon secretion. Although diabetes treatment has mainly focused on regulating hyperglycemia through artificial insulin therapy, previous evidence has identified that persistent hyperglucagonemia may worsen hyperglycemia and thus the disease prognosis. Research into glucagon inhibition indicates insulin, GABA, and glucose as potent negative regulators of glucagon. Additionally, previous work from our lab identified a novel role for the stathmin2 protein in the negative regulation of glucagon by promoting its degradation through the endolysosomal pathway. In the present study, we investigate whether paracrine inputs promote degradation of glucagon through activation of stathmin2 activity.

**Methods:** We use epifluorescence microscopy to examine the colocalization of glucagon and stathmin2 in αTC1-6 cells under high glucose conditions after treatment with insulin and GABA. Using the NIS element software to compute a Pearson's correlation coefficient value, we quantify the degree of any colocalization within lamp2a-marked lysosomes and syntaxin1-marked sites of exocytosis.

**Results:** Pervious studies observe high colocalization between glucagon and stathmin2 in αTC1-6 cells in components of the endolysosomal pathway, which appears to increase when stathmin2 is overexpressed. Consistent with the purposed role of stathmin2 as a negative regulator, our findings show that treatment with insulin and GABA under high glucose concentrations results in a high Pearson's correlation coefficient value for colocalization between stathmin2 and glucagon within αTC1-6 cells.

**Discussion:** Our findings provide further support for the role of stathmin2 as a negative regulator of glucagon and offer additional insight on the impact of paracrine inhibitors on its activity. This study builds upon the current understanding of glucagon regulation and may be helpful to identify potential ways for preventing hyperglucagonemia and thus exacerbated hyperglycemia in diabetes.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Jackson, Matthew

**Additional Author(s):** Khan ZA, Menassa R, Kiser P.

**Abstract Title:** Use of a VHH-IgA Fc fusion protein targeting surface protein Intimin to block E. coli O157:H7 colonization in GI tract of mice

**Abstract:**
**Introduction:** Shiga toxin-producing Escherichia coli (Enterohemorrhagic E. coli (EHEC); O157:H7 and related serotypes) is a human foodborne bacterial pathogen that can inhabit the gastrointestinal (GI) tract of common livestock. Due to a lack of effective treatments for EHEC, control of the pathogen prior to zoonotic transmission is critical for public health networks. The aim of this study is to test the safety and efficacy of a new nanobody-expressing plant matter (DNB) as an oral passive immunization method for livestock. The nanobody, or VHH-IgA Fc fusion protein, is designed to target and bind to the E. coli O157:H7 surface protein intimin. DNB has been shown to effectively block E. coli O157:H7 from binding to human cells in vitro, with in vivo testing occurring in this study on mice. We hypothesize that DNB will reduce E. coli O157:H7 colonization and shedding in mice when administered prophylactically.

**Methods:** To test this hypothesis, multiple experiments will be run to determine the effects of DNB on both the mice and the bacteria. A safety trial was run first to rule out any toxicity or off-target effects. Safety of DNB administration was assessed using clinical signs (i.e. ill thrift, weight loss), with post-mortem gross and histologic assessment for abnormalities relative to untreated mice. Efficacy testing will involve E. coli O157:H7 challenges after DNB supplementation. The measure of DNB efficacy will involve quantification of GI tract colonization and fecal shedding of the bacteria as well as gross and histologic assessment of the mice following infection and/or treatment.

**Results:** The results of the safety trial showed that administering DNB caused no off-target injuries or toxicity in the mice. Daily monitoring showed no changes in behaviour or appearance, and there was no aversion to the feed supplemented with 20% w/w DNB. In the future challenge trials, we are hoping to see the same inhibitory effect in the infected mice as was seen in vitro.

**Discussion:** DNB was developed to provide a high yield, cost-effective food additive that prevents colonization of E. coli O157:H7 in livestock GI tracts, thereby reducing the pathogen's contamination of the food chain. This study is the next step in determining whether DNB can be used to help reduce or eventually eliminate E. coli O157:H7 in a passive, inexpensive manner, as successful results from this study can lead to further testing on livestock animal models.

**Research theme 1:** Infection, Immunity, and Inflammation
**Research theme 2:** One Health
**Research theme 3:**

**Presenter's Name:** James-McDonald, Christian

**Additional Author(s):** Larsen F, Asfaha S

**Abstract Title:** Investigation of the Effects of DNA Demethylating Drugs on DCLK1+ Cell Derived Tumor Organoids

**Abstract:**
DCLK1+ tuft cells can serve as a cell of origin for colorectal cancer in mouse models when deletion of tumour suppressor adenomatous polyposis coli (APC) is coupled with a colitis inducing agent. Epigenetic alterations can alter tumor progression; DNA hypomethylation can increase gene expression including expression of endogenous retroviruses that have been maintained in the human genome. Utilizing a DCLK1 tumor organoid model, mechanisms behind epigenetic effects on tumor outcomes will be explored. Predictively, DNA and histone hypomethylation will decrease colitis-associated tumour organoid growth via the stimulation of an anti-viral response. DCLK1+ cell derived tumours will be isolated from a colitis-associated colorectal cancer mouse model to start tumor organoid cultures in vitro. Tumor organoids will be treated with DNA or histone hypomethylating agents and images will be taken across timepoints to evaluate effects on tumor organoid size. RNA will be isolated, and RT-qPCR will be performed to assess expression patterns of endogenous retroviruses and anti-viral genes. AMAVS knockout mouse model will also be generated to assess viral mimicry as a mechanism. DNA and histone hypomethylation are expected to produce a reduction in tumor organoid size. Increased expression of endogenous retroviruses is predicted to drive promotion of an anti-viral response state characterized by increased expression of interferons and interferon-stimulated genes. The MDA-5/RIG-I anti-viral signalling pathway (united by downstream signalling protein MAVS) is anticipated to be the mechanism in which viral mimicry is established. Despite extensive prevalence, morbidity, and mortality of colorectal cancer there remains gaps in understanding how epigenetic alterations effect tumour progression. Mechanisms in which changes in methylation state impact colitis-associated colorectal cancer will be explored.

**Research theme 1:** Epigenetics
**Research theme 2:** Infection, Immunity, and Inflammation
**Research theme 3:**

**Presenter's Name:** Ji, Helen

**Additional Author(s):** Lin S, Romagnoli T, Coats J, Cecchini M

**Abstract Title:** Simulated biopsy cores in lung cancer resections to understand cellularity distribution across tumours and adequacy for molecular testing

**Abstract:**
**Introduction:** Pathologic diagnosis of lung cancer is critical to ensure patients receive the optimal therapy and molecular testing. To perform molecular testing, it is ideal for cases to have at least 1,000 tumor cells to ensure adequate cellularity for molecular testing. In this study, we simulated biopsies across resected lung cancers to understand the adequacy of cores across tumor. We utilized this conservative threshold of 1000 cells to identify cores that would be optimal for molecular testing.

**Methods:** 50 resection cases diagnosed with lung squamous cell carcinoma were obtained from the archival records at London Health Sciences Center. In QuPath, a cell detection was performed to detect all cells on and areas of tumor and non-tumor were annotated that served as the basis of an object classifier to identify tumor cells from background stroma and inflammatory cells. We then simulated ideal core needle biopsies of 0.25 mm x 2.5 mm across the entire slide. Optimal biopsy core was defined as having greater than or equal to 10% tumour cellularity and 1000 tumour cells. The number of cores that met the threshold was recorded for each case.

**Results:** In our cohort, 44 out of 50 cases had at least one core with greater than 1000 tumour cells and >10% tumor cellularity. There was a range of optimal cores in each case that ranged from 0.65% to 85.71%. The average number of optimal cores in each specimen was 26%. Cores with less than optimal cellularity often had areas of dense fibrosis or necrosis present in the simulated core needle biopsy.

**Discussion:** This study showed that a majority of the core needle biopsies performed on squamous cell carcinoma lung nodules had optimal tumor cores for molecular testing, however, there exists a high degree of non-optimal cores that would not meet the threshold. The absolute minimum number of tumor cells is 100-200 cells and a cellularity of 5%, therefore, it is possible that some of these cores may have been sufficient for molecular testing. Future and ongoing work will study the distribution of cellularity in the core and correlate with imaging students to better guide CT-guided core needle biopsies to ensure optimal tissue sampling.

**Research theme 1:** Cancer Biology
**Research theme 2:** Digital Pathology
**Research theme 3:**





**Presenter's Name:** Jin, Bernie

**Additional Author(s):** Poon AFY

**Abstract Title:** Comparing Intrinsic Disorder of Core and Accessory Viral Proteins

**Abstract:**
**Introduction:** Intrinsic disorder is an important concept in molecular biology, which describes proteins that do not have a well-defined, stable three-dimensional structure under physiological conditions. Previous studies have shown that species from all domains of life have abundant amounts of intrinsically disordered proteins (IDPs) in their genomes. In particular, viruses often exhibit highly disordered genomes, which have been suggested to confer various benefits. However, the mechanism for the evolution of IDPs in viruses is unclear. In this study, we attempt to investigate the difference in intrinsic disorder between homologous clusters of conserved and accessory proteins in different viral families. We hypothesize that accessory proteins, being less conserved and more flexible in function, will tend to have a higher amount of intrinsic disorder, while core proteins that are more highly conserved will have a more defined structure and a lower level of intrinsic disorder.

**Methods:** To test our hypothesis, we first extracted homologous clusters of proteins based on their k-mer distance. We then used Metapredict, an intrinsic disorder predictor, to generate intrinsic disorder scores for all viral amino acid sequences. Next, we performed Permutational Multivariate ANOVA (PERMANOVA) to determine if any significant variation in disorder scores exists between clusters of homologous proteins. Finally, we tested for correlation between disorder scores and cluster size, and also between disorder scores and mean amino acid entropy.

**Results:** Preliminary results suggests that there may be a relationship between cluster size and intrinsic disorder. Linear regression reveals that some families exhibit a moderate correlation, although the direction of the correlation differs between families. Results for mean amino acid entropy is unclear, and a clear correlation was not found.

**Discussion:** Our findings show that there is some correlation between cluster size and intrinsic disorder. These results tentatively show that intrinsic disorder may be influenced by evolutionary factors.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Lam, Victor

**Additional Author(s):** Lam VHK, Misra T, Wu N, Cecchini MJ

**Abstract Title:** Digital Quantification of Tumor Density in Relation to Human Papillomavirus status in Head and Neck Squamous Cell Carcinoma

**Abstract:**
**Introduction:** The incidence of head and neck squamous cell carcinoma (HNSCCs) has been increasing, yet the prognosis remains poor with a 5-year survival rate around 50%. Human Papillomavirus (HPV) is a significant risk factor to HNSCCs with HPV positive (HPV+) cases having a better 5-years survival rate (80%) compared to HPV negative (HPV-) HNSCCs. Of the strains, HPV16 is mainly associated with HPV+ HNSCCs, while tobacco and alcohol consumption are responsible for HPV- HNSCCs. Currently, staging is based on the size and spread of the tumor, which may be a surrogate measure for the tumor cellularity. Cell counting to stage tumors is unfeasible for pathologists. However, our previous work demonstrated the viability of image analysis tools to facilitate quantification of cells in digital histology slides. Although primary HPV+ HNSCCs are generally smaller in size than HPV- HNSCCs, the tumor density between these groups is unclear but is relevant for current staging methods. In this study, we investigate the tumor cellularity of HPV+ and HPV- HNSCCs.

**Methods:** 12 total digital slides were obtained from The Cancer Genome Atlas (TCGA) HNSC dataset with 7 HPV+ and 5 HPV- cases. HPV statuses were compiled by Dr. Nichols' lab. Tumors were annotated using QuPath and reviewed by an anatomical pathologist. Annotations were then used to train machine learning-based cell detection algorithms to obtain total tumor cell counts. Accounting for the surface area, tumor density (cells/mm2) was used to normalize the data.. Each digital slide was divided into 1260 µm x 1260 µm grids and treated as an individual datum. Three grids of relative average tumor count from each case were used for a total of n=36.

**Results:** Automated tumor classification was accurate as reviewed by an anatomical pathologist. In this preliminary work, a significant increase in tumor density was observed in HPV+ HNSCCs compared to HPV- HNSCCs using Mann-Whitney test ($p<0.001$).

**Conclusion:** Digital tools efficiently facilitate cell classification automation for tumor density. In this preliminary analysis, we observed a significant trend towards higher density being associated with HPV+ HNSCCs. Higher cellularity suggests that HPV+ HNSCCs may have denser tumor cells despite a generally smaller primary tumor size reported in HPV+ cases. Ongoing/future work will explore this relationship in further detail and correlate cellularity with prognoses.

**Research theme 1:** Digital Pathology
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Levy, Michael

**Additional Author(s):** Relator R, McConkey H, Kerkhof J, Sadikovic B.

**Abstract Title:** Quantification of DNA methylation episignatures for the diagnosis of Mendelian neurodevelopmental disorders

**Abstract:**
The diagnosis of neurodevelopmental disorders can be challenging due to overlapping clinical phenotypes and uncertain pathogenicity of genetic variants. An expanding number of such genetic disorders are characterized by genome-wide disruptions in DNA methylation referred to as episignatures. We have previously developed 57 unique episignatures which are currently in clinical use as the EpiSign test to assist with the diagnosis of 65 genetic syndromes. These assessments involve the use of unsupervised clustering and supervised machine learning techniques to determine whether a clinical test sample matches any of the 57 episignatures. To decrease the subjectivity of interpreting clustering results and to increase the efficiency of processing large numbers of samples we have developed an episignature meta score. The meta score combines quantified clustering plot results with support vector machine classifier results to distill each test result to a single number. This enables quick identification of which samples are likely positive or negative, and which may need further manual review. Overall, the episignature meta score allows us to more quickly and accurately process the increasing number of samples submitted for Episign testing.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:** Test Utilization, Optimization and Quality Assurance
**Research theme 3:** Epigenetics

**Presenter's Name:** Liddy, Amanda

**Additional Author(s):** Maleki Vareki S, Burton JP

**Abstract Title:** Bacterial-Based Therapy with Akkermansia muciniphila to Modulate Tumour and Gut Microbiome and Activate T-Cells in Pancreatic Cancer

**Abstract:**
Pancreatic adenocarcinoma (PDAC) is becoming a common cause of cancer mortality in Canada and around the world. Due to the poor long-term outcomes and limited treatment options for PDAC, establishing new treatments is necessary to improve the survival of patients. Recently, the gut microbiome has been shown to play an important role in the body's response to tumors by influencing the immune system. Bacterial-based adjunct therapy has the potential to transform the TME to sensitize cancers to immunotherapy when present in the gut. Akkermansia muciniphila is one of the bacterial species that is routinely shown to be enriched in successful immunotherapy responders when present in the gut. A. muciniphila enhances anti-tumor immunity by transforming PDAC into immune hot tumors by increasing the recruitment of CD8+ T cells and stimulating dendritic cells to promote IL-12 secretion. This study aims to investigate the effect of A. muciniphila, in modifying the gut- and tumor-microbiome and activating T-cells in PDAC. Additionally, we will determine whether the combination of bacterial-based therapy with anti-PD1 treatment can sensitize immunotherapy-refractory PDAC tumors to immunotherapy. To determine the effects of A. muciniphila on PDAC tumor-bearing mice, A. muciniphila or PBS will be orally administered to PK mice with pancreatic tumors three times per week for two weeks. Stool will be collected pre- and post-treatment to assess the changes in the gut microbiota by 16S rRNA gene sequencing. PDAC tumor tissues will also be harvested for profiling by 16S rRNA gene sequencing, as well as flow cytometry. To further understand the immune activation and tumor infiltration related to A. muciniphila, mixed lymphocyte reaction assays will be completed with dendritic cells from naïve mice and treated with A. muciniphila or co-cultured with splenocytes harvested from tumor-bearing animals. Finally, to examine whether oral bacterial therapy can sensitize PDAC tumors to immunotherapy with anti-PD1, PK tumor-bearing mice will be treated with A. muciniphila or PBS in combination with anti-PD1 immunotherapy or an isotype control antibody injection. Two weeks following the completion of the treatment, tumors will be excised and weighed. This study will provide a better understanding of the link between the gut microbiome and cancer therapeutics and will test novel combination therapy for the treatment of pancreatic cancer that is otherwise untreatable with current regimens.

**Research theme 1:** Cancer Biology
**Research theme 2:** Infection, Immunity, and Inflammation
**Research theme 3:**





**Presenter's Name:** Lin, Sherman

**Additional Author(s):** Tran C, Chu M, Romagnoli T, et al.  Cecchini MJ

**Abstract Title:** 1000 Mitoses Project: An International Consensus on Mitotic Figures

**Abstract:**
**Background:** The identification of mitoses is essential for the diagnosis and classification of many different tumors. Despite its important role, there is a paucity of data examining the consistency in interpreting mitotic figures amongst pathologists. In this study, we leverage open-source publicly accessible datasets and social media to recruit an international group of pathologists to collectively score an image database of 1000 mitotic figures.

**Design:** The study was announced on Twitter to recruit practicing pathologists across the world. A survey was sent to obtain practice information, including institution affiliation, country, years in practice, and subspecialty training. Each pathologist was instructed to select a digital slide from The Cancer Genome Atlas (TCGA), and annotate 10-20 mitotic figures within a 2 mm^2 area. The first 1000 submitted mitotic figures were used to create an image dataset, with each figure transformed into an individual tile at 40x magnification. The dataset were redistributed to all pathologists to review, and determine whether each tile constituted a mitotic figure. The agreement rate for each pathologist and tile were created, and descriptive statistics were calculated.

**Results:** The scoring of mitotic figures was completed on 1010 tiles by 85 pathologists from 33 different countries. Pathologists had a median agreement rate with 80.22% of the mitotic figure tiles (mean 78.52), with an agreement range from 42.03 to 95.65%. For the mitotic figure tiles, there was a median agreement rate of 87.06% and 41.60% of the submitted tiles had a high agreement score in the 90-100% category. The range of agreement for the tiles ranged from 1.18 to 100%, and reflects a subset of tiles with mixed or low agreement.

**Conclusion:** This dataset stands as the largest international consensus study for mitotic figures to date. The agreement range reflects a spectrum of opinions on what constitutes a mitotic figure, which may have potential implications in tumor classification and clinical management. This variability also presents a barrier to developing machine learning tools, as current datasets are based on the opinion of only a small number of observers. Future and ongoing work seeks to abstract features that can be utilized to build more robust training systems for machines and pathologists.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:** Cancer Biology
**Research theme 3:** Digital Pathology

**Presenter's Name:** Liu, Amber

**Additional Author(s):** Shooshtari P

**Abstract Title:** Benchmarking BABEL Deep Learning Method Against Various Cell Types in Humans and Mice

**Abstract:**
**Introduction:** Multi-omic profiling within a single cell has the potential to improve our understanding of biological mechanisms of gene regulation compared to profiling a single modality. However, the multi-omics experiments can be quite expensive. In addition, existing joint profiling methods also often produce convoluted data when multiple modalities are extracted due to cell sensitivity. BABEL is a deep learning model developed by Wu et al. that can generate desired modalities from a single measured modality. Although this algorithm addresses an important problem in the field, it is unclear to what extent BABEL is applicable to different cell types and tissues. The aim of my study is to benchmark BABEL's predictions against the observed values, in a diverse set of cell types in human and mouse. The goal is to evaluate the accuracy of gene expression (scRNA-seq) predictions that BABEL outputs, when given an "unpaired" scATAC-seq dataset as input.

**Methods:** To accomplish this aim, I have found 2 jointly profiled datasets from human and 3 from mouse. These datasets include kidney, bone marrow, and brain cells. I treated these paired datasets as 'test' and 'benchmarking' sets of data. I first pre-processed and formatted the scATAC-seq data to be consistent with the input data format for BABEL. From this input, BABEL then generated scRNA-seq prediction outputs. I aim to use Pearson and Spearman's correlation coefficients to compare the level of correlation between the predicted and observed gene expressions for individual cells.

**Results:** Our expected result is that BABEL will generate the most accurate scRNA-seq predictions on datasets most like its training set. The original BABEL model was trained on peripheral blood mononuclear cells (PBMCs), thus we expect the correlation coefficients to be highest for the human bone marrow mononuclear cell (BMMC) dataset. It would also be interesting to see if the accuracy of predictions for mouse dataset will be lower than that of human datasets, given that BABEL was trained on human data.

**Discussion:** Our benchmarking study will demonstrate the strengths and limitations of the BABEL model in predicting an unmeasured modality in a single cell (i.e. scRNA-seq), given an input of a different modality (i.e. scATAC-seq). This will provide insight into cell types that BABEL is able to predict the most accurately, and the potential to increase the model's accuracy by changing its training dataset.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Lockau, Laura

**Additional Author(s):** Mui L, Joseph M, Cecchini M

**Abstract Title:** The use of fiducial markers to improve orientation and facilitate preparation of cell block specimens in cytopathology

**Abstract:**
**Introduction:** Cell blocks are important specimens for molecular studies that enhance diagnosis and determine eligibility for targeted treatments in many cancer types, including lung and pancreatic tumors. Lack of a point of reference in conventional preparation techniques leads to limited orientation for molecular extraction; in hypocellular samples where embedded tissue is not visible during sectioning, the block can easily be over- or under-cut. Some studies have used organic or inorganic fiducial markers to provide a point of reference for orientation purposes and to ensure that blocks are cut at the correct depth. This abstract describes a project in progress, aiming to evaluate the use of such markers to optimize cell block preparation methods at our institution.

**Methods:** Fresh specimens will be harvested via FNA biopsies at Victoria Hospital to generate study material. Samples will be fixed in CytoLyt medium, then diluted in ratios of 1:2, 1:5, and 1:10 to simulate varying degrees of cellularity in clinical samples. Histogels will then be created using either a standard protocol with no fiducial marker, an organic marker consisting of banana peel dyed with India ink, or an inorganic marker consisting of dark suture material. Each sample will then be assessed in terms of analysts' ability to localize and extract DNA. These groups will be compared to determine whether including a fiducial marker significantly improves the performance of molecular studies on cell block samples, any effect of the type of marker used, and variation based on specimen cellularity.

**Results:** Based on the results of prior studies, we expect that adding a fiducial marker may improve the ability to localize material for molecular testing. This may be most significant for samples with low cellularity.

**Discussion:** The addition of a fiducial marker to established histogel preparation methods may address common limitations of cell block specimens relating to both ease of identifying the location of cell concentrations, as well as determining orientation for comparison between serial sections. The methods tested here will make use of inexpensive and readily available materials. This simple and cost-effective solution demonstrates promise to improve the yield of molecular samples, which can enhance our ability to provide accurate diagnosis and determine eligibility for targeted treatments in a variety of cancer types.

**Research theme 1:** Test Utilization, Optimization and Quality Assurance
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Lu, Bonnie

**Additional Author(s):** Palmer J, Poon AFY

**Abstract Title:** Bayesian analysis of generative models of sequence insertion events in HIV-1 envelope glycoproteins

**Abstract:**
**Introduction:** Insertions play an important role in the adaptation of HIV-1 to the adaptive immune system. Specifically, the HIV-1 env gene that encodes the surface-exposed envelope glycoprotein (gp120) contains several hypervariable loops with unusually high insertion rates. However, we understand little about where insertions come from. What shapes the nucleotide composition of an inserted sequence? Are they derived from adjacent sequence in the virus genome, or are they simply random samples of nucleotides? Most models of molecular evolution in common use do not explicitly model insertion events, focusing instead on the replacement of one nucleotide with another (substitution events). We propose to address these questions by fitting generative models to insertion events that have been reconstructed from the phylogenetic analysis of HIV-1 evolution within hosts.

**Methods:** A custom Metropolis-Hastings Markov Chain Monte Carlo (MCMC) sampling algorithm was implemented in R to conduct Bayesian inference. We validated this algorithm by using the MCMC method to fit alternative models to simulated insertion data sets. Next, we applied the validated method to the insertion sequence data retrieved from the branch length consensus trees of a previous within hosts study. In total, 364 insertion sequences were used to estimate the posterior probabilities of the real sequence data.

**Results:** The model was run for $2 \times 10^5$ MCMC iterations on simulated and real-sequence data. The posterior probabilities of the four parameters describing the finalized empirical model of insertion sequences (probability of entering the slip state, probability of staying in the slip state, rate of nucleotide substitutions, and probability of seeing a frameshift-inducing insertion length) were found to be relatively concordant with the true values of the simulated data.

**Discussion:** The model is able to simulate nucleotide substitutions and insertions in sequences in a manner that reasonably reflects the trends observed in a patient-derived sequence data. The use of a two-state model system provided the flexibility needed to capture the unique trends of very rare insertion events that were simultaneously quite long. Although these mechanisms still require tuning, our model is able to account for the strong bias against frameshift-inducing insertion events and explore additional insertion configurations by moving independent slip events.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** MacDonald, James

**Additional Author(s):** Perampalam P, MacDonald JI, Zakirova K, Passos DT, Ramos-Valdes Y, Mehlen P, Shepherd TJ, Rottapel R, Dick FA

**Abstract Title:** Netrin signaling mediates survival of dormant epithelial ovarian cancer cells

**Abstract:**
Dormancy in cancer is a clinical state in which residual disease remains undetectable for a prolonged duration. At a cellular level, rare cancer cells cease proliferation and survive chemotherapy and disseminate disease. We utilized a suspension culture model of high grade serous ovarian cancer (HGSOC) cell dormancy and devised a novel CRISPR screening approach to identify genetic requirements for cell survival under growth arrested and spheroid culture conditions. In addition, multiple RNA-seq comparisons were used to identify genes whose expression correlates with survival in dormancy. Combined, these approaches discover the Netrin signaling pathway as critical to dormant HGSOC cell survival. We demonstrate that Netrin-1 and -3, UNC5H receptors, DCC and other fibronectin receptors induce low level ERK activation to promote survival. Furthermore, we determine that Netrin-1 and -3 overexpression is associated with poor prognosis in HGSOC and demonstrate overexpression elevates survival in dormant conditions. Lastly, we show that Netrin signaling contributes to chemotherapy resistance and metastasis in cell culture and xenograft models. This study highlights Netrin blockade and MEK inhibition as promising future directions for targeting cancer cell dormancy.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** McLoughlin, Allison

**Additional Author(s):** Taray-Matheson D, Diao H (2), Min W

**Abstract Title:** CircHUWE-1 as a Regulator of Prostate Cancer Growth

**Abstract:**
Prostate cancer is a major health concern for men worldwide and is often asymptomatic in its early stages. Small cell carcinoma of the prostate (SCCP) is a highly aggressive form of prostate cancer that can be studied in vitro using PC3 cell lines. Circular RNAs (circRNAs) have been previously shown to regulate tumor growth. CircRNAs can regulate transcription and splicing, sequester RNA binding proteins, code for proteins or function as microRNA sponges. CircHUWE-1 has been implicated in the regulation of colorectal cancer and non-small cell lung cancer (NSCLC), where it was shown that silencing circHUWE-1 inhibited the ability of colorectal cancer cells and cisplatin-resistant NSCLC cells to proliferate, migrate and invade in vitro. The present study aims to investigate the role of circHUWE-1 in the regulation of small cell carcinoma of the prostate, which has not previously been characterized. We hypothesize that circHUWE-1 causes increased tumor proliferation, invasion, and migration in PC3 cells. The PC3 cells were cultured and baseline expression of circHUWE-1 was examined using qPCR. PC3 cells were transfected with circHUWE-1 siRNA to silence circHUWE-1 mRNA expression. Knockdown of circHUWE-1 mRNA levels by siRNA transfection was confirmed by qPCR. Proliferation of transfected PC3 cells will be measured using a CCK8 assay, migration will be measured using a scratch assay, and invasion will be measured using a transwell assay. Each assay will consist of the three treatment groups an addition to a negative control group. We expect that silencing circHUWE1 with siRNA will cause the PC3 cells to exhibit a decreased ability to proliferate, migrate and invade. This research could increase our understanding of how circular RNA contributes to prostate cancer proliferation, migration and invasion and could allow researchers to block these pathways by providing targets for specific therapies.

**Research theme 1:** Cancer Biology
**Research theme 2:** Epigenetics
**Research theme 3:**





**Presenter's Name:** Muralitharan, Anushga

**Additional Author(s):** Wehrli B

**Abstract Title:** Reflexive ABPAS Staining of Esophageal Biopsies is Not Cost-Effective

**Abstract:**
**Introduction:** The Alcian Blue/Periodic Acid-Schiff stain (ABPAS) is a histochemical stain that is frequently used to identify acid mucopolysaccharides and has been performed reflexively on all esophageal biopsies at LHSC to help identify metaplasia seen in Barrett's esophagus and also fungal infections. Approximately 4300 esophageal biopsies were examined in 2021 for which reflexive ABPAS staining was performed at a cost of $12 per slide. While ABPAS staining makes it easier to diagnose Barrett's esophagus and fungal esophagitis, a standard hematoxylin and eosin (H&E) stain may be sufficient. We hypothesize reflexive ABPAS staining of esophageal biopsies is not cost-effective.

**Methods:** Pathology reports of esophageal biopsies from 2021 were reviewed. H&E and ABPAS stained slides of 96 cases with various pathologies including those with Barrett's esophagus and fungal infections were retrieved from the pathology archive. The H&E slides of the 96 cases were first randomly reviewed by the study pathologist who was blinded to the diagnoses. The study pathologist provided an initial diagnosis for each case based solely on the H&E review, then reviewed the corresponding ABPAS stained slides for each case and provided a final diagnosis.

**Results:** It was observed that the correct diagnosis was made 100% with solely the H&E stain and with the ABPAS stain for biopsies with Barrett's' esophagus. Esophageal biopsies with fungal infections were diagnosed correctly 25% of the time with just the H&E stain and 63% with the APBAS stain.

**Discussion:** Reflexive ABPAS staining of all esophageal biopsies is not necessary and instead can be ordered selectively as a confirmatory test in order to diagnose questionable or indeterminate cases of Barrett's esophagus. An ABPAS stain should likely be ordered in all cases with a clinical suspicion of fungal infection.

**Research theme 1:** Test Utilization, Optimization and Quality Assurance
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Parikh, Prey

**Additional Author(s):** Hamilton DW, Darling M

**Abstract Title:** The Characterization of a 'Scar Tissue' Phenotype of Fibrous Proliferations of the Oral Mucosa and Gingiva

**Abstract:**
Gingival and oral mucosal tissues are thought not to scar, a widely held view held by biologists. However, in pathology practice, fibrotic tissues are relatively frequently encountered in the gingiva and oral mucosa. Animal models suggest that phenotypic differences exist in primary wound healing cells, fibroblasts and myofibroblasts, between the skin and the oral mucosa. These differences have been thought to be the driving force behind minimal scarring or scar free healing in the oral mucosa. We hypothesize that human gingival lesions will show a differential phenotypic fibroblast and myofibroblast associated protein and cytokine profile compared to the typical scar tissue phenotype seen in skin lesions. Immunohistochemical methods will be applied to formalin fixed paraffin embedded tissue sections to test for the presence or absence of various biomarkers commonly seen in cutaneous wound healing. Immunofluorescence will be used to visualize smooth muscle actin, TGF beta, and periostin. Immunohistochemical stains that include Piccrosirus red and Masson's trichome will be used to test for collagen. An open image analysis software will then be used to quantify the number of cells per unit area that show positive staining. Since gingival wound healing still undergoes the same stages as cutaneous wound healing, we expect to see positive staining for all the biomarkers stated above. However, we expect differential expression of each biomarker compared to the typical expression in cutaneous lesions. Scar formation is an unwanted potential outcome of cutaneous healing which can cause a variety of negative physiological and psychological effects. Understanding how the gingiva heals in a way that avoids or minimizes scar formation can serve as a possible basis for the treatment of scars sustained during surgical procedures or through mechanical trauma like burns.

**Research theme 1:** Infection, Immunity, and Inflammation
**Research theme 2:** Oral Biology and Medicine
**Research theme 3:**





**Presenter's Name:** Pavlovic, Milica

**Additional Author(s):** Frisbee S, Fleet J

**Abstract Title:** Diabetes and the Relationship Between Post-Stroke Cognitive Impairment and Falls

**Abstract:**
**Introduction:** Diabetes, stroke, cognitive impairment, and the risk of falls are all interconnected and thus, there is a critical need to understand these relationships. Associations have been separately established, however, the importance of diabetes control post-stroke to decrease the risk of cognitive impairment and falls is crucial to investigate. Individuals with diabetes are at an increased risk of stroke and cerebral small vessel disease. Stroke survivors are at risk of cognitive impairment, which is known as post-stroke cognitive impairment. In general cognitive impairment increases the risk of falls and fractures. The main goal of this research project was to determine the impact on cognitive function and the risk of falls when patients with diabetes have a stroke compared to individuals without diabetes.

**Methods:** To conduct the research project, a retrospective patient chart review was completed. The study population included adults over the age of 18 with at least a moderate severity of stroke from the inpatient stroke rehabilitation unit. When reviewing patient charts, current medications, lab reports, and patient history was documented. Patient scores from the Montreal Cognitive Assessment (MoCA) were utilized to measure cognitive function and the Berg Balance scale was used to assess the risk of falls.

**Results:** The expected results indicate that if a patient has diabetes, then a stroke occurs they will have an increased risk of falls and cognitive impairment. Overall, diabetes increases the risk of stroke, and jointly these conditions will decrease an individual's cognitive function, which leads to an increased risk of falls and fractures.

**Discussion:** This research project will provide information needed to perform future research and establish treatment plans to control diabetes in post-stroke patients to avoid cognitive impairment and falls. Furthermore, clinicians and patients will understand the impact of animals and environmental health on stroke rehabilitation and diabetes. Overall, this project will encourage individuals and physicians to strictly manage diabetes, especially post-stroke to prevent falls and cognitive impairment.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** One Health
**Research theme 3:**

**Presenter's Name:** Relator, Raissa

**Additional Author(s):** Verma A, Riccio A, Sadikovic B

**Abstract Title:** Methylation status of imprinted regions in neurodevelopment disorders

**Abstract:**
**Introduction:** Genomic imprinting is parental-specific gene expression and plays an important role in development, with abnormal methylation of control regions (DMRs) resulting in imprinting disorders. Some imprinting disorders are linked to genetic variants, while others have unknown causes. An expanding number of neurodevelopmental disorders (NDDs) have been associated to distinct epigenetic profiles known as episignatures. These NDDs are mostly caused by epigenetic regulator genes that have been shown to affect imprinting control, however, methylation of imprinted loci in NDDs has been poorly investigated. In this study, we examined the status of imprinting DMRs in individuals with positive episignature profiles to investigate the function of epigenetic modifiers in maintaining genomic imprinting.

**Methods:** We performed a comparative analysis of 50 known imprinting DMRs in individuals positive for an EpiSign disorder and unaffected controls. We computed the difference in mean methylation for each locus and tested for significance using a two-sided z-test. In silico validation was also implemented.

**Results:** Our analysis revealed that several epigenetic modifier genes maintain imprinting status similar to controls. However, a few results stand out, including Down syndrome and immunodeficiency-centromeric instability-facial anomalies syndrome (ICF), which mostly present hypomethylated profiles for EpiSign cases compared to controls in imprinted regions. Independent analysis also confirmed differential methylation status outcomes.

**Discussion:** The genes associated with imprinting disturbances can provide functional insights into the imprinting mechanism during human development and phenotypic correlations with NDDs. The identified epigenetic modifier genes/regions may aid in understanding the etiology of imprinting disorders.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:** Epigenetics
**Research theme 3:**





**Presenter's Name:** Richmond, Julie

**Additional Author(s):** Cecchini MJ

**Abstract Title:** Correlation between Gross and Radiologic Size of Lung Cancers

**Abstract:**
**Introduction:** The treatment for lung cancers is largely driven by the stage which is largely based on the size of the tumor. Radiologic size determines the extent of lung resection required at the time of surgery, while the gross tumor size confirmed by microscopic examination provides a definitive stage that can dictate need for additional therapy. In most cases there is a good correlation between the size of lesions on radiology and on the surgical resection. However, there can be some discordances including in cases where there is a prolonged delay between imaging and resection. This study aims to investigate the difference in recorded tumor size and the association with the interval between imaging and resection.

**Methods:** Lung cancer cases (n= 70) at LHSC were retrospectively analyzed in one-year pre- and post- COVID-19 pandemic. Focusing on the pandemic for a portion of our data enabled us to consider cases that have had a possible delay of surgery after radiologic discovery. The most recent recorded size on imaging was compared to the gross tumor size in cases of varying lung cancer types. We considered the lung cancer type so that more aggressive tumors could be highlighted in our data. The time interval between imaging and resection was analyzed to appreciate the impact on size correlation, with or without the potential for surgical delay during the post pandemic year.

**Results:** The majority of cases in our series did not have a significant difference in size between that observed on imaging and the subsequent resection specimen. A small subset of cases (n= 17) had > 1 cm difference in size compared to the pre-operative imaging. The interval between imaging and resection was 72.2 days during COVID and 58.2 days pre-COVID, however, this did not translate into a statistically significant difference in size variance. The trend showed an increased size difference in the pre-COVID subset.

**Conclusions:** In most cases the radiologic size correlates well with the final size of the tumor on resection. There is a subset of cases in which there is a difference in size. Despite the increase time between imaging and resection during COVID we did not identify a difference in size discrepancies.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:** Test Utilization, Optimization and Quality Assurance
**Research theme 3:**

**Presenter's Name:** Silva, Ananilia

**Additional Author(s):** Levy MA, Relator R, Haghshenas S, Kerkhof J, McKonkey H, Skinner SA, Vitobello A, Valenzuela I, Scheffer I, Myers K, Tedder ML, Sadikovic B.

**Abstract Title:** DNA methylation episignature for Neurodevelopmental Disorder with Hypotonia, Stereotypic Hand Movements, and Impaired Language, NEDHSIL, syndrome

**Abstract:**
**Background:** Epigenetic mechanisms, such as DNA methylation, have become promising targets in the search for potential biomarkers for rare diseases, including genetic neurodevelopmental disorders. The discovery of DNA methylation episignatures has become a key tool in clinical diagnosis of monogenic syndromes. This study describes a DNA methylation episignature for the Neurodevelopmental Disorder with Hypotonia, Stereotypic Hand Movements, and Impaired Language (NEDHSIL), caused by mutations in MEF2C gene, which encodes a transcription factor known to play a crucial role in molecular pathways affecting neuronal development. Pathogenic MEF2C variants cause a range of clinical phenotypes including different degrees of developmental delay, various types of seizures, hypotonia, characteristic facial factors, and behavioral abnormalities.

**Methods:** DNA was extracted from the blood of 8 patients with the MEF2C-related syndrome and control individuals and methylation levels were measured using Illumina Infinium EPIC bead chip arrays. For the methylation analysis, R MatchIt package was used to find a total of 56 matched- controls by age, sex, batch, and array and clustering of cases and controls were investigated using heatmaps and multidimensional scaling (MDS). A support vector machine (SVM) was used to assess the sensitivity and specificity of the episignature to the NEDHSIL cohort.

**Results:** The analysis showed 106 most differentiated probes, with hypermethylation evidence, and from selected probes, the heatmap and MDS plots showed a significant and clear separation between cases and controls. Calculating methylation variant pathogenicity (MVP) scores for each training sample, through cross-validation step, it was observed a high sensibility and specificity for the NEDHSIL cohort compared to other neurodevelopmental disorders.

**Conclusion:** A robust episignature in NEDHSIL syndrome was identified, that enables diagnosis and genetic variant classification, while providing insights into the molecular pathophysiology of this disorder.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:** Epigenetics
**Research theme 3:**





**Presenter's Name:** Tapp, Brandon

**Additional Author(s):** Jessani A

**Abstract Title:** Questionnaire Design for the Identification of Oral Health Status and Oral Health Service Utilization Among Rwandan Pregnant Women

**Abstract:**
**Introduction:** Oral health is vital to overall health, especially during pregnancy. Pregnancy can cause changes in a woman's oral health, and untreated dental problems like periodontitis or gum disease can have severe consequences, including preterm labour and low birth weight. However, across low-income nations, particularly in East African countries like Rwanda, pregnant women are not adequately informed of the importance of their oral health. In addition, no self-reported data has been collected to measure the consequences of poor oral health knowledge in Rwandan pregnant women, either behavioural or clinical. Thus, the main goal of this study was to construct a questionnaire for use in examining oral healthcare needs and patterns of oral health service utilization by pregnant women in Rwanda.

**Methods:** Andersen and Newman's Framework of Health Services Utilization, which highlights predisposing and enabling psychosocial factors, was applied in constructing questions regarding socioeconomic status/support and health service utilization. Nominal variables, ordinal variables and the Likert scale were employed in a closed-ended question format. Representatives and researchers from the University of Rwanda and the Rwandan Ministry of Health were consulted to incorporate local context in the question design. Expected honorarium and participant motivation were considered to finalize the questionnaire length and order.

**Results:** Six sections were constructed for the questionnaire containing 39 questions in total, including demographic information (5), education and income (3), social support (3), general health (8), prenatal screening (7), and oral health (13). Consultation with researchers from the University of Rwanda reduced the questionnaire length from an original 67 questions and incorporated local Rwandan terms within question formulation, notably, the inclusion of Ubudehe categories as a measure of socioeconomic status.

**Discussion:** The designed questionnaire can generate the first baseline data describing the self-reported oral health status of Rwandan pregnant women and their utilization of dental services. The distribution of this questionnaire and data collection is expected to occur as early as July 2023, pending ethical approval in Rwanda and the finalization of the protocol. Identifying the needs and actions of Rwandan pregnant women in terms of their oral health will be helpful in improving overall maternal and fetal health outcomes.

**Research theme 1:** One Health
**Research theme 2:** Oral Biology and Medicine
**Research theme 3:**

**Presenter's Name:** Tran, Michael

**Additional Author(s):** Hallett M

**Abstract Title:** Candescence 2.0, developing an accessible deep learning approach to identifying Candida albicans morphology

**Abstract:**
Candida albicans is a common species of yeast found in the human gut flora, which can become pathogenic and cause fungal infections of the mouth or vagina in certain environmental conditions. C. albicans is a commonly studied model organism for pathogenic yeast due to its unique properties, one of which is its ability to shapeshift into various morphologies in response to environmental changes. Identifying and annotating the morphological states in culture microscopy imagery can be time-consuming and challenging, not to mention subjective to the observer's interpretation. To address this issue, our lab developed Candescence, a tool that utilizes deep learning to objectively detect and classify C. albicans' morphological states. With the ability to detect and label cells in culture with 85% recall and 81% precision, Candescence can also generate visual data of intermediary stages between morphologies and help clarify visual differences between them. Currently, the tool is being restructured and organized to expand its usability outside our lab and possibly to other Candida species. In collaboration with other labs in Tel Aviv, Candescence visions a workflow of identifying and classifying C. albicans cells accessible and reproducible through module installation and from the command line. Candescence has the potential to advance research on pathogenic yeasts and beyond.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Trautrim, Erik

**Additional Author(s):** Hammond R

**Abstract Title:** Anxiety in the workplace: handling abnormal prions and common infectious agents

**Abstract:**
Transmissible spongiform encephalopathies (TSEs) are limited to those exposed to the abnormal prions that cause them. In humans, transmission of the abnormal prion that causes Creutzfeldt-Jakob Disease (CJD) can result from a workplace exposure due to needlestick or sharps injuries (NSSIs). This transmission vector includes healthcare workers (HCWs) in the operating room and other pathology and laboratory medicine staff that handle the potentially infectious tissue. As CJD can only be diagnosed via ante-mortem cortical biopsy or post-mortem internal exam, tissue can only be presumed to be infected with abnormal prions at the time of handling. Those who are at risk of such an exposure also handle tissues containing common infectious agents. Higher anxiety scores are seen in those who have had a NSSI, however anxiety scores related to handling of tissues without incurring an injury have yet to be investigated. To understand this population, their opinions, knowledge levels, and anxiety scores were compiled using an anonymous and voluntary online survey. This study seeks to measure anxiety among staff who handle potentially infectious tissues through a modified Hospital Anxiety and Depression subscale (HADs). Scoring anxiety acts as a component of a larger survey which provides demographic and qualitative data. Years in healthcare/research, as well as individual knowledge base and experience are also analyzed for variations in anxiety scores. Participants were from the Department of Pathology and Laboratory Medicine (PaLM) with London Health Sciences Centre (LHSC), London, ON. We hypothesize that a significant difference exists between anxiety scores associated with handling abnormal prions (CJD) and the anxiety scores associated with handling common infectious agents (i.e., bacterial, viral, fungal), across groups. Given the results of the study, we indicate some best practices for the handling of infectious tissues as they relate to lower anxiety scores. Furthermore, we identified the role that in-service sessions play in staff understanding of abnormal prions and common infectious agents.

**Research theme 1:** Pathobiology of Neurologic Diseases
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Vaibhav, Venkat

**Additional Author(s):** Asfaha S

**Abstract Title:** The role of 5-lipoxygenase (5-LO) expressing cells in colitis-associated colorectal cancer

**Abstract:**
**Introduction:** Patients with prolonged ulcerative colitis (UC) exposure are 20% more likely to develop colorectal cancer (CRC). Tuft cells, a rare epithelial cell type within the intestinal crypt, may be the origin for colitis-associated cancer (CAC). To study this, I will be working with a new transgenic mouse model 5-LO-GFP-DTR-CreERT2 mice, wherein tuft cells are marked by 5-lipoxygenase (5-LO) expression. 5-LO expression is also seen in macrophages, which has been shown to play a role in tumorigenesis. The transgenic construct also contains GFP for detection by microscopy, DTR for selective cell ablation, and CreERT2 for conditional expression. Due to the abundance of genetic tools, this can be an effective mouse model for studying CAC.

**Methods:** 1) Characterize the location and expression profile of 5-LO+ cells within the intestinal epithelium and bone marrow for all three mouse lines. Immunofluorescent staining of the colon and bone marrow (BM) was conducted to quantify the number of GFP+ cells per 100 crypts across the rectum, distal colon, and proximal colon. Colonic slides were stained for the tuft cell marker, Dclk1. 2) Determine whether 5-LO+ epithelial cells give rise to colitis-associated CRC. 5-LO-GFP-DTR-CreERT2 mice crossed to APC fl/fl mice were treated with three doses of 6mg tamoxifen, followed by five days of 2% DSS to induce colitis. 14 weeks following DSS treatment, the mice were sacrificed for histology, tumor number and size.

**Results:** Immunofluorescent staining of the colon and BM shows endogenous GFP fluorescence of in all three lines, with the highest frequency of GFP+ cells seen in Line 3 mice (n=7), followed by Line 2 (n=6) and 6 (n=3). Dclk1 costaining in the colon is observed in Line 3 mice (n=3), but quantification and statistical analyses are yet to be conducted. For the tumor experiments, mice from Line 2 (n=7) and Line 6 (n=4) showed no tumor formation, with no histological signs of dysplasia detected. However, one Line 3 mouse did successfully generate a tumor, which has been verified through histology. This mouse will be analyzed further to optimize the protocol for generating tumors in Line 3 mice.

**Discussion:** With the highest number of GFP+ cells observed in the colon of Line 3 mice, it could be the most effective of the three mouse lines at studying CAC. High GFP+ labelling in the BM of Line 3 mice also opens the door for investigating the role of macrophages in CAC.

**Research theme 1:** Infection, Immunity, and Inflammation
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Vo, Meggie

**Additional Author(s):** Peng T

**Abstract Title:** Doxorubicin induces SerpinA3 expression in cardiomyocytes

**Abstract:**
**Introduction:** Doxorubicin is a chemotherapeutic drug widely prescribed for the treatment of various cancers, including solid tumours and haematological malignancies. However, its clinical applications are limited due to its cardiotoxic effects on the heart and the precise mechanism underlying this effect is not fully understood. SerpinA3 is a serine protease inhibitor currently used as a diagnostic factor in some cancers due to its overexpression in various cancer types. Our lab has previously shown that serpinA3 expression increases following doxorubicin treatment in neonatal mice cardiomyocytes. In the present study, we have attempted to see if similar results are observed in human cardiomyocytes. We hypothesize that doxorubicin will increase the expression of serpinA3 protein in human cardiomyocytes.

**Methods:** To test this hypothesis, we first cultured AC16 cells and treated them with varying doses of doxorubicin to investigate cytotoxicity. We then collected the cells and performed western blots to assess the expression of serpinA3 in treated versus untreated cells.

**Results:** Our results show that AC16 cells treated with doxorubicin have an increased expression of serpinA3 compared to untreated cells.

**Discussion:** These findings show that serpinA3 expression increases in AC16 cells following treatment with doxorubicin. While the mechanism is not fully understood, these results suggest a relationship between serpinA3 and doxorubicin-induced cardiotoxicity.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Vora, Sachee

**Additional Author(s):** Wathens CN

**Abstract Title:** Applying a One Health Approach to Investigating Refugee Health Models and Evaluating the Efficacy of the Newcomer Clinic and Integration Program

**Abstract:**
**Introduction:** The refugee crisis is currently one of the most prominent global issues. As such, it is imperative to think about ways to provide accessible and comprehensive health services for refugees. Community health centres (CHCs) provide health services for underserved communities and address the root causes of adverse health in their communities, such as upstream, non-clinical factors. The London Newcomer Clinic and Integration Program (NCCIP) works to provide primary care for newly arrived Government-Assisted Refugees (GARs) within their first six months. There is a critical need to understand how well the clinic achieves its goal of providing accessible, comprehensive, and culturally sensitive care to GARs. This project aims to provide recommendations to the NCCIP on their practice by investigating existing refugee health models and conducting an evaluation to assess the clinic's ability to provide appropriate primary care to GARs in London. This project will utilize and incorporate the One Health framework into the creation of the evaluation and recommendations.

**Methods:** Multiple literature scans will be conducted to gather information on refugee health models and investigate the One Health connection to refugee health. Interviews and meetings will be held with integral stakeholders to advise the construction of the evaluation and to appropriately engage all stakeholders. Finally, the evaluation will be created and conducted.

**Results:** The expected results are to identify the most appropriate and comprehensive way to conduct the evaluation of the NCCIP, as well as information on best practices within CHCs and refugee health. Different ways to integrate the One Health approach within CHCs and how it connects to refugee health on a bigger scale will also be addressed.

**Discussion:** The results from the evaluation and the literature search will aid in the formation of recommendations for the NCCIP. This will enable them to observe how their model of health is working and what could be improved. It will also provide suggestions for areas of growth and innovation regarding services specific to refugee health. Finally, the results will convey the importance of One Health within refugee health, specifically in terms of prevention, detection, and treatment of zoonotic infectious diseases.

**Research theme 1:** One Health
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Vytlingam, Kevin

**Additional Author(s):** Ji X, Peng T

**Abstract Title:** Determining the interaction between junctophilin-2 and junctin by the bimolecular fluorescence complementation (BiFC) assay

**Abstract:**
**Introduction:** Junctophilin-2 (JPH2) and junctin play important structural roles in stabilizing type 2 ryanodine receptors (RyR2) in the heart. This, in turn, regulates calcium influx into cardiomyocytes, which is important for maintaining normal cardiac contractility. Decreased JPH2 and junctin levels have been well-documented in cardiac disease. However, despite the proximity and overlapping functions of these two proteins, the possibility of an interaction between them has yet to be explored. Our study aims to determine whether binding between JPH2 and junctin occurs using the bimolecular fluorescence complementation (BiFC) assay.

**Methods:** A549 cells were cultured and transfected with two plasmids: one containing ASPH (encoding cardiac junctin) fused to the N-terminal fragment of green fluorescent protein (GFP), and the other containing JPH2 fused to the C-terminal fragment of GFP. Western blotting was used to confirm JPH2 and junctin expression, and cells were visualized in vitro using fluorescence microscopy to observe whether an interaction occurred. Co-immunoprecipitation in A549 cells was performed to verify the result of the BiFC assay.

**Results:** Western blotting confirmed the expression of JPH2 and junctin at expected levels. A fluorescent signal was observed when the JPH2 and junctin constructs were co-transfected into A549 cells and imaged using fluorescence microscopy. No fluorescent signal was observed when the JPH2 and junctin constructs were transfected separately into cells.

**Discussion:** A novel interaction between JPH2 and junctin was demonstrated using the BiFC assay. Given the importance of each protein in maintaining calcium homeostasis in cardiomyocytes and thus normal heart contractions, inhibition of this interaction may contribute to the pathogenesis of heart failure. Future studies should be directed at identifying genetic mutations capable of interrupting this interaction. Finally, the implications of a disrupted interaction on cardiovascular dynamics could be examined in animal models to deduce the functional importance of this binding event.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** Infection, Immunity, and Inflammation
**Research theme 3:**

**Presenter's Name:** Wang, Eric

**Additional Author(s):** Feng B, Chakrabarti S

**Abstract Title:** miR-9 regulates endothelial-to-mesenchymal transition in diabetic complications

**Abstract:**
**Background:** Diabetes causes chronic complications such as diabetic retinopathy, cardiomyopathy, and nephropathy. These complications, though different in location and features, share a common origin: glucose induced endothelial damage. Endothelial cells are highly susceptible to hyperglycemia, and endothelial damage paves the way for further dysfunction. Throughout this process, endothelial cells are influenced by tissue-specific factors, leading to variations in outcomes across different complications. Understanding the unique and common responses of various endothelial cells to hyperglycemia will inform better ways to address diabetic complications. miR-9 is a small RNA regulator of gene expression that influences inflammatory and profibrotic signalling. miR-9 is downregulated in endothelial cells in response to diabetes and may play an important role in regulating glucose-induced endothelial dysfunction across diabetic complications.

**Methods:** Diabetes was induced in 6-week-old C67BL/6 mice. Diabetic and age-matched non-diabetic mice were sacrificed after 2 months. Eyes, heart, and kidneys were collected, formalin-fixed, and sent for Nanostring Digital Spatial Profiling analysis. Data were analyzed using the GeoMx DSP analysis suite. Human retinal endothelial cells (HRECs) were cultured in normal (5mM) and high glucose (25mM) conditions to confirm the downregulation of miR-9 and occurrence of endothelial-to-mesenchymal transition (EndMT), a pathway of interest determined by Nanostring analysis. miR-9 activity was experimentally altered in HRECs (via transfection of miRNA mimics or siRNAs) and in mice (using transgenic endothelial-specific miR-9 overexpressing mice) to assess regulatory role of miR-9 in glucose-induced EndMT.

**Results:** Different organs showed differential enrichment of various genes and pathways in response to diabetes. EndMT and related pathways were commonly seen and contributes to endothelial dysfunction. High glucose suppressed miR-9 and induced EndMT in HRECs; EndMT was prevented by miR-9 mimics. Overexpression of miR-9 prevented glucose-induced EndMT and rescued retinal barrier function in diabetic mice.

**Discussion:** Endothelial cells of different origins have different specific responses to high glucose in diabetes, but EndMT may be an underlying connection between the various diabetic complications. miR-9 prevents EndMT and may represent a key regulator across diabetic complications.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** Epigenetics
**Research theme 3:**





**Presenter's Name:** Wasif, Sumaiyah

**Additional Author(s):** MacDonald J, Dick FA

**Abstract Title:** Investigating the Role of Netrin Signalling in High-Grade Serous Ovarian Cancer Spheroid Survival and Chemotherapy Resistance

**Abstract:**
High-grade serous ovarian cancer (HGSOC) comprises of more than 70% of all ovarian cancer cases. HGSOC is challenging to treat due to its late-stage diagnosis when metastases are already present. HGSOC is different from other human cancers due to tumour cells disseminating from ovaries into the peritoneal cavity. In epithelial ovarian cancer (EOC), transcoelomic route is the most common route of metastasis. Ascites from ovarian cancer patients contain a cell-cycle dormant population of cancer cells. These cells show altered metabolism, reduced proliferation, and certain unexplored mechanisms of survival that allow insight into HGSOC spheroid biology. Therefore, new models to study spheroids allow us to explore basic molecular questions related to HGSOC dormancy and chemotherapy resistance.
A previous study done in our lab used a genome wide CRISPR screen to identify genes that are essential for spheroid survival, including netrin family of proteins. Netrins could signal through MEK/ERK pathway and mediate dormancy in HGSOC spheroids. Netrins have been previously shown to be only overexpressed in malignant ovarian tumors and not in benign ovarian cancers, indicating the importance of their role as potential clinical biomarkers.

Therefore, we hypothesize that netrins are upregulated in ovarian cancer spheroids, enhance spheroid viability in ascites, support cancer dormancy, and contribute to chemotherapy resistance.
We will investigate the effects of netrin inhibition and overexpression on ovarian cancer spheroid viability. We plan to compare RNA expression of netrin knockout spheroids and control spheroids, to determine significant pathways of netrins that affect spheroid survival. We plan to compare RNA expression of netrin-overexpressing spheroids and control spheroids. This approach will identify critical pathways that netrins use, that ultimately effect spheroid biology.

We will also study the regulation of netrins and identify useful upstream and downstream mediators as potential therapeutic targets. We show that spheroid survival is reduced after inhibiting the downstream effector molecule MEK, by treating spheroids with a MEK inhibitor. By studying spheroid biology and the molecular mechanisms of netrins, we will identify novel pathways and molecules as therapeutic targets, to overcome chemotherapy resistance and improve patient outcome.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Wang, Isabel

**Additional Author(s):** Gibson C

**Abstract Title:** What We Can Learn From the Victorians: A Comparison of Modern and Victorian Epidemic Response and Prevention

**Abstract:**
Since the rise of modern medicine and the use of vaccination and drug therapies, non-therapeutic methods of inhibiting the spread of infectious disease have largely been ignored or considered archaic. The period between the outbreak of an epidemic and the advent of a treatment for the disease is critical to its containment and control. In the modern (2000–present) era, the healthcare of Victorian (1837–1901) England is often demonized for the lack of acceptance of germ theory and poor hygienic practices, and their role in rapid disease propagation. This qualitative literature review evaluates the elements of modern and Victorian era epidemic response for their successes and failures in disease control within a One Health framework. This comparative qualitative narrative review will identify selected human, animal and environmental factors that contribute to disease control from both eras. Grey literature such as novels, popular media and satire will be consulted in addition to medical literature, hospital records and recorded population vital statistics to gain an understanding of health perspectives and attitudes, as well as the medical traditions and superstitions practiced by laypeople. Findings thus far include the importance of adequate ventilation in preventing airborne disease spread, soap marketing techniques as encouragement for good sanitation habits, and the balance of patient-physician authority in health outcomes. Results will be summarized and compiled into a prescription of non-therapeutic, but effective, methods of disease control and a list of potentially ineffectual modern practices to be abandoned or improved that could be used in response to future outbreaks of infectious disease. This prescription and list will be instrumental in promoting early prevention and response to new disease outbreaks, especially in populations with health disparities and/or reduced access to new therapies.

**Research theme 1:** One Health
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Wang, Shirley

**Additional Author(s):** Khan ZA

**Abstract Title:** Unlocking cellular potency in human cells through chemical reprogramming

**Abstract:**
Chemically induced pluripotent stem cells (CiPSCs) serve as an alternative method to the traditional method of transfecting pluripotency genes. This CiPSCs approach involves targeting select cell signalling pathways and epigenetic modifiers using small molecules to reprogram somatic cells. Although promising, current limitations include the inability to induce pluripotency by small molecules in human somatic cells. This inability is believed to be due to stable human epigenomes. My study aims to investigate whether the starting cell type such as lineage committed but undifferentiated human cells, which may demonstrate epigenome flexibility, can make a difference when exposed to reprogramming chemicals and display pluripotency. To achieve my objective, I utilized a recently characterized undifferentiated cell type from infantile hemangiomas. These hemangioma-initiating cells differentiate into vascular endothelial cells and provide an excellent model to study chemically-induced pluripotency. I compared the response of hemangioma cells to fully mature dermal microvascular endothelial cells (HDMEC). Cells exposed to novel chemical reprogramming cocktails at 2 time points, 48 hours and 9 days to induce pluripotency. I analyzed transcript levels of pluripotency associated gene : POU5F1, SOX2, KLF4, NANOG. My results indicate an increased expression of SOX2 and NANOG in hemangioma cells when compared to HDMEC at the 48 hour time point. However, no changes were observed when cells were exposed to the chemical cocktail for 9 days. Although the study is on-going with detailed analysis. The results to date indicate that uncommitted cells may be induced to exhibit pluripotency using small molecules. The results of this study may contribute towards developing regenerative therapeutic strategies that utilize chemical reprogramming as an alternative chemical reprogramming of lineage-restricted human cells approach to change human cell fates.

**Research theme 1:** Regenerative and Transplantation Medicine
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Wang, Honglin

**Additional Author(s):** Feng B, Chakrabarti S

**Abstract Title:** CircRNA_012164 interacts with microRNA-9-5p to mediate diabetic cardiac fibrosis.

**Abstract:**
**Introduction:** Diabetic cardiac myopathy (DCM) is a potent and independent risk factor in developing cardiovascular disease and heart failure. Despite successful management of comorbid cardiovascular risks, diabetic patients still see increased incidents of heart failure. The first stage of DCM is cardiac fibrosis, which is characterized excessive deposition of extracellular matrix proteins into the basement membrane and interstitium of the heart. Hyperglycemia results in inflammatory signaling and transcriptional derangement in endothelial cells, leading to the activation of various cells in the heart that contribute to the production of fibrosis. Previous research has shown that the noncoding RNA (ncRNA) MicroRNA-9 (miR9) regulates the expression of various fibrotic and inflammatory genes related to DCM. CircularRNAs are a new class of ncRNA which function by sponging up and downregulating microRNAs. CircRNA_012164 is a circRNA which has been found by an assay to be upregulated in diabetic murine heart tissue, and has a binding affinity to miR9. We hypothesize that circRNA_012164 interacts with miR9 to mediate the expression of genes associated with cardiac fibrosis in diabetes.

**Methods:** We induced diabetes in normal and endothelial-specific miR9-overexpressing mice to quantify the downstream effects of hyperglycemia and miR9 on the expression levels of fibrotic genes and circRN_012164. CircRNA will be quantified following digestion of linear RNA with RNase. Next, we assessed the expression of circRNA_012164 in mouse cardiovascular endothelial cells (MCECs) to observe the endothelial-specific expression of circRNA_012164 in response to hyperglycemic and normoglycemic conditions. Finally, we will establish a causational relationship between circRNA_012164, miR9 and downstream fibrotic genes with transfection experiments.

**Results:** Our results show that endothelial-specific miR9-overexpressing mice show significantly reduced expression of FN1, Col1A1 and FSP1 in both diabetic and non-diabetic mice, with miR9 overexpression being able to restore gene expression to baseline non-diabetic levels. CircRNA_012164 was confirmed to be overexpressed in diabetic murine hearts. In MCECs, hyperglycemia resulted in an increase in circRNA_012164 and downstream fibrotic gene expression. We expect to see that knockdown of circRNA_012164 would result in rescuing the expression of miR9 following exposure to hyperglycemia and reducing the downstream fibrotic response.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Win, Phyo

**Additional Author(s):** Zeng S, Xie J, Newcomb C, Arking D, Castellani C.

**Abstract Title:** The role of mitochondrial DNA modifying agents on the nuclear epigenome and transcriptome

**Abstract:**
**Introduction:** Mitochondrial DNA copy number (mtDNA-CN) reflects the quantity of mtDNA and serves as a proxy for mitochondrial function. Previous studies have shown that mtDNA-CN variation can influence nuclear DNA (nDNA) methylation and gene expression. Interestingly, both mtDNA and the nDNA epigenome are modifiable by exogenous and endogenous environmental stimuli. The hypothesis of this project is that exogenous environmental chemical modifications to mtDNA-CN alters nDNA methylation and gene expression in a dose-dependent manner and in some cases, is reversible. Identification and characterization of these dynamics will uncover the biological mechanisms contributing to these relationships

**Methods:** Exogenous mtDNA-CN modifying chemical compounds were applied to HEK293T cells in culture, these included resveratrol (Resv), acetaminophen (Acet) and ethidium bromide (EtBr) at increasing doses (N=112). The effect of removal of EtBr following exposure for four recovery timepoints was also tested. DNA and RNA from exposed lines were analysed for DNA methylation via the Illumina Methylation EPIC Beadchip, and RNA sequencing via the Illumina NovaSeq 6000, respectively. Linear mixed model and negative binomial regression analyses were used to assess the relationship between mtDNA-CN variability and methylation/gene expression, with nDNA measures as the outcome. Integrated association analysis between differentially methylated and expressed genes was performed to determine significant CpG-Gene pairs.

**Results:** Acet and Resv exposure resulted in dose-dependent mtDNA-CN increases, whereas EtBr led to dose-dependent mtDNA-CN decreases. 332 CpGs were identified to be differentially methylated ($p<1e-7$) and significant CpGs showed enrichment for a positive correlation between mtDNA-CN and methylation (313 CpGs, $p<2e-16$). In EtBr recovery experiments, top CpGs display methylation changes that correlate with mtDNA-CN changes and for many loci, mtDNA-CN and nDNA methylation revert to initial levels within 96 hours. Integration of methylation and gene expression identified 423 pairs including association between cg0918651 with three differentially expressed nearby genes (NUDT3, UQCC2, C6orf1, $p<6e-9$).

**Discussion:** Environmentally induced mtDNA-CN variation correlates with nDNA methylation and gene expression changes suggesting that the mechanism driving these changes is not independent, and further demonstrating that in many cases, these changes are reversible.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:** Epigenetics
**Research theme 3:**

**Presenter's Name:** Woo, Elissa

**Additional Author(s):** Cecchini MJ, Halliday G

**Abstract Title:** Use of flexible transparent film as a novel physical support for histologic slides to facilitate next generation slide scanning

**Abstract:**
**Introduction:** Current practices in many institutions continue to utilize traditional methods of light microscopy for the analysis and diagnosis of specimens received in their pathology department. However, with increasing volumes of specimens the need for consideration of new techniques could revolutionize pathology as it is known today. Digital pathology requires the integration of processes which can entirely eliminate traditional methods causing discomfort for pathologists as this technology is very unfamiliar for the majority of them. The study of potential alternatives to traditional glass microscopes slides could allow for ease of integration of digitized techniques.

**Methods:** The proposed system involves cutting embedded tissue directly only rolled transparent film which can travel through staining solutions prior to being scanned. Three phases will be conducted to evaluate the feasibility of this concept. Phase one will identify film with key characteristics that are necessary for histologic processing. Phase two will assess the selected film during staining and its optical characteristics, while continually optimizing protocols to achieve the most desirable result. The final phase involves the creation of a prototype that can facilitate automated microtomy and labeling of tissue sections.

**Results:** Tissue-Tek coverslipping film has been identified to meet the key criteria for this project. Various techniques have been explored to improve tissue adhesion to the film, finding that baking the tissue sections onto the film yields the best result. Challenges during staining have been observed with xylene and other solutions that have affected tissue adhesion. Additionally, the optical characteristics of the film are sufficient for viewing utilizing light microscopy.

**Discussion:** Microtomy issues such as bubbles between the support medium and tissue section have proven to have a more significant impact on adherence with film when compared to traditional glass slides. Ensuring that the tissue section lays flat with no bubbles is essential to achieving a good end product. Staining each tissue section individually allowed for the easiest way to monitor tissue adherence between reagents to see where issues arise. This novel innovation proves to be possible but still requires additionally testing prior to initiating phase three.

**Research theme 1:** Digital Pathology
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Yang, Ha Ryun

**Additional Author(s):** Nichols M, Hsia C, Chin-Yee B, Bhayana V, Chin-Yee I

**Abstract Title:** Anemia associated with Decreased Plasma Zinc Levels is Likely Secondary to Acute Inflammation

**Abstract:**
**Introduction:** Zinc (Zn) is an important trace metal for normal hematopoiesis, and deficiencies in Zn can result in anemia. Many conditions can disrupt the balance of metals in the body, such as impaired absorption in the gut. Plasma Zn levels are also negative acute phase reactants decreasing with systemic inflammation. In this study, we aimed to determine the effects of Zn deficiency on hematopoiesis and define risk factors for Zn deficiency. We hypothesized that 1) plasma zinc deficiency would be associated with anemia and 2) that patients with low plasma Zn would have conditions affecting Zn absorption such as bowel disease, be on medications such as protein pump inhibitors (PPI), or alternatively show signs of systemic inflammation.

**Methods:** We performed a retrospective cohort study on 606 adult patients (age > 18 years), 303 each from zinc deficient ($c < 9.4$ umol/L) and normal plasma Zn groups, who had levels measured at London Health Sciences Centre (LHSC) between 2017 and 2021. We recorded plasma zinc, hemoglobin, malabsorptive pathologies including celiac disease, Crohn's disease, pancreatic insufficiency, short gut, and gastric bypass, usage of PPIs, serum albumin, serum c-reactive protein (CRP), and serum ferritin for all patients. Differences in mean hemoglobin levels (single-sided t-tests) and mean measurements of risk factors between zinc deficient and zinc normal patients (double-sided t-tests) were compared. We also examined the relationship between Zn plasma concentration across risk factors and compared trace metal levels and hematologic parameters.

**Results:** Our results showed that a deficiency in plasma Zn is associated with significantly lower hemoglobin concentration in blood ($p < 0.001$), lower levels of albumin ($p < 0.001$) and higher CRP ($p < 0.001$). No significant relationships were identified with malabsorption or proton pump inhibitors ($p > 0.05$).

**Discussion:** Decreased plasma Zn is commonly associated with other markers of systemic inflammation such as low albumin and high CRP in keeping with Zn as a known negative acute phase reactant. Although patients with low plasma Zn had significantly lower hemoglobin, the lack of correlation between plasma Zn levels and degree of anemia suggest that Zn deficiency was not causing the anemia, but rather reflected a common factor, systemic inflammation. In evaluating patients with anemia, plasma Zn should be interpreted cautiously in patients with signs of active inflammation.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** Infection, Immunity, and Inflammation
**Research theme 3:**

**Presenter's Name:** Yu, Manus

**Additional Author(s):** MohdWessam AJ, French A, Cameron L

**Abstract Title:** IL-21 and TGFβ Influence Glucocorticoid Insensitivity in Th2-Th17 double-positive cells.

**Abstract:**
**Introduction:** Glucocorticoids are used to treat inflammatory conditions seen in asthma, but Th17 cells have been shown to be less responsive than Th2 cells. Previously, we found that the addition of IL21 and TGFβ can differentiate Th2 into Th2-Th17 double-positive cells, and we believed that Th17 differentiating cytokines may be influencing glucocorticoid resistance. The degree to which IL21, TGFβ, and even IL1β influences glucocorticoid response and whether this relates to induction of glucocorticoid response genes (TXNIP, FKBP5) is unknown; thus, we sought to investigate it through this study.

**Methods:** To test this hypothesis, we cultured human blood Th2 cells in the presence of both Th17 differentiating cytokines (IL21, TGFβ) and glucocorticoids. Chronic steroid response was simulated by adding hydrocortisone over 2 weeks, and acute steroid response was simulated by adding dexamethasone over 24 hours. Induction of glucocorticoid response genes (TXNIP, FKBP5) was measured using quantitative RT-PCR. Effects of individual Th17 differentiating cytokines (IL21, TGFβ) were tested against addition of IL1β.

**Results:** Th2 cells grown with IL21 and TGFβ showed less responsiveness to glucocorticoid. These Th17 differentiated cells had significantly decreased levels of TXNIP, a glucocorticoid response gene involved in glucocorticoid-induced apoptosis, in response to chronic hydrocortisone treatment compared to Th2 cells. Induction of FKBP5 in response to chronic hydrocortisone treatment was not significantly reduced in Th17 differentiated cells compared to Th2 cells; however, FKBP5 levels were reduced by 30% in Th17 differentiated cells in response to acute dexamethasone treatment compared to Th2 cells. Additional IL1β did not have significant effects or influence notable trends to the FKBP5 gene expression.

**Discussion:** These results show that insensitivity to glucocorticoids in Th17 differentiated cells is in part due to a decreased induction of glucocorticoid response genes regulated by the glucocorticoid receptor. Both acute and chronic steroid responses decreased with addition of IL21 and TGFβ, indicating that these cytokines lead to T cell resistance against both single-dose treatments for asthma exacerbations and longer-term exposure from chronic stress. Addition of IL21 and TGFβ alone were also shown to be sufficient for differentiating Th2 cells and reducing their responsiveness to glucocorticoid treatment.

**Research theme 1:** Infection, Immunity, and Inflammation
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Zahid, Danish

**Additional Author(s):** Poon AFY

**Abstract Title:** Assessing the Robustness of Episignature-Based Disease Prediction Methodology to Random Variation: A Feasibility Study on Artificially Forging an Episignature in the Absence of Disease

**Abstract:**
Recent studies have developed computational methods to identify sets of DNA methylation probes (episignatures) capable of predicting patient disease status. The prior successful implementation of episignature-based disease prediction methods highlight the potential of episignatures to serve as diagnostic markers. However, the robustness of existing methodology to random variation (i.e., the false positive rate of prediction) remains largely unexplored. Our study assessed the current methodology's susceptibility to random variation by examining the feasibility of artificially forging an episignature in the absence of a disease. In this study, we used Illumina 450K DNA methylation data from 101 healthy control individuals. Samples were then artificially labeled at random as either cases (50%) or controls (50%). Following published workflows, initial quality control steps were performed and an episignature was identified through a series of linear regression, receiver operating characteristic (ROC) curve analysis, and the removal of highly correlated probes. We used the identified episignature to train a linear support vector machine (SVM) classifier. Prior to analysis, the data was divided into four equal parts, three of which were used for probe selection and SVM training, and the fourth was set aside for testing the SVM's performance. This procedure was repeated four times, with each part being used only once to test the SVM (i.e., four-fold cross validation). Additionally, two-fold cross-validation was used to tune the SVM cost parameter. Preliminary results indicate that SVM classifiers trained on artificially forged episignatures achieved an accuracy comparable to the expected accuracy of random classification. These findings suggest that the current methodology is unlikely to generate false positive predictions due to random variation in the data. We are currently modifying individual steps in the workflow to assess their impact on the overall sensitivity of the methodology. Our research identifies critical steps and best practices for episignature-based disease prediction. However, we suggest that further research with larger and more diverse datasets be conducted to more conclusively explore the existing methodology's sensitivity to random variation.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:** Epigenetics
**Research theme 3:**

**Presenter's Name:** Zemingui, Angela

**Additional Author(s):** Kiser P

**Abstract Title:** Characterizing the Impacts of Lifelong Western Diet Exposure on Maternal and Fetal Renal Tissues

**Abstract:**
**Introduction:** Poor metabolic health is on the rise due to overconsumption of the Western diet, that is, a diet high in carbohydrates and fats but low in plant-based fibres like fruits and vegetables. Consumption of this diet has been thought to contribute to poor glycemic control in pregnant women and adverse metabolic health. Importantly, offspring born to these women are predisposed to developing metabolic diseases, such as type 2 diabetes, later in life. While these effects can in part be explained by genetic and epigenetic changes, increasing evidence suggests that adverse in utero development is also responsible. There is a great need to thoroughly analyze the impacts of maternal overconsumption, especially, on the organs involved in our metabolism such as the kidneys given that their development is especially susceptible to suboptimal maternal nutrition. As such, we will be attempting to characterize the renal abnormalities associated with lifelong Western diet consumption separate from weight gain, to help elucidate its impact on metabolic health.

**Methods:** Female Dunkin Hartley guinea pigs were bred in the laboratory and weaned at 15 days of age, they were subsequently randomized into a control or experimental group. Guinea pigs in the experimental group were fed a diet mimicking Western diet consumption, whereas Guinea Pigs in the control group were fed a diet mimicking a balanced diet. Ultrasounds were performed to confirm both pregnancy and the litter size. The animals were eventually sacrificed, and the renal tissues of both the mothers and offspring were collected. These tissues were fixed, sectioned, and stained for histomorphologic characterization and semi-quantitative analysis. Finally, a TUNEL assay was performed to evaluate the magnitude of apoptotic events in the paraffin-embedded tissue sections.

**Results:** We expect that a lifelong Western diet will result in several histomorphologic abnormalities, of which include, fibrosis, inflammation, and oxidative stress. Moreover, we expect structural abnormalities in the kidneys such as glomerulopathy and vacuolization.

**Discussion:** This study will contribute novel data to the small but expanding literature characterizing the effects of a lifelong Western fed Diet, and therefore advance our understanding of the metabolic impact of maternal overnutrition during pregnancy.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** Infection, Immunity, and Inflammation
**Research theme 3:**

# Poster Presentations
# Session B
# 3:00 pm - 4:30 pm



| # | First Name | Last Name | Title |
|---|---|---|---|
| 1 | Rober | Abdo | The Spatial Transcriptomic Landscape of Breast Cancer Brain Metastasis |
| 2 | MohdWessam | Al Jawhri | The effects of Glucocorticoids on Th2 cell phenotype and function |
| 3 | Nelson | Chang | Lysosomal networks regulate glucagon trafficking and secretion in pancreatic alpha cells |
| 4 | Samantha | Collings | The role of DLC1β in attenuating cardiac ischemia-reperfusion injury during heart transplantation |
| 5 | Natalia | Dabrowski | Differential Expression of Myeloid and Lymphoid Lineage-Associated Genes in the Adipocytic Bone Marrows of Ageing Mice |
| 6 | Salma | Dammak | H&E features that predict TMB in lung squamous cell carcinoma |
| 7 | Angela | Dan | Understanding the KIM-1 shedding function in renal cell carcinoma |
| 8 | Allie | Dawson | MACROD2 Inhibition Leads to Treatment Resistance in Human Papillomavirus-Related Head and Neck Cancer |
| 9 | Dominic | Ghantous | Single-trial analysis of express visuomotor responses in Parkinson's Disease |

| # | First Name | Last Name | Title |
|---|---|---|---|
| 10 | Sadegheh | Haghshenas | Heterozygous POGZ variants are associated with a DNA methylation episignature |
| 11 | Lu | Haitao | Cell-free DNAs induce panoptosis through activating Z-DNA binding protein 1 (ZBP1) and may cause heart allograft rejection |
| 12 | Francine | He | One Health Approach on the Pharmacotherapy of Carcinoid Heart Disease in Neuroendocrine Tumours |
| 13 | Megan | Hong | Fc-dependent depletion of Tregs promotes anti-CTLA-4 activity against neuroblastoma tumours with induced DNA mismatch repair deficiency |
| 14 | Jacob A | Houpt | Intraneural Perineurioma of the Sciatic Nerve: A Report on Two Cases |
| 15 | Mackenzie | Hsu | Cellular and molecular mechanisms underlying ageing-related stem cell deficits in the bone marrow |
| 16 | Zi Huai | Huang | cGAN – Driven Radiomic Prediction of Mutation Status Based on MR Images of Breast Cancer |
| 17 | Lucy | Hui | Impact of data access models on the detection of emerging SARS-CoV-2 variants of concern |





| # | First Name | Last Name | Title |
|---|---|---|---|
| 18 | Sugitha | Janarthanan | Action Categorization in the Mind Across Vision and Language |
| 19 | Jessica | Jeong | Assessing the Presence of Bacterial Cas9 in MLH1-knockout Neuroblastoma Cells |
| 20 | Helen | Ji | Struma Ovarii: A rare teratoma of the ovary |
| 21 | Karim | Karimi | Identification of DNA methylation episignature for the autosomal dominant mental retardation 21 syndrome caused by mutations in the CTCF gene |
| 22 | Daniel | Kawa | Assessing in Vivo Off-Target Binding of a Novel Oral Antibody Vaccine Developed to Prevent Colonization of Enteric Pathogen E. Coli O157:H7 |
| 23 | Joon | Kim | EZH2 inhibition stimulates viral mimicry causing immune destruction of splenic B cells |
| 24 | Jakub | Kuczek | Investigating Nuclear Morphometry in Diffuse Astrocytic Gliomas |
| 25 | Xinru | Li | Evaluation of S100A7 as a Biomarker of Malignant Transformation from Oral Epithelial Lesions, and Relation to Oral Cancer in Dogs |

| # | First Name | Last Name | Title |
|---|---|---|---|
| 26 | Yueyang | Li | Sonification of Pathology: From Slides to Sound |
| 27 | August | Lin | Clinical Significance of Granular Mitoses in Glioblastoma |
| 28 | Chin-Jung | Lin | Nicotinamide Mononucleotide prevents neutrophil aging and reduces bacterial burden in sepsis |
| 29 | Haley | McConkey | Clinical Epigenomic Testing in Canada: Discovery and Clinical Assessment of Episignatures |
| 30 | William | McCullagh | Immunological Impact of Carbon Monoxide Releasing Molecules on In-Vitro Renal Ischemia Reperfusion Injury |
| 31 | Melissa | Menard | A Case of Unsuspected Peritoneal Mesothelioma Presenting as Rectal Polyp |
| 32 | Amanda | Morin | The effect of in vitro models of mitochondrial DNA variation on the nuclear epigenome and transcriptome |
| 33 | Anushga | Muralitharan | Polycystic Liver Disease: A Case Study |
| 34 | Julia | Nguyen | Association between mitochondrial DNA haplogroups and nuclear DNA methylation in cardiovascular disease and aging |





| # | First Name | Last Name | Title |
|---|---|---|---|
| 35 | Lindsay | Ninivirta | Maximizing Diagnostic Yield in Biliary Brush Cytology: Implementation of a Quality Improvement Project |
| 36 | Timothy | Nunes | Lifelong maternal Western Diet impairs placental and fetal development in a non-obese guinea pig (Cavia porcellus) model |
| 37 | Nachuan (Harrison) | Pan | The role of miR-9 in diabetic cardiomyopathy |
| 38 | Samina | Panjwani | Exploring the neurocircuitry mechanisms underlying stimulus-response learning in mice, and its relevance to Parkinson's disease |
| 39 | Daniel | Passos | Disrupting the DREAM transcriptional repressor complex induces apolipoprotein overexpression and systemic amyloidosis in mice |
| 40 | Kendra | Prasad | Characterizing Human Papillomavirus Associated Oral Epithelial Dysplasia: An Evaluation of Biomarkers |
| 41 | Neha | Raina | Identifying non-HLA antibodies and their role in kidney transplantation outcomes |

| # | First Name | Last Name | Title |
|---|---|---|---|
| 42 | Jordan | Ramnarine | Who Speaks for the River?: An Indigenous Feminist Approach to the One Health Impacts of Climate Colonialism on Two-Spirit Peoples in Deshkan Ziibi |
| 43 | Cassandra | Rastin | Utility of NGS Testing in Epilepsy Patients: A Two-Year Review of the LHSC Experience |
| 44 | Liam | Ratushny | Investigation of molecular mechanisms of the cancer cell cycle and their impact on treatment resistance and disease progression |
| 45 | Sevanthi | Ravichandran | Efficacy of repositioned drugs in the management of renal ischemia reperfusion injury using sIRI-cold and sIRI-RT in vitro models |
| 46 | Julie | Richmond | Malignant mesothelioma of the omentum: a case report |
| 47 | Kathleen | Rooney | DNA methylation episignature and comparative epigenomic profiling of HNRNPU-related neurodevelopmental disorder |
| 48 | Sarah | Ryan | Two Steps Forward: A New Generation of Targeted Therapy in Anaplastic Thyroid Cancer |





| # | First Name | Last Name | Title |
|---|---|---|---|
| 49 | Nader | Shaker | Expression of S100A7 in verrucous hyperplasia |
| 50 | Gracie | Sun | Evaluation of the gaps in the continuum of stroke care in southwestern Ontario across the three pillars of clinical care, advocacy, and research – A qualitative needs-assessment study |
| 51 | Danielle | Taray-Matheson | The role of TEX-derived circHUWE1 in prostate cancer migration and metastasis |
| 52 | Erik | Trautrim | The value of genetic panels in a case of pediatric Spitzoid melanoma |
| 53 | Carolyn | Twible | Characterizing the hippocampal dentate gyrus involvement in temporal lobe epilepsy |
| 54 | Andrew | Wang | Assessment of Pathology Domain Specific Knowledge of ChatGPT and Comparison to Human Performance |
| 55 | Tan Ze | Wang | Role of circular RNA ASPH in macrophage polarization and response in sepsis |
| 56 | Komila | Zakirova | Identification of molecular mechanisms of spheroid dormancy in epithelial ovarian cancer |
| 57 | Peter | Zeng | The clinical, transcriptomic, and cellular architecture of idiopathic subglottic stenosis |

**Presenter's Name:** Abdo, Rober

**Additional Author(s):** Li SS, Zhang Q

**Abstract Title:** The Spatial Transcriptomic Landscape of Breast Cancer Brain Metastasis

**Abstract:**
**Background:** Brain metastases (BM) are responsible for majority of the cancer mortality. Despite the advances in systemic therapies, BM is notoriously refractory to treatment. Breast cancer is one of the most common primary sites for brain metastasis. Metastatic cancer cells are known to diverge genetically and phenotypically from their primary counterpart. Together with the unique tumor brain microenvironment (TBME), this poses additional challenges in treatment of BM. Here, we aim to decipher the mechanisms of cancer cell evolution and brain tumor microenvironment remodeling.

**Methods:** We identified 30 cases of patient-paired, surgically resected brain metastasis with breast origin. Ten cases of non-tumoral brain control were also included. Two tissue microarray (TMA) blocks were constructed to include all cases. NanoString GeoMX Digital Spatial Profiling (DSP) using whole-transcriptome atlas (WTA) were performed to determine the expression of 18,694 genes. PanCK, CD45 and GFAP were used as morphology markers to visualize and annotate the regions of interest (ROIs). For each patient, five ROIs were analyzed: primary breast cancer (BC), primary breast cancer microenvironment (BCME), metastatic tumor cells (MTC), immediate TBME (iTBME), and distant TBME (dTBME).

**Results:** 1) Gene expression profiles of BC replicated the clinical biomarker status of most of the cases. Triple negative breast cancers (TNBC) demonstrated distinct gene signature, in both primary and metastatic sites. 2) When PAM50 gene signature was analyzed, there were 9 BC shifted genetic profile and were reclassified into different molecular subtypes at their matched brain metastatic site. Functional enrichment analysis revealed enriched EMT, ECM-receptor interaction, and complement system in these profile shifting-BC cases. In contrast, the BC cases that preserved their original profiles (non-shifting BC) shared upregulated pathways of ribosome biogenesis, cell cycle, and neutrophil extracellular traps (NETs). 3) TBME underwent cellular and molecular plasticity characterized by elevated neutrophils, reactive astrocytes, and activated microglia. In the TBME homing TNBC, cancer-associated fibroblasts (CAF) represented a hub in the cellular interaction between MTCs and TBME.

**Conclusion:** This study provides transcriptomic evidences of breast cancer plasticity during brain metastasis. The brain microenvironment underwent significant remodeling to host metastatic breast cancer cells.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:** Cancer Biology
**Research theme 3:** Pathobiology of Neurologic Diseases





**Presenter's Name:** Al Jawhri, MohdWessam

**Additional Author(s):** French A, Cameron L

**Abstract Title:** The effects of Glucocorticoids on Th2 cell phenotype and function

**Abstract:**
**Introduction:** Asthma is a global health problem affecting millions of people and placing a significant burden on healthcare systems. The T helper 2 (Th2) cell subset plays a crucial role in Type 2 high asthma, with their function regulated by type 2 cytokines. Glucocorticoids (GCs) are the primary treatment for Type 2 high asthma, but the impact of their long-term use on Th2 cells is unclear. Severe asthmatics who receive high-dose GC treatment still experience persistent symptoms, which are thought to be associated with an increased presence of Th2-Th17 dual-positive cells. Our preliminary data examining Th2 cells showed that exposure to GC increased the expression of several Th17-related genes. We hypothesized that chronic GC treatment enhances Th2 transition to Th2-Th17 cells when exposed to Th17 differentiating cytokines.

**Methods:** Primary human Th2 cells were generated from donor peripheral blood mononuclear cells (PBMCs). Th2 cells were treated with IL-21 and TGFB1 with/without GC every 2 days (0.5 μM hydrocortisone) to assess Th2-Th17 differentiation. We examined expression changes and differentiation status by assessing Th2 (CRTh2 and IL-13) and Th17 (CCR6, IL-21R, IL-1R, RORc, and IL-17A) markers using qRT-PCR, flow cytometry, and ELISA.

**Results:** Our differentiation experiments revealed that Th2 cells transition to IL17A-producing Th2-Th17 cells when cultured with IL-21 and TGFb1, with a 2-fold increase in IL13+IL17+ cells. These conditions also induced IL-21R, CCR6, and IL-1R1 expression, while decreasing CRTh2 and IL-13 expression. Th2-Th17 cells were more viable in chronic GC than Th2 cells and had higher IL1R levels (3.5-fold), indicating they may be less susceptible to GC-induced apoptosis.

**Discussion:** These findings provide insights into the mechanisms driving Th2-Th17 cell development in vitro, and the results may be useful for studying these pathways in vivo in Type 2 high severe asthma. If long-term GC exposure enhances responsiveness to Th17 factors, leading to increased Th2-Th17 cell development and pathogenicity, this could provide new therapeutic strategies for severe asthma and potentially a cure.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** Infection, Immunity, and Inflammation
**Research theme 3:**

**Presenter's Name:** Chang, Nelson

**Additional Author(s):** Dhanvantari S

**Abstract Title:** Lysosomal networks regulate glucagon trafficking and secretion in pancreatic alpha cells

**Abstract:**
**Introduction:** There is a rising consensus that the etiology of diabetes mellitus involves both insulin deficiency and hyperglucagonemia contributing to hyperglycemia. Our lab investigates the cellular mechanisms of glucagon secretion, with a focus on intracellular trafficking pathways to reveal clues about glucagon's role in hyperglycemia. Our previous work found a neuronal protein, Stathmin2(Stmn2) in the secretory granules of alpha cells when glucagon secretion was inhibited. We showed that overexpression of Stmn2 co-localized with glucagon to the degradative lysosome, suggesting that Stmn2 may regulate glucagon secretion through lysosomal trafficking. In the present study, I hypothesize that Stmn2 regulates glucagon secretion by up-regulating degradative lysosomal biogenesis and trafficking while reduced Stmn2 mimics diabetes by re-routing glucagon to secretory lysosomes, resulting in excess secretion.

**Methods:** AlphaTC1-6 cells will be treated with glucagon secretion stimulators and paracrine factors to test the physiological regulations of Stmn2. The co-localization of Stmn2, glucagon and other lysosomal, and exocytosis marks will be analyzed by confocal microscopy. The nuclear translocation of the transcription factors involved in lysosomal biogenesis will also be assessed to determine the level Stmn2 functions at. Cells will be treated to mimic diabetic states, and the exposure of the luminal epitope 1DB4 will be used as an indicator for secretory lysosomal secretion. Glucagon secretion and co-localization with the secretory lysosomal marker LAMP1 will be assessed.

**Results:** Our preliminary results show that these alpha cells are responsive to potassium-stimulated glucagon secretion. On the other hand, secretion experiments with known paracrine factors such as insulin and GABA surprisingly do not inhibit glucagon secretion alone, perhaps because they are co-secreted physiologically. Our results also show that the immunostaining pattern overlaps between glucagon and Stmn2 as they were hypothesized to co-localize. More markers will be co-stained to visualize trafficking under various conditions.

**Discussion:** These preliminary findings show that there is an interaction between Stmn2 and glucagon physiologically. This will set the baseline for further experiments to test their interaction in the diabetic conditions. In addition, these results will validate the significance of more paracrine interactions and the role of glucagon in hyperglycemia.

**Research theme 1:** Digital Pathology
**Research theme 2:** Pathobiology of Neurologic Diseases
**Research theme 3:**



**Presenter's Name:** Collings, Samantha

**Additional Author(s):** Min WP, Zheng X, Liu Q, Li SC, Joshi R, Diao H, Taray-Matheson D, Won S

**Abstract Title:** The role of DLC1β in attenuating cardiac ischemia-reperfusion injury during heart transplantation

**Abstract:**
**Introduction:** Heart failure (HF) is a disease consequence of multiple etiologies. Ultimately, the only curative means for HF is heart transplantation (HTx). However, HTx efficacy is impacted by intra-operative ischemia-reperfusion injury (IRI). Cardiac IRI grafts display histopathological changes such as apoptosis, inflammatory cell infiltrate, and infarction. Currently, the pathomechnism of cardiac IRI remains elusive but previous research has implicated the PI3K/Akt and RhoA/ROCK pathways. Therefore, deleted-in-liver-cancer 1 protein's beta-isoform (DLC1β) may be associated with cardiac IRI due to its regulation of RhoA/Akt1. It is hypothesized that DLC1β overexpression (OE) attenuates cardiac IRI by abrogating apoptotic injury via the PI3K/Akt & RhoA/ROCK pathways.

**Methods:** The study aims 1) to investigate DLC1β's role in cardiac IRI, 2) to analyze if DLC1βis a novel cardioprotective target and 3) to explore pathways involved in IRI pathogenesis. The in-vitro design used H9C2 (rat) and HL-1 (mouse) cardiac cell lines. Cells were transfected (3 groups: blank, control (pc3 plasmid) or DLC1β OE plasmid) and placed in a hypoxia-oxygenation reperfusion chamber (H/OR). IRI/no IRI cells were then compared via Western blot (WB)/qPCR/flow cytometry. In-vivo, mouse heterotopic HTx's were performed on C57/BL6 male mice. The HTx groups included wild-type (blank) mice/control mice (pc3 tail-vein (TV) injection)/DLC1β OE TV injection mice. 24hrs post-TV, donors were sac'd for HTx and grafts were stored for 24hrs at 4°C in UW solution. Recipient mice were sac'd 24hrs/7days post-HTx and grafts were analyzed via histopathology/qPCR/WB.

**Results:** In-vivo, significant differences in injury score at 24hr/7days were seen when comparing DLC1β mice versus control mice. In-vitro, there was a reduction in early/late apoptosis and cell death in DLC1β OE groups compared to controls via Annexin V flow cytometry/incucyte. Additionally, DLC1β groups display upregulated anti-apoptotic targets (BCl2, Akt1, etc.) and downregulated pro-apoptotic targets (Bax, Casp3, etc.) compared to control groups via qPCR (in-vivo and in-vitro). Further western blot analyses of pathway targets are currently ongoing.

**Discussion:** The current histopathology data is supportive of DLC1β's role as a potential cardioprotective target. This may have further translational/clinical applications in the future; however, reducing intra-sample variability and exploring the pathomechnism is still of interest.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** Regenerative and Transplantation Medicine
**Research theme 3:**

**Presenter's Name:** Dabrowski, Natalia

**Additional Author(s):** Khan ZA

**Abstract Title:** Differential Expression of Myeloid and Lymphoid Lineage-Associated Genes in the Adipocytic Bone Marrows of Ageing Mice

**Abstract:**
**Introduction:** The bone marrow (BM) is a rich source of stem cells. There are, at least, two different stem cell populations in the BM: hematopoietic stem cells and non-hematopoietic multipotent cells. Hematopoietic stem cells (HSCs) are capable of self-renewal and of giving rise to myeloid and lymphoid cell precursors. With age, HSCs increase in number; meanwhile their potential for self-renewal decreases and their differentiation potential skews towards the myeloid lineage. Histologically, BM ageing is characterized by an increase in adiposity and a decrease in hematopoietic area. Clinically, it is associated with the development of autoimmune disorders and myeloid leukemias, and a decrease in adaptive immunity efficiency. Evidence suggests there may be a link between increased adipogenesis in the BM and HSC-ageing. Thus, I will determine whether hematopoietic stem cell bias towards the myeloid lineage is secondary to BM adiposity, possibly indicating causality.

**Methods:** To achieve my goal, I obtained femur tissues from C57BL/6N mice of various ages. One set of tissues was fixed in formalin and embedded in paraffin. The other set was used to create BM flush samples. I used the BM flush to isolate RNA and measure transcript levels of genes associated with the myeloid and lymphoid lineages and with adipogenesis. For the fixed tissues, I will stain with hematoxylin and eosin and perform histomorphometry. In addition, tissue slices will be used to localize myeloid and lymphoid antigens.

**Results:** My analysis of BM flush from 67–71-week-old mice showed increased levels of lymphoid-associated gene transcripts, along with increased levels of Igf1 and Cxcl12 transcripts. No change was observed in myeloid-associated transcript levels, while an increase in Igf2 transcript levels was observed in male but not female middle-aged mice. In terms of adipogenesis-associated transcripts, I expect there to be increased levels in middle-aged mice. Lastly, I expect morphometric analysis to show an increase in lymphoid antigens in 67–71-week-old mice.

**Discussion:** These findings may indicate that expansion of the HSC and common lymphoid progenitor compartments occurs in middle age. The significance of differential Igf2 transcript levels between male and female mice is unknown, but an exciting avenue to pursue. My study will generate novel insight into the association of BM adiposity and HSC aging, and thus may identify potential targets for anti-myeloid-skewing treatments.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** Infection, Immunity, and Inflammation
**Research theme 3:**





**Presenter's Name:** Dammak, Salma

**Additional Author(s):** Cecchini M, Ward AD

**Abstract Title:** H&E features that predict TMB in lung squamous cell carcinoma

**Abstract:**
**Introduction:** The PD-L1 score is used to guide treatment decisions, but it does not accurately predict response to immunotherapy in all cases. While adding tumor mutational burden (TMB) to PD-L1 improves response prediction, it is costly and typically requires high tumor cellularity. In our previous work, we demonstrated that a neural network could be trained to distinguish the TMB-high and TMB-low cancers based solely on digitized standard-of-care H&E slides1. However, it was not clear what features it used to visually distinguish them. In this study, we hypothesized that occluding and highlighting certain aspects of the tissue would allow us to better understand the underlying relationship between TMB and cancer morphology.

**Methods:** We utilized digital slides of tumour resections from the Cancer Genome Atlas lung squamous cell carcinoma. The dataset had 70 patients across 35 centers which we split into 50 training and 20 testing slides. We calculated the TMB with a 10 mutations/Mb threshold utilized to separate TMB-high and low cases. First, we trained and tested the model on the raw images to establish a performance baseline. We then modified the images of the entire dataset then retrained the model and retested it with these modified-image sets. These were: a nucleus mask dataset (the nuclei pixels are replaced with white pixels and everything else is blacked out), a nucleus content dataset (nuclei appear normally but everything else is blacked out), and a cytoplasm dataset (nuclei are blacked out but everything else appears normally).

**Results:** On the raw-image test set, the model had an area under the receiver operating characteristic curve (AUC) of 0.87. On the nucleus-mask test set, its AUC was 0.75, which dropped to 0.70 on the nucleus-content test set and increased to 0.80 on the cytoplasm test set.

**Discussion:** This study suggests that complex genetic features of a tumor are encoded in the morphologic appearance on H&E slides across multiple centers and uncovers the features driving that relationship. It shows that nucleus shape, size and/or location are highly important features for this relationship, as is the appearance of the cytoplasm, and it shows that intra-nuclear appearance is misleading. This motivates additional work to further understand this relationship and leverage it to build a system that can be used to help physicians decide which patients would benefit from immunotherapy.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:** Digital Pathology
**Research theme 3:**

**Presenter's Name:** Dan, Angela

**Additional Author(s):** Ding M, Gunaratnam L

**Abstract Title:** Understanding the KIM-1 shedding function in renal cell carcinoma

**Abstract:**
**Introduction:** Renal cell carcinoma (RCC) arises from renal proximal tubule epithelial cells (PTECs). Kidney Injury Molecule-1 (KIM-1) is a transmembrane receptor that is upregulated in PTECs during injury and dedifferentiation events, such as the development of RCC, but is not detectable in the healthy kidney. Upon binding to phosphatidylserine, an "eat me" signal on apoptotic cell surfaces, KIM-1 facilitates apoptotic cell phagocytosis by PTECs. The ectodomain of KIM-1 is shed constitutively and through phorbol ester (PMA) induction via membrane-proximal cleavage by metalloproteases to release soluble KIM-1 into the urine and blood. Shed KIM-1 in the urine is a biomarker for acute kidney injury and RCC, but the pathophysiological function of KIM-1 shedding is not well understood. The aim of this study is to develop a shedding-defective mouse KIM-1 (mKIM-1) mutation and determine the relevance of shedding for RCC phagocytosis and invasion. Our lab has previously identified a potential cleavage site at I202 and generated a mutant mKIM-1 construct with a three amino acid deletion at the site (amino acids 201-203) using site-directed mutagenesis. We hypothesize that the fj201-203 mutated mKIM-1 protein will decrease shedding of KIM-1 in mouse RCC PTECs and decrease invasion and phagocytosis.

**Methods:** We transfected and generated stable murine RCC Renca cells expressing wild-type (KIM-1-Renca) and fj201-203-mutant KIM-1 (fj201-203-Renca) and determined shedding function through Western blotting of conditioned media with and without PMA-induced shedding. The role of shed KIM-1 in migration and invasion will be determined using Transwell migration and invasion assays and imaging with light microscopy. To determine phagocytic ability, we will incubate KIM-1-Renca and fj201-203-Renca cells with pHrodo Red-labeled apoptotic thymocytes, and phagocytosed cells will be quantified using flow cytometry.

**Results:** The fj201-203-Renca cells exhibited decreased ectodomain shedding of KIM-1, and we expect the cells to have inhibited invasive and phagocytic ability.

**Discussion:** The mutant mKIM-1 gene with defective shedding function generated in this study will elucidate the role of KIM-1 shedding for phagocytosis and invasion by RCC PTECs. This allows for the further study of the pathophysiological function of KIM-1 shedding and the production of an in vivo mouse model with dysfunctional KIM-1 ectodomain shedding.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Dawson, Allie

**Additional Author(s):** Shaikh M, Zeng P, Barrett J, Nichols AN

**Abstract Title:** MACROD2 Inhibition Leads to Treatment Resistance in Human Papillomavirus-Related Head and Neck Cancer

**Abstract:**
**Introduction:** Head and neck squamous cell carcinoma (HNSCC) is the 6th most common cancer worldwide. Recently, infection by human papillomavirus (HPV) has caused a rapid rise in HNSCC cases. Although patients with HPV+ HNSCC generally respond well to chemoradiation treatment, a cohort of patients exhibit treatment resistance leaving them more susceptible to tumour recurrence and metastasis. At present, no known molecular drivers to treatment resistance in HPV+ HNSCC have been identified. We have completed a genomic and transcriptomic characterization of a local HPV+ HNSCC patient cohort. We observed that copy number losses of MACROD2 have been identified in the treatment failure dataset. Thus, we hypothesize that inhibition of MACROD2 drives resistance to chemoradiation in HPV+ HNSCC.

**Methods:** Functional validation studies in vitro have been completed to assess MACROD2 as a candidate gene for treatment resistance in HPV+ HNSCC. Inhibition of MACROD2 expression was tested by both small interfering RNA (siRNA) and short hairpin RNA (shRNA) in multiple HPV+ HNSCC cell lines. Functional assays were then performed to assess proliferation, clonogenic ability, invasion/migration, cisplatin-sensitivity, and radiation-sensitivity between scramble control and knockdown models. Exploration of the mechanistic role of MACROD2 in tumour evolution and chemoradiation resistance are currently underway to compare control and knockdown models by RNA sequencing and reverse-phase protein array (RPPA).

**Results:** Preliminary siRNA screens suggested that MACROD2 significantly drives cell proliferation, clonogenic potential, migration, and chemoradiation resistance in several HPV+ HNSCC cell lines. Stable knockdown of MACROD2 expression using targeted shRNA have shown more complete knockdown and significantly increased cell proliferation, colony forming potential, and chemoradiation resistance in multiple HPV+ HNSCC.

**Discussion:** These findings provide a better understanding of the molecular basis of treatment resistance in HPV+ HNSCC. Our research has the potential to enhance treatment efficacy, direct future targeted therapy and may allow clinicians to use MACROD2 as a clinical stratification biomarker in treatment protocols for HPV+ HNSCC.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Ghantous, Dominic

**Additional Author(s):** Corneil BD

**Abstract Title:** Single-trial analysis of express visuomotor responses in Parkinson's Disease

**Abstract:**
**Introduction:** Parkinson's Disease (PD) is a progressive neurodegenerative disease presenting with bradykinesia, rigidity, tremor, and freezing of gait as a result of the degradation of dopaminergic neurons in the substantia nigra pars compacta. This leads to loss of control over volitional movements, however some reflexive movements have been shown to be conserved in PD and unaffected by dopamine replacement therapy. This study focuses on a reflex known as the express visuomotor response (EVR), the fastest stimulus-driven muscle activity observed in upper limb muscles, appearing as a small burst of activity ~100 ms after onset of a visual stimulus. Express responses are thought to be controlled by subcortical pathways through the superior colliculus while still being subject to modulation by cortical movement pathways. The goal of our study is to use novel analysis techniques to assess how EVRs are affected by the motor and cognitive symptoms of PD. We hypothesize that express visuomotor responses will be conserved in PD yet control over the reflex will be impaired.

**Methods:** We applied a novel single-trial analysis to electromyographic data previously collected from sixteen PD patients and eighteen healthy controls (HC), allowing for direct quantification of latency, variance, prevalence, and magnitude of express responses within a single subject. Comparisons were made between PD and HC participants as well as between different dopamine statuses. We will also assess cognitive control by analyzing how these metrics are affected based on the condition of the previous trial.

**Results:** As we predicted, our results show no significant differences in latency, variance, and prevalence of EVRs between PD patents and healthy controls as well as across dopamine conditions. Moving forward, we expect to observe differences between PD and HC subjects in the modulation of EVR prevalence and magnitude by the previous trial condition, demonstrating the impairment of cognitive control in PD.

**Discussion:** Our current results support the hypothesis that express responses are conserved in PD. Additionally, this study will further our understanding of the relationship between reflexive responses and PD and will potentially serve as a new biomarker for conserved motor pathways. This may act as the foundation for research into new treatments for Parkinson's disease.

**Research theme 1:** Pathobiology of Neurologic Diseases
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Haghshenas, Sadegheh

**Additional Author(s):** Shillington A, Levy MA, Relator R, Kerkhof J, McConkey H, Merla G, Simpson BN, Faivre L, Sadikovic B

**Abstract Title:** Heterozygous POGZ variants are associated with a DNA methylation episignature

**Abstract:**
The diagnosis of Mendelian neurodevelopmental disorders is associated with many challenges, due to factors including overlapping phenotypic characteristics and variants of uncertain significance. Recently, DNA methylation biomarkers, also known as episignatures, have become a powerful technique to assist physicians in providing a more definitive diagnosis to individuals with rare genetic disorders. White-Sutton syndrome (WHSUS) is a neurodevelopmental disorder inherited in an autosomal dominant manner, associated with loss of function variants in POGZ. This disorder has variable clinical features, often overlapping with other genetic syndromes. In this work, a robust episignature for WHSUS is identified and a highly sensitive and specific binary classifier is constructed. The methylation pattern of three individuals with POGZ VUSs were then assessed using the constructed model, demonstrating the ability of the episignature in classifying ambiguous cases. Moreover, the differentially methylated probes detected for WHSUS were compared to those of 56 other syndromes with known episignatures, potentially providing insight into the etiological pathways of WHSUS.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:** Epigenetics
**Research theme 3:**

**Presenter's Name:** Haitao, Lu

**Additional Author(s):** Zhang Z

**Abstract Title:** Cell-free DNAs induce panoptosis through activating Z-DNA binding protein 1 (ZBP1) and may cause heart allograft rejection

**Abstract:**
**Background:** Transplant rejection is associated with various forms of programmed cell death. Donor-derived cell-free DNAs (dd-cfDNAs) are novel biomarkers for monitoring allograft rejection, which was confirmed by endomyocardial biopsy to allograft samples. However, current reports have not illustrated the injuries induced by cfDNAs to heart transplantation rejection yet as cfDNAs were demonstrated to cause tissue injuries through various cell death pathways. Therefore, it is validating to study if cfDNA lead to various death programs and aggravate transplantation rejection.

**Methods:** We conduct cell death assays in human cardiovascular endothelial cells with the treatments of purified cfDNAs. Then we tried to determine whether cfDNAs promote cell death by activating various DNA/RNA sensors by qRT-PCR, gene silencing and Western Blotting. Next, we used protein-protein interaction technology, like coIP, to determine how cfDNAs-DNA/RNA sensors axis induces cell death. Continuously, we used Western blotting to measure key molecules for pyroptosis, apoptosis or necroptosis respectively to determine the occurrence of PANoptosis (a crosstalk among pyroptosis, apoptosis and necroptosis). Inflammation responses and in vivo experiments will be performed for wild-type controls and gene knockout group with heart allograft.

**Results:**We found markedly elevated levels in the number of cell death in endothelial cells treated with cfDNAs. With this treatment, PCR and blotting results showed Z-DNA binding protein 1 (ZBP1) has a significant increase. In addition, ZBP1 silencing reduced the number of cell death in cfDNAs-treated cells. Interestingly, coIP results showed ZBP1 interacts with Receptor-Interacting Protein Kinase 3 (RIPK3) and Adenosine deaminases acting on RNA 1(ADAR1). which are believed to be the essential complexes inducing cell death. Furthermore, we found that GSDMD (p30), caspase 7(p20), and pMLKL, key molecules of pyroptosis, apoptosis or necroptosis, showed a significant increase in cfDNA-treated cells. Surprisingly, their protein levels were reduced in ZBP1silencing cells treated with cfDNA. Interestingly, the protein level of ADAR1 was increased in ZBP1 silencing group.

**Conclusion:** cfDNAs induce cell death by activating ZBP1, then interacting with RIPK3 to initiate cell death in the form of PANoptosis. CfDNA-induced PANoptosis predicts histological injuries outcome and may mechanistically propagate dd-cfDNAs-induced heart allograft rejection.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** Regenerative and Transplantation Medicine
**Research theme 3:**





**Presenter's Name:** He, Francine

**Additional Author(s):** Frisbee SJ

**Abstract Title:** One Health Approach on the Pharmacotherapy of Carcinoid Heart Disease in Neuroendocrine Tumours

**Abstract:**
**Introduction:** Neuroendocrine tumours (NETs) are a complex group of neoplasms in neuroendocrine cells which may secrete excess hormones, neurotransmitters, and other neuroendocrine factors. While once considered rare, NETs are now recognized as the fastest growing cancers. NET patients commonly develop carcinoid heart disease (CHD), leading to poor quality of life and prognosis. Due to the rarity of this disease, diagnosis usually occurs in the late stages with 50% of NETs metastasized, when the only curative treatment, surgical intervention, is no longer an option. Currently, biotherapy with somatostatin analogues is the most efficient treatment to achieve palliation. As more novel therapies are being developed, it is important to address the gap in understanding the relationship of NETs, CHD, and pharmacotherapy.

**Methods:** A scoping literature review will be conducted to determine the current state of knowledge from primary studies about the pharmacotherapy for NET patients with CHD. Interconnectedness between human and animal treatment, social behavioral factors, including the role of diet, socioeconomic and environmental factors associated with NETs will be addressed. Relevant stakeholders beyond scientific research will be identified and analyzed, showing the need for an interdisciplinary approach.

**Results:** The expected result of the study is to find correlation and trends between different pharmacotherapies used. An ideal management schedule and plan for NET patients with CHD is expected. With the integration of the One Health approach, evidence gaps that currently exists between NETs, CHD, and pharmacotherapy will be addressed.

**Discussion:** Recognizing that pharmacotherapy of NETs and CHD is affected by animal-human-environment interactions, it is important for NETs and CHD to be assessed with a One Health approach to address all pillars of health. This project will lead to the development of early clinical management and interventions that will substantially improve patient outcomes and quality of life.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** One Health
**Research theme 3:**

**Presenter's Name:** Hong, Megan

**Additional Author(s):** Figueredo R, Maleki Vareki S

**Abstract Title:** Fc-dependent depletion of Tregs promotes anti-CTLA-4 activity against neuroblastoma tumours with induced DNA mismatch repair deficiency

**Abstract:**
**Introduction:** Expression of immune checkpoint molecules such as CTLA-4 on T-cells can suppress anti-tumour immune responses by inhibiting T-cell activation and function. Anti-CTLA-4 is an immune checkpoint inhibitor (ICI) that enhances patients' anti-tumour immune responses to eliminate cancer cells. ICIs have revolutionized the treatment of cancer in the last decade; however, their use is limited by their efficacy to only a small fraction of patients.

The DNA mismatch repair (MMR) pathway corrects mismatched base pairs that occur during DNA replication. Notably, patient response to ICIs is positively associated with those with MMR-deficient (dMMR) tumours in several solid cancers. However, studies have not addressed why dMMR tumours are more sensitive to ICIs than their pMMR counterparts. We have previously shown that inducing MMR deficiency in ICI-refractory and MMR-proficient (pMMR) neuroblastoma tumours rendered them sensitive to anti-CTLA-4 therapy. This study investigates the importance of anti-CTLA-4-mediated regulatory T-cell (Treg) depletion in its efficacy against induced dMMR (idMMR) neuroblastoma tumours.

**Methods:** MMR repair deficiency was induced in the murine neuro-2a cell line by knocking out MLH1 expression using CRISPR/Cas9. pMMR or idMMR tumours were grown in immunocompetent syngeneic mice and treated with anti-CTLA-4 once tumours were palpable. Tumour growth was measured followed by immunophenotyping of tumours and spleens by flow cytometry.

**Results:** Anti-CTLA-4 therapy increased CD3+ cells and decreased Tregs in idMMR neuroblastoma tumours but had no effect on pMMR tumours. idMMR tumours had an increase of macrophages compared to pMMR tumours and FcγRIV expression was increased on pro-inflammatory Ly6cHigh macrophages. Treatment with an anti-CTLA-4 clone that does not have an affinity towards FcγRIV did not deplete Tregs in idMMR tumours and failed to control tumour growth.

**Discussion:** These results suggest that the therapeutic effect of anti-CTLA-4 against idMMR tumours is mediated by Fc-dependent mechanisms that deplete Tregs. The increase of macrophages and FcγRIV expression may enhance anti-CTLA-4-mediated Treg depletion in idMMR tumours. These results further our understanding of the biology of pMMR and dMMR tumours and tumour immune microenvironment features that facilitate ICI sensitivity. Targeting the MMR pathway may be a therapeutic approach to improve ICI response in patients with ICI-refractory tumours.

**Research theme 1:** Cancer Biology
**Research theme 2:** Infection, Immunity, and Inflammation
**Research theme 3:**





**Presenter's Name:** Houpt, Jacob A.

**Additional Author(s):** Ang LC

**Abstract Title:** Intraneural Perineurioma of the Sciatic Nerve: A Report on Two Cases

**Abstract:**
Intraneural perineuriomas are solitary benign neoplasms of the perineurium accounting for approximately 1% of all peripheral nerve sheath tumours. Of these, only around 13% were found to occur in the sciatic nerve, making sciatic nerve intraneural perineuriomas a rarity among other tumours of the peripheral nervous system. While their course is typically indolent, the presence and growth of intraneural perineuriomas can, over time, lead to muscle weakness and wasting, decreased sensation, and loss of nerve function distal to the lesion. We report two unsuspected cases on radiological imaging eventually diagnosed as intraneural perineuriomas on subsequent neuropathological evaluation. Neither patient had a history of known neurofibromatosis (type 1 or 2). The first case is a 45-year-old female originally suspected to have a sciatic nerve schwannoma based on MRI findings. Exploratory surgery, however, revealed involvement of multiple nerve fascicles uncharacteristic of schwannomas. The second case is a 27-year-old male with MRI findings suggestive of a fibrolipomatous hamartoma with appreciable mass effect who also obtained a biopsy. In both instances, microscopy revealed multiple concentric layers of spindle cells arranged around individual axons forming pseudo-onion bulbs which predominated in the neoplasm. These spindle cells were immunopositive for epithelial membrane antigen (EMA) indicative of a proliferative lesion of the perineurial cells. The S100 protein was only expressed in Schwann cells associated with axons within the pseudo-onion bulbs. GLUT1 and claudin-1 immunohistochemistry were also of particular utility as they were found to be reliably expressed by perineurial cells, allowing both cases to be reliably distinguished from more common peripheral nerve sheath tumours such as schwannomas and neurofibromas. These two cases underscore the need for neuropathological assessment in the face of the wide differential diagnosis that sciatic nerve intraneural perineuriomas might carry both clinically and radiologically.

**Research theme 1:** Cancer Biology
**Research theme 2:** Pathobiology of Neurologic Diseases
**Research theme 3:**

**Presenter's Name:** Hsu, Mackenzie

**Additional Author(s):** Howlett C, Khan ZA

**Abstract Title:** Cellular and molecular mechanisms underlying ageing-related stem cell deficits in the bone marrow

**Abstract:**
**Introduction:** As we age, our bodies lose the ability to repair tissue damage, which contributes to the occurrence of age-related diseases in elderly people. Ageing and impairment of regenerative stem cells may contribute to our inability to repair tissues. Recent studies have indicated that stem cell fate is indirectly influenced by the composition of their cellular environment, the niche. Since the bone marrow houses different regenerative stem cell and has a rich microenvironment that is known to change with ageing, it is an excellent model to investigate the mechanisms which may contribute to stem cell deficits during ageing. Hence, I hypothesize that age-related cellular changes in the bone marrow are associated with the marrow resident stem cell ageing phenotype.

**Methods:** To understand how ageing negatively impacts regenerative stem cells, I examined the bone tissues of male and female C57BL/6 mice at different ages. I harvested the femur and tibia of mice at 8, 24, 48, 58-61, and 67-71 weeks of age. These timepoints correspond to approximately 20 to 75 human years. To examine the effect of ageing on the cellular composition of the bone marrow, I first performed histomorphometry (digital pathology) and immunostaining on the fixed bone tissues. I then prepared a single cell suspension from the bone marrows of the mice for gene expression profiling to identify molecular changes that may govern stem cell deficits.

**Results to date:** My morphometric analyses show an increased percent adiposity in the bone marrow with advanced ageing in both male and female mice. Bone tissues also showed increased immunoreactivity to stem cell antigen SCA-1 at middle age in female mice. However, gene expression studies show no changes in transcript levels of various stem cell antigens. Detailed molecular studies are underway to elucidate potential changes in marrow-resident stem cells.

**Significance:** This research will allow for a better understanding of how ageing effects the composition and function of marrow resident stem cell populations. I anticipate that these studies will lead to the identification of targets for the prevention of ageing-related ailments.

**Research theme 1:** Digital Pathology
**Research theme 2:** Regenerative and Transplantation Medicine
**Research theme 3:**





**Presenter's Name:** Huang, Zi Huai

**Additional Author(s):** Liu Q, Hu P

**Abstract Title:** cGAN – Driven Radiomic Prediction of Mutation Status Based on MR Images of Breast Cancer

**Abstract:**
**Introduction:** Breast cancer is a heterogenous cancer. It is crucial to capture both multi-omic information and the tumor's phenotypic heterogeneity to construct personalized treatment options. Radiogenomics is an emerging filed that integrates medical images and genomic measurements, However, most radiogenomic studies face the challenging issue where the data frame is missing either imaging data, genomic data or clinical outcome data. We hypothesize that a well trained conditional generative adversarial network (cGAN) model will be able to address the missing data problem in radiogenomic analysis of breast cancer. The model can be used to predict breast cancer magnetic resonance images (MRI) based on breast cancer patient's multi-omic profiles. The imputed images can be further used to predict the mutation status of breast cancer driver genes.

**Methods:** We chose matched MRI and multiomic (RNA gene expression, DNA methylation, and copy number variation) profiles of 61 breast cancer patients from The Cancer Imaging Archive (TCIA) and The Cancer Genome Atlas (TCGA), respectively. The multiomic data was integrated and factorized into 17 latent features in our previous study. A cGAN model was trained based on the matched MRI and latent features. The MRI data are based on the side view of the tumor tissue. The prediction of MRI is performed based on a given patient's multiomic latent features using the trained model. The produced images are compared to real patient images and evaluated for its quality using the performance metric Frechet's Inception Distance (FID).

**Results:** We built the cGAN model that conditioned on the 17 latent multiomic features using 58 patients with the matched MRI and multiomic data. The FID of the trained model based on the test set with 58 patients is 2.782. Using the trained model, we also performed predictions for the patients with only multiomic profiles but no MRI data. We will train a convolutional neural network (CNN) based on the imputed MRI to predict the mutation status of various selected breast cancer driver genes (on-going)

**Discussion:** These findings solidify cGANs as a potential tool to generate synthetic breast cancer MRI. It also lays the foundation for future breast canIt also lays the foundation for future breast cancer related machine learning studies as the imputed images can significantly augment the existing MRI data and avoid any privacy issue for data sharing.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Hui, Lucy

**Additional Author(s):** Poon AFY

**Abstract Title:** Impact of data access models on the detection of emerging SARS-CoV-2 variants of concern

**Abstract:**
To date, nearly 15 million SARS-CoV-2 genomes have been published through the GISAID (Global Initiative for Sharing All Influenza Data) database. These data have played a central role in tracking the spread of this virus, and the identification of "variants of concern" (VoCs) associated with rapid outbreaks. However, there has been controversy around GISAID's model for data access, which is controlled by a user registration system and Terms of Use that restricts the re-distribution of data or derived results. As a result, some researchers have advocated for more open models of data sharing, including the Nextstrain open data resource that curates SARS-CoV-2 genomes in the NCBI Genbank database. However, there are substantial differences in the rates that genomes are uploaded to these databases.

Our objective was to examine the impact of different data access models on the time until an emerging VoC could be detected from genomic data. We obtained variant classifications and sample collection and genome submission dates for 10.6 and 4.7 million genomes from GISAID and Nextstrain, respectively. For each WHO-defined VoC (Alpha, Beta, Gamma, Delta and Omicron), we used logistic regression to determine the earliest dates at which a significant difference in relative growth rates could be detected for an emerging VoC. These dates were consistently earlier using the GISAID database (mean 3 months, range 1-6 months). Therefore, the expected delay in detecting a new VoC - if one was limited to using an open access database - can be on the same time scale as the emergence and establishment of the VoC.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Janarthanan, Sugitha

**Additional Author(s):** Dima DC, Mohsenzadeh Y

**Abstract Title:** Action Categorization in the Mind Across Vision and Language

**Abstract:**
**Introduction:** Previous research shows that there are shared neural mechanisms for action processing across both vision and language. Multiple behavioral studies have indicated that visual, semantic, and social features play a predominant role in action categorization. However, we don't yet understand how action concepts are organized in the mind, and whether this organization is shared across vision and language. In an attempt to fill these gaps, the focus of this study was to 1) Understand the features in actions that affect how they are categorized in the brain and 2) Understand the similarities and differences between how action videos and action sentences are categorized in the mind.

**Methods:** We first assembled a stimulus set of 95 naturalistic clips and corresponding sentences of everyday actions that varied along multiple feature axes. Visual features were extracted from the action videos using Convolutional Neural Networks (CNN), and Natural Language Processing (NLP) models were used to extract semantic features from the action sentences. Experimental data were collected from 41 participants (for videos) and 35 participants (for sentences) who performed multiple arrangement tasks, arranging each stimulus set according to the actions' similarity in meaning. We then assessed the contribution of each feature to the behavioral similarity data and compared action processing across vision and language.

**Results:** Our results show that multiple features influence action categorization in the brain, with the most influential being semantic features such as action category, both across vision and language. Multiple neural networks correlated well with video similarity judgments, with clip-ViT and resnet50 having the best performance. BERT was the best-performing NLP model, correlating very well with sentence similarity judgments.

**Discussion:** Features on the semantic axis appear to be the most influential in action categorization across vision and language. The same features predicted similarity judgments in both modalities, suggesting that action processing occurs very similarly across both. The complexity of artificial intelligence models contributes to their performance, as the more complex ones are better at replicating human similarity judgments and thus can be used as models for the human brain.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Jeong, Jessica

**Additional Author(s):** Figueredo R, Maleki S

**Abstract Title:** Assessing the Presence of Bacterial Cas9 in MLH1-knockout Neuroblastoma Cells

**Abstract:**
**Introduction:** CRISPR-Cas9 is a prokaryotic adaptive immunity mechanism that has been adapted by scientists into a revolutionary gene editing tool. Previous work in our lab has used this process to knockout MLH1, a primary mismatch repair gene, in neuro-2a neuroblastoma cells to study whether these cells would then be sensitized to the immune system due to the formation of neoantigens. Immune monitoring of these neuroblastoma tumours indicated that the MLH1 knockout (KO) neuroblastoma cells were more immunogenic and had higher infiltration of T-cells. Nevertheless, there is a possibility that unintended Cas9 plasmid insertion and expression in these cells was the underlying cause of this increased immunogenicity, leading to confounding immune sensitization due to foreign bacterial protein presence. This study aims to assess the presence of bacterial Cas9 protein and transcripts from the CRISPR-Cas9 system in the MLH1-KO neuro-2a clones.

**Methods:** To detect Cas9 protein presence, we isolated protein from neuro-2a cells and ran a Western Blot to stain for Cas9 protein. To detect Cas9 mRNA presence, we isolated RNA from neuro-2a cells, generated cDNA from the RNA, and amplified this cDNA using PCR. Then, we performed DNA gel electrophoresis to identify Cas9 DNA presence.

**Results:** Our results demonstrate that neither Cas9 protein nor transcripts are present in our MLH1-KO cells.

**Discussion:** These findings provide evidence that Cas9 proteins and transcripts were not present in our MLH1-KO neuroblastoma cells. Therefore, Cas9 immunogenicity was not an interfering factor in the MLH1-KO cells, reinforcing previous findings of increased immune involvement due to neoantigen formation.

**Research theme 1:** Cancer Biology
**Research theme 2:** Test Utilization, Optimization and Quality Assurance
**Research theme 3:**





**Presenter's Name:** Ji, Helen

**Additional Author(s):** Ninvirta L, Armstrong CE, Zhang A, Hogarth L

**Abstract Title:** Struma Ovarii: A rare teratoma of the ovary

**Abstract:**
**Introduction:** Teratoma is a germ-cell-derived ovarian neoplasm categorized into mature, immature, and monodermal subtypes. Struma ovarii, an extremely rare monodermal teratoma primarily or exclusively comprised of thyroid tissue, accounts for 5% of teratomas and 1% of all ovarian tumours. It usually occurs in the fifth decade and presents as a pelvic mass. The thyroid tissue present in struma ovarii can be benign or malignant, with papillary and follicular carcinoma subtypes being the most common.

**Case:** A 73-year-old female patient presented to the hospital with a sudden onset of lower abdominal cramping, nausea, and back pain. She had no urinary tract infection and gynecologic symptoms. Her family history indicated a significant breast cancer history. Upon imaging, a complex adnexal mass was identified. Surgery was subsequently performed to remove the mass, and further histological examination revealed the tumour to be a malignant struma ovarii.

**Discussion:** Although hyperthyroidism can be a possible side effect of malignant struma ovarii, many cases documented are asymptomatic and incidental. Due to the rarity of this disease there is no consensus for management, and surgical treatment is commonly the primary approach. At the grossing bench, the ovarian mass can be multiloculated and cystic with possible focal brown-tan and solid components grossly representing thyroid tissue. However, this is not common feature for every case. In conclusion, struma ovarii is a benign neoplasm with a small percentage capable of undergoing malignant transformation. Due to the rarity of the disease, further case-based research is needed to determine the optimal treatment and diagnosis process for malignant struma ovarii.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Karimi, Karim

**Additional Author(s):** Haghshenas S, Kerkhof J, McConkey H, Tedder ML, Patterson W, Vissers L, Bouman A, Mussa A, Trajkova S, Merla G, Alders M, Sadikovic B

**Abstract Title:** Identification of DNA methylation episignature for the autosomal dominant mental retardation 21 syndrome caused by mutations in the CTCF gene

**Abstract:**
**Introduction:** CCCTC-binding factor (CTCF) protein plays important roles in gene transcription and global chromatin organization. Germline mutations in CTCF gene cause autosomal dominant mental retardation 21 syndrome (MRD21; OMIM 615502), characterized by intellectual disability, short stature, microcephaly, and congenital heart defects. The main objective of this study was to establish a DNA methylation episignature using a binary support vector machine (SVM) model as a diagnostic biomarker for MRD21.

**Methods:** DNA samples were extracted from peripheral blood of 11 individuals with genetic variants in CTCF and clinical features consistent with MRD21. DNA methylation analysis was performed using the Illumina Infinium Methylation EPIC Bead Chip microarrays. Controls were randomly selected from EpiSign Knowledge Database (EKD) at the London Health Sciences Centre (LHSC). The methylation levels were fitted in a multivariate linear regression model to identify the differentially methylated probes.

**Results:** Collectively, 103 differentially methylated probes were selected to construct a binary SVM classification model. DNA methylation analysis indicated a clear and robust separation between patients with pathogenic variants and controls. In addition, two variants of uncertain significance (VUS) were mapped to the MRD21 episignature, and were reclassified as likely pathogenic. The SVM model was able to distinguish patients with the MRD21 syndrome from other neurodevelopmental disorders from the EKD, confirming the high sensitivity and specificity of the model.

**Discussion:** This study presents a distinct DNA methylation episignature associated with MRD21-neurodevelopmental syndrome, which not only expanded the EpiSign diagnostic test but also can be utilized as biomarker for early diagnosis of this syndrome.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:** Epigenetics
**Research theme 3:**





**Presenter's Name:** Kawa, Daniel

**Additional Author(s):** Jackson-Boeters L, Kiser P.

**Abstract Title:** Assessing in Vivo Off-Target Binding of a Novel Oral Antibody Vaccine Developed to Prevent Colonization of Enteric Pathogen E. Coli O157:H7

**Abstract:**
Characterized by Shiga toxin production and intimin-mediated binding to host gastrointestinal (GI) epithelium, enterohemorrhagic Escherichia Coli (EHEC) O157:H7 is frequently responsible for foodborne outbreaks. While it colonizes the GI tracts of humans and livestock alike, it is largely asymptomatic in the latter, while in severe cases potentially fatal hemolytic uremic syndrome manifests in the former. The ineffectiveness and potential for symptom exacerbation by current therapies, and a drive to prevent pathogenic E. coli colonization before it moves up the food chain have driven the development of DNB, a novel plant-derived chimeric single-domain antibody (VHH)-secretory IgA fusion protein designed for use as a feed additive. Previous in vitro experiments have shown DNB's VHH to specifically target the 277 C-terminal residues of intimin on select EHEC strains including O157:H7, neutralizing their adherence to human epithelial cells. Based on sequence search with NCBI BLAST, no notable homology was noted between the 277 C-terminal intimin residues and any mammalian protein, suggesting specific off-target DNB-to-GI-epithelium binding to be unlikely. Currently, we are optimizing an immunohistochemistry assay to detect DNB in CD-1 mouse GI tissues to determine if there is any such binding, which could indicate possible interference with normal cellular functions such as nutritional uptake. Primary antibody specificity will be further validated by western blotting. This assay will be tested on GI tissues from experimental groups of 5 male and female mice fed a diet of 20% DNB or standard mouse chow for two weeks. The female mice fed DNB initially underwent weight loss peaking at -5.9% on day 7 ($p < 0.05$) but which was restored by day 14, none being observed in males. Comprehensive histologic assessment of mouse organ tissues from this experiment, however, did not identify any notable abnormalities. If DNB is associated with the intestinal mucosa of female mice, this could help explain the weight loss observed in the in vivo experiment. This assay will contribute toward the in vivo validation of DNB's safety as a livestock feed additive and provide information about DNB localization during future E. coli O157:H7 challenge studies. If off-target DNB binding is detected along the intestinal mucosa, this could highlight potential contraindications against its administration and drive further refinements in the biologic's development.

**Research theme 1:** One Health
**Research theme 2:** Test Utilization, Optimization and Quality Assurance
**Research theme 3:**

**Presenter's Name:** Kim, Joon

**Additional Author(s):** Kim SJ, Kiser PK, Asfaha S, DeKoter RP, Dick FA

**Abstract Title:** EZH2 inhibition stimulates viral mimicry causing immune destruction of splenic B cells

**Abstract:**
EZH2 is a histone methyltransferase that deposits H3K27me2/3 in heterochromatin and it is misregulated in tumorigenesis. Inhibition of heterochromatin can induce viral mimicry in cancer cells, where upregulated repetitive elements are detected by cytosolic pattern recognition receptors (PRRs) to activate inflammatory signaling. Here we demonstrate that EZH2 inhibitors stimulate inflammation and immune self-recognition of resting splenic B cells. We generated a PRR loss-of-function mouse model called RIC with mutations in Rigi, Ifih1 (MDA5), and Cgas. In both WT and RIC mutant B cells, EZH2 inhibition caused loss of H3K27me3 at repetitive elements and upregulated their expression. However, expression of inflammatory chemokines in B cells was interrupted by the RIC mutations. Furthermore, recruitment of cytotoxic T cells and neutrophils in response to EZH2 inhibition was blocked in RIC mutants preserving viability of B cells. This study demonstrates a pharmacologically induced mechanism of inflammation that causes self-recognition and B cell death.

**Research theme 1:** Epigenetics
**Research theme 2:** Infection, Immunity, and Inflammation
**Research theme 3:**





**Presenter's Name:** Kuczek, Jakub

**Additional Author(s):** Zhang Q

**Abstract Title:** Investigating Nuclear Morphometry in Diffuse Astrocytic Gliomas

**Abstract:**
**Introduction:** Diffuse astrocytomas are a subtype of glioma that are highly infiltrative into the surrounding brain parenchyma. Together with mitotic counts, nuclear atypia is one important histological feature that distinguishes World Health Organization (WHO) grade 2 and grade 3 astrocytomas. However, determining the degree of nuclear atypia is subjective and prone to mistakes. Detailed nuclear morphometry studies are lacking. This study aims to investigate how nuclear morphometry of diffuse gliomas correlates to the tumor genetic alteration, the WHO grading and patient prognosis.

**Methods:** 100 H&E stained diffuse astrocytoma whole slide images (WSI) will be obtained from The Cancer Genome Atlas (TCGA) public dataset. Image analysis software QuPath will be used to analyze nuclear morphometry. The tumor core will be annotated using QuPath to segment 1000 tumor nuclei. The nuclear parameters measured include nuclear area, nuclear roundness, nuclear perimeter, and nuclear chromatin density. WHO grading designated at time of diagnosis, patient's clinical outcome and genetic testing results (DNA sequencing and chromosomal status) are available for correlation.

**Results:** 80 WSI images were downloaded and annotated. Nuclear morphometry analysis is ongoing. We expect that diffuse astrocytic gliomas that possess more atypical nuclear morphometry will correlate to a higher WHO grading, poorer patient prognosis and higher chromosomal abnormalities.

**Discussion:** The results of this study may contribute towards improving the WHO grading and patient prognosis of diffuse astrocytoma patients using nuclear morphometric analysis, which may also serve a surrogate marker for genetic changes in glioma cells.

**Research theme 1:** Cancer Biology
**Research theme 2:** Digital Pathology
**Research theme 3:**

**Presenter's Name:** Li, Xinru

**Additional Author(s):** Darling M

**Abstract Title:** Evaluation of S100A7 as a Biomarker of Malignant Transformation from Oral Epithelial Lesions, and Relation to Oral Cancer in Dogs

**Abstract:**
**Introduction:** Worldwide, head and neck cancer accounts for up to 4% of all cancer cases and it is estimated that over 90% of all oral neoplasms are squamous cell carcinoma (OSCC). The majority of OSCC cases are detected at an advanced stage, with 5-year survival rate ranging from 40-50%. The protein S100A7 has been shown to be over-expressed in oral potentially malignant disorders (OPMD) and has been linked to the MAPK and Wnt signaling pathways. In this study, we aim to identify whether S100A7 is a reliable predictor of malignant transformation, to investigate its association with the MAPK and Wnt pathways, and to identify epithelial-mesenchymal transition (EMT).

**Methods:** Tissue blocks of normal oral epithelium and biopsies of patients with OPMD were retrieved from the archives. Samples were stained using immunohistochemistry for S100A7, BRAF, e-cadherin, vimentin, beta-catenin, MCM2, geminin and Ki-67. A risk stratification system based on S100A7 overexpression will be used to determine probability of malignant transformation. Image analysis using QuPath software was employed to determine degree of expression of these biomarkers. RNA Scope will be used to determine evidence of protein synthesis.

**Results:** Preliminary results indicate that vimentin expression in oral epithelium of OPMD doubled when compared to normal oral epithelial tissue. Ki67 nuclear staining was also significantly higher in OPMD. There was lower expression of both E-cadherin and BRAF in OPMD; while B-catenin expression had no significant difference.

**Discussion:** These findings show that an EMT phenotype is observed in OPMD. One of the most distinguishing features for the establishment of an EMT phenotype is up-regulated expression of mesenchymal markers and down-regulated expression of structural adhesion proteins. The cellular mitotic activity is also dysregulated in OPMD epithelium shown by increased Ki-67. These results show promise for predicting further malignant transformation.

**Research theme 1:** Cancer Biology
**Research theme 2:** Oral Biology and Medicine
**Research theme 3:**





**Presenter's Name:** Li, Yueyang

**Additional Author(s):** Lin S, Shi T, Strijbos M, Huang J, Jeong A, Chen M, Liu R, Cai T, Kuang D, Khov L, Cecchini M.

**Abstract Title:** Sonification of Pathology: From Slides to Sound

**Abstract:**
**Introduction:** Sonification is the process of converting data into sound, and has been used as a tool in medicine to track EKG and EEG changes. In pathology, the diagnosis of diseases is based on the recognition of distinct morphological features. The use of image analysis software and data sonification may be leveraged to convert slides into sound representations that may be capable of discerning differences between cell types. In the present study, we test the hypothesis that the sound of the malignant cells can be distinguished from that of normal lung tissue.

**Methods:** A single digital slide of lung adenocarcinoma with abundant tumour and normal lung areas was selected from the Cancer Genome Atlas dataset. Using QuPath, the slide was divided into 100 nm2 tiles, and intensity features including average optical density, hematoxylin concentration, eosin concentration, and saturation were extracted. Representative rows of tiles that transitioned between normal lung parenchyma and tumour were selected and inputted into the TwoTone sonification program. Audio tracks were generated and the exact transition point was recorded. 3 tracks were selected to serve as the training set and the remaining tracks were randomized. Participants were asked to listen to the training tracks, then listen to the 30 tracks and indicate what they believed was the transition point.

**Results:** The survey was completed by 10 participants with varying levels of musical and pathology training. The mean distance from the true transition point across all tracks and participants was 0.42 seconds, with a standard deviation of 0.50 seconds. Of the 10 participants, 7 have had music training (mean=0.39, stdev=0.18) and 3 have not had music training (mean=0.51, stdev=0.02). 5 have had pathology training (mean=0.39, stdev=0.18) and 5 have not had pathology training (mean=0.46, stdev=0.15). Neither subgroup did significantly better than the other. Track 9 and 29 were challenging for participants, with mean differences of 1.90 and 2.30 seconds respectively, which may have been primarily due to tumour heterogeneity.

**Discussion:** The sonification of pathology represents a novel tool to interpret pathological features using a multi-sensory approach. Areas of normal lung parenchyma and tumour can be discerned with a high degree of accuracy. Future and ongoing work aims to develop machine learning algorithms from sonified pathohistology slides to identify critical pathologic features.

**Research theme 1:** Digital Pathology
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Lin, August

**Additional Author(s):** Zhang Q, Wang F

**Abstract Title:** Clinical Significance of Granular Mitoses in Glioblastoma

**Abstract:**
**Introduction:** Gliomas are the most common primary central nervous system (CNS) neoplasm. Prognosis varies greatly based on grading and molecular profile. Tumour proliferative index is one of the four WHO tumour grading criterias and is characterized by the presence of mitotic figures. Particularly, atypical figures can be considered an indicator for high tumour aggressiveness. Granular mitoses are a form of atypical mitotic figure characterized by minute chromosomal bodies unique to high grade gliomas such as glioblastoma. Although granular mitoses have been previously described histologically in gliomas, their mechanisms, genetic alterations and its effects on treatment are largely unknown.

**Methods:** 4 slides were reviewed from the public Cancer Genome Atlas (TCGA) glioblastoma slide dataset. All atypical mitoses were identified from using QuPath, a digital slide analysis software. From these annotations, granular mitoses, normal mitotic figures and apoptotic bodies were categorized by a pathologist. Clinical data was obtained from cBioPortal.

**Results:** Although three slides presented with 1 granular mitosis, the number of granular mitoses ranged from 1 to 15 (15, 1, 3, 1 granular mitosis). The case with 15 granular mitoses displayed an overall survival of 2 months. The other overall survival for the other cases were 4, 6, and 43, respectively.

**Discussion:** The survival rate of glioblastomas with many granular mitoses are similar than few. However, there is one outlier from the 4 slides analyzed (43 months). Further research is required to correlate the transcriptomic profiles of these cases (cBioPortal) to the presence and number of granular mitoses. Additionally, as more slides are annotated and reviewed, the significance of granular mitoses in clinical data may become clearer.

**Research theme 1:** Cancer Biology
**Research theme 2:** Digital Pathology
**Research theme 3:**





**Presenter's Name:** Lin, Chin-Jung

**Additional Author(s):** Lin CJ, Ni R, Peng T

**Abstract Title:** Nicotinamide Mononucleotide prevents neutrophil aging and reduces bacterial burden in sepsis

**Abstract:**
**Introduction:** Sepsis is a life-threatening and highly complex disease that caused by the host response to the pathogen infection. During sepsis, C-X-C chemokine receptor type 4 positive (CXCR4+) aged neutrophils produce high levels of reactive oxygen species and neutrophil extracellular traps (NETs). NETs can protect the host through the antimicrobial activities; however, the excessive NETosis can lead to disseminated intravascular coagulation and multiple organ dysfunction syndrome. Nicotinamide mononucleotide (NMN) is natural biosynthetic precursor of NAD+ that can regulate the oxidative stress and inflammatory response. Studies has shown that NMN can prevent the bacterial infection and improve the survival in sepsis. In the present study, we sought to investigate whether and how NMN modulates the neutrophil aging in sepsis. We hypothesize that NMN prevents neutrophil aging thereby attenuating bacterial dissemination and protecting organs in sepsis.

**Methods:** Neutrophils were isolated from the bone marrow of mice. Neutrophils aging was induced by lipopolysaccharides (LPS) or culturing for 24 (or 48 hours?). CXCR4+ aged neutrophils were analyzed by flow cytometry. Sepsis was induced in mice by feces-injection-into-peritoneum. Bacterial burden in blood was determined.

**Results:** Incubation with LPS or culture for 24 hours resulted in a significant increase in the proportion of CXCR4+ neutrophils, indicative of aging, which was prevented by co-incubation with NMN. In a mouse model of sepsis, the percentage of CXCR4+ neutrophils increased in blood. Treatment with NMN reduced CXCR4+ neutrophils and concomitant bacterial burden in blood of septic mice.

**Discussion:** These findings indicate that NMN can prevent neutrophil aging both in vitro and in vivo, and that suppression of neutrophil aging may help limiting bacterial dissemination in sepsis. Thus, NMN may be a therapeutic agent for sepsis.

**Research theme 1:** Infection, Immunity, and Inflammation
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** McConkey, Haley

**Additional Author(s):** Kerkhof J, Levy MA, Relator R, Rooney K, Haghshenas S, Au B, Antonishyn N, Boycott K, Dyment D, White-Brown A, Chacon I, Li C, Tarnopolsky M, Nezarati M, Goobie S, Ben Amor M, Badalato L, Sadikovic B

**Abstract Title:** Clinical Epigenomic Testing in Canada: Discovery and Clinical Assessment of Episignatures

**Abstract:**
**Introduction:** Neurodevelopmental disorders (NDDs) often present with overlapping presentations, making a clinical diagnosis difficult. First-tier genetic testing includes microarray or gene sequencing based on the phenotypic presentation. 65 to 75% of patients do not receive a diagnosis from this testing and must undergo reflex testing, such as whole exome sequencing (WES). This can take months or years and is costly, and patients can be left with no variants detected or a variant of uncertain significance (VUS). DNA methylation is another mechanism that can impact gene expression. An expanding number of NDDs exhibit unique DNA methylation patterns in peripheral blood, called episignatures, which can be used as diagnostic biomarkers.

**Methods:** The EpiSign test uses whole-genome methylation analysis to compare detected methylation changes in a patient to known NDD episignatures. A current national trial is in progress with the main goal of obtaining real-world prospective evidence to validate the utility of EpiSign in both the first-tier and reflex setting, collecting detailed clinical and health economics data.

**Results:** The EpiSign test contains 57 episignatures associated with 65 genetic syndromes . So far 372 patients have been enrolled in the study, 76% first-tier and 24% reflex, with 264 results issued. Current episignature positivity rate is 12% and the turnaround time for test results after receiving sample is 30 days on average, highlighting efficient study workflow. Positive EpiSign cases demonstrate usefulness in first-tier setting, the re-classification of VUSs, as well as unresolved cases with no candidate variants. A recent case study detailed an unresolved patient with a positive EpiSign for a deletion syndrome despite no detected genetic deletions. When the clinical team reviewed the WES data within the deleted region, they found a variant in a new disease gene, one that was not characterized at time of previous clinical analyses.

**Discussion:** The use of EpiSign in Canadian genetics clinics provides an additional strategy for physicians to assess patients with ambiguous clinical presentation or genetic findings. The highlighted positive case demonstrates the use of EpiSign in directing efficient exome reanalysis, reducing cost for reassessment of backlog of unsolved patients. EpiSign has the potential to impact healthcare resource allocation and provide a more cost-effective approach for the diagnosis of rare disease.

**Research theme 1:** Epigenetics
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** McCullagh, William

**Additional Author(s):** Bhattacharjee RN, Ravichandran S

**Abstract Title:** Immunological Impact of Carbon Monoxide Releasing Molecules on In-Vitro Renal Ischemia Reperfusion Injury.

**Abstract:**
**Introduction:** Over 50000 Canadians are currently living with kidney failure making demand for kidney donations extremely high. Kidneys donated after cardio-circulatory death are being used to cope with this demand, despite the fact that these kidneys lead to poorer outcomes when compared to kidneys from living and brain-death donors. Kidneys donated after cardio-circulatory death undergo ischemic reperfusion injury (IRI) during the transplantation process, mediated by the innate immune system, notably via toll-like receptors (TLR). Our lab has previously shown CORM-401 has the ability to reduce TLR signalling and by extension IRI in ex-vivo porcine kidney models and in-vivo murine models. We therefore hypothesize that CORM-401 pre-incubation will significantly reduce inflammatory marker levels in Human Kidney cell lines.

**Methods:** To test this hypothesis we incubated human kidney cells with CORM-401 for 12 hours before treating the cells with lipopolysaccharide, a TLR-4 ligand. ELISA was then conducted on the cell supernatant after 6 hours to measure levels of IL-6 and TNF-alpha. Relative IL-6 and TNF-alpha levels were then compared against a negative control, positive control, and inactive CORM-401 vector control.

**Results:** In our experiment we expect CORM-401 to attenuate TLR-4 signalling. This should result in decreased IL-6 and TNF-alpha levels in CORM-401 treated human kidney cells when compared to control conditions.

**Conclusion:** This study will demonstrate whether CORM-401's ability to reduce ischemic reperfusion injury in in-vivo murine models and ex-vivo porcine is able to transfer to in-vitro human models, paving the way for future studies into CORM-401's effectiveness on human models. If CORM-401 can safely be used in human transplants, a reduction in ischemic reperfusion injury would decrease instances of graft failure, making donation after cardio-circulatory death a more reliable treatment for kidney failure.

**Research theme 1:** Regenerative and Transplantation Medicine
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Menard, Melissa

**Additional Author(s):** Lin S, Vincent M, Cecchini M

**Abstract Title:** A Case of Unsuspected Peritoneal Mesothelioma Presenting as Rectal Polyp

**Abstract:**
**Introduction:** Malignant peritoneal mesothelioma (MPM) is an aggressive rare tumor associated with poor prognosis. Even rarer is MPM presenting as a rectal polyp in the sigmoid discovered through a screening colonoscopy. To our knowledge, we present the first case of MPM discovered through colonoscopy that was resolved through a detailed medical history, distinct histopathological features, and immunohistochemistry panel.

**Case:** The patient is a 69-year-old man with a past history of resected melanoma that underwent a screening colonoscopy after a positive fecal immunochemical test revealing a 2-3 cm round ulcerating mass 20 cm from the anal verge. Biopsy of the mass showed nests of atypical epithelioid cells negative for melanoma immunohistochemical markers but positive for mesothelial markers. There is a family history of pleural mesothelioma in his father and there was loss of BAP1 on biopsy. Surgical resection of the sigmoid colon revealed a polypoid mass (2 cm) that was arising from the serosa and extending into the wall, submucosa, and surrounding pericolonic adipose tissue. Genetic testing was done which revealed a germline BAP1 mutation. Although the patient did not have a definite history of exposure to asbestos, a family history of pleural mesothelioma in conjunction with BAP1 loss and immunohistochemical biomarkers showing epithelial origin is consistent with the diagnosis of MPM.

**Discussion:** There is currently a scarcity of literature that describes the diagnosis and management of early stage MPM. There is a strong association between mesothelioma and asbestos exposure, however, patients with a BAP1 germline mutation suggest a familial predisposition for mesothelioma. Increased awareness should be placed on considering MPM in the differential diagnosis during routine colonoscopy given appropriate familial history. Given MPM usually presents at a late stage, a detailed medical history in correlation with identifying key pathohistological findings and appropriate immunohistochemical mesothelioma markers is critical in diagnosing this rare entity at an early stage.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Morin, Amanda

**Additional Author(s):** Castellani CA

**Abstract Title:** The effect of in vitro models of mitochondrial DNA variation on the nuclear epigenome and transcriptome

**Abstract:**
Bidirectional crosstalk between the nuclear genome (nDNA) and the mitochondrial genome (mtDNA) is required for proper cell functioning and homeostasis. Altering the quantity (mtDNA-CN) or the quality (heteroplasmy) of mtDNA leads to nDNA methylation and histone acetylation changes resulting in differential gene expression. mtDNA variation is associated with variability in health and disease and all-cause mortality. Replication of mtDNA is regulated by nDNA-encoded genes, including TFAM (mitochondrial transcription factor A) and POLG (DNA polymerase γ). TFAM knockout (KO) models previously developed in the lab show an 18-fold reduction in mtDNA-CN and subsequent variation in nDNA methylation and nuclear gene expression. It has also been shown that expression of exonuclease-deficient (D198A) and polymerase-deficient (D1135A) dominant-negative POLG (DN-POLG) mutants results in up to a 5-fold increase in heteroplasmic load and up to 75% reduction in mtDNA-CN, respectively. To uncover mechanisms driving these associations, we are leveraging 1) Stable cell lines with mtDNA-CN reduction (TFAM KOs, N=6) and inducible models of mtDNA-CN modulation (POLG D1135A), 2) Inducible models of heteroplasmy modulation (POLG D198A), and 3) mtDNA modifying chemicals and drugs. mtDNA-CN variation is measured with qPCR, and heteroplasmy variation is called with Whole Genome Sequencing. The effect of mtDNA variation on nDNA will be assessed by the generation of DNA methylation profiles using the Illumina Infinium EPIC Methylation Array and gene expression profiles via RNA sequencing. We are also generating profiles of histone acetylation and acetyl-CoA levels in TFAM KO lines. Regarding POLG mutants, both stable and transient inducible expression will be achieved by co-transfecting Flp-In T-Rex293 cells (HEK293 derivative with integrated tetracycline repressor expression and a FRT site) with an expression vector containing a FRT site and a DN-POLG mutant under tetracycline operator control, and a vector expressing Flp recombinase, mediating recombination between the FRT sites in the genome and the expression vector. Our preliminary chemical treatments on HEK293 cells with chloroform show a significant increase in mtDNA-CN ($p=0.03$). These models will allow us to uncover mechanisms mediating the effect of mtDNA variation on health and disease through the integration of DNA methylation and gene expression profiles, as well as functionally characterize relevant genes and pathways.

**Research theme 1:** Epigenetics
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Muralitharan, Anushga

**Additional Author(s):** Walsh J

**Abstract Title:** Polycystic Liver Disease: A Case Study

**Abstract:**
**Introduction:** Polycystic liver disease (PCLD) is a rare genetic disease with a prevalence of 1:158 000 and is characterized by the development of at least 20 cysts affecting the liver parenchyma. Most cases occur in conjunction with autosomal dominant polycystic kidney disease (ADPKD), but 20% are isolated PLCD cases. While it doesn't always present clinically, there are cases where severe symptoms show causing many effects on the patient.

**Case:** A 46 year old male presented with abdominal pain and distension. He has already been diagnosed with autosomal polycystic kidney disease which is combined with his polycystic liver. The enlarged state of his liver (~10 kg) put pressure on surrounding organs, and it was decided that a simultaneous liver and kidney transplant was to be done to help alleviate his symptoms.

**Discussion:** As a liver transplantation is the cure for polycystic liver disease, there is not much that needs to be done post treatment and instead most pathology testing will be confirmatory tests. One finding in this case that was interesting to note was the size and weight of the liver as it was exponentially larger than a healthy liver. The cut surface of the liver showed numerous benign cysts filled with clear, serous fluid and minimal normal parenchyma identified. As such, not many sections of the liver were needed for histology and 6 samples from different regions of the liver such as from near the capsule and porta hepatis were taken for histology. The findings from the sections taken showed multiple intrahepatic cysts lined with simple cuboidal cells and scattered bile duct hamartomas.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Nguyen, Julia

**Additional Author(s):** Morin A, Castellani C

**Abstract Title:** Association between mitochondrial DNA haplogroups and nuclear DNA methylation in cardiovascular disease and aging

**Abstract:**
Given the vital role of the mitochondria towards regulating physiological processes, measures of mitochondrial DNA (mtDNA) are associated with complex disease outcomes. mtDNA haplogroups are categorizations of regions of mtDNA that cluster based on maternal lineage, and they are independently associated with complex disease risk. The biological mechanisms by which mtDNA measurements, including mtDNA haplogroup classifications, lead to phenotypic variation have not been well established. Previously, we have shown that mtDNA variability can drive differential epigenetic modifications and associate with aging-related disease outcomes. Matched baseline visit methylation derived from the Illumina Infinium EPIC array and genotyping data from the Affymetrix Axiom microarray from over 1,400 prospective participants from the Canadian Longitudinal Study on Aging (CLSA) were used to evaluate the effect of nuclear DNA (nDNA) methylation on the association between mtDNA haplogroups (classified by HaploGrep) and disease. Further, we conducted association analyses between environmental indicators, mtDNA haplogroup classifications, and disease traits, including cardiovascular, cancer and all-cause mortality outcomes, for over 26,000 participants. We identified site-specific nuclear DNA CpG methylation which are significantly associated with mtDNA haplogroups. The functional regions and ontologies that are overrepresented in these associations were also determined. Using follow-up information ascertained 3 years after baseline visits, we conducted survival analyses on disease outcomes of interest in relationship to both mtDNA haplogroups and nDNA methylation. These findings have implications for the role of mtDNA variability in disease etiology and have the potential to facilitate the translation of mtDNA evaluations into clinical practice as biomarkers of disease risk and manifestation.

**Research theme 1:** Bioinformatics and Data Science
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Ninivirta, Lindsay

**Additional Author(s):** Li H, McFarland S, Murphy K, McRae S, Weir M, Joseph M

**Abstract Title:** Maximizing Diagnostic Yield in Biliary Brush Cytology: Implementation of a Quality Improvement Project

**Abstract:**
**Introduction:** High diagnostic atypical rate in Biliary Brush (BB) cytology samples in patients with pancreaticobiliary diseases, often poses a clinical diagnostic dilemma. In 2016, we introduced a Quality Improvement (QI) project in our cytopathology division in an attempt to reduce the high atypical rate in BB cytology. We evaluated the collection techniques and diagnostic performance data for BB cytology for six years and implemented an in-service education in 2017 for clinicians and cytopathology staff. Our objectives were 1) to determine whether the in-service education strategy had an impact on BB atypical rates and 2) to assess the positive predictive values (PPV) for atypical diagnoses based on surgical and cytological (EUS-FNA) follow-up.

**Methods:** A retrospective cohort data analysis of BB cytology cases was performed using LHSC cytopathology database. Pre-education cohort was defined as cases collected from 2013 to 2016; while post-education cohort included cases collected from 2018 to 2021. In-service training for cytology staff and clinicians was given during 2017. The diagnostic categories were: insufficient, negative, atypical, suspicious and positive for malignancy. Statistical analysis was performed to compare BB diagnoses with surgical & EUS/FNA follow-up diagnoses in both cohorts.

**Results:** The pre-education cohort had fewer BB cases per month compared to post-education cohort (7.3 versus 19.2). There were significant differences across the diagnostic categories between the cohorts; atypical (36.5% versus 30.7%), positive (9.8% versus 18.5%), suspicious (13.2% versus 13.0%), and negative/insufficient samples (2.9% versus 1.7%). The PPV for detecting malignancy and dysplasia on atypical cytology diagnosis was (91% versus 85%) on surgical follow-up and was (62% versus 97%) on EUS-FNA follow-up.

**Discussion/Conclusion:** Execution of in-service education effectively decreased the atypical rate, as some cases shifted to positive and suspicious categories. Given the high PPV for malignancy associated with an atypical BB cytology diagnosis, additional useful diagnostic procedures such as EUS-FNA for final diagnosis should be considered for appropriate patients. This type of in-house QI strategy will allow for more effective sampling/interpretation of BB cytology samples and guide clinicians to diagnose patients with pancreaticobiliary diseases, thereby optimizing patient care and improving resource allocation.

**Research theme 1:** Test Utilization, Optimization and Quality Assurance
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Nunes, Timothy

**Additional Author(s):** Nygard KL, Courchesne MCJ, Richardson BS, Regnault TRH, Kiser PK

**Abstract Title:** Lifelong maternal Western Diet impairs placental and fetal development in a non-obese guinea pig (Cavia porcellus) model

**Abstract:**
**Background:** Independent of body mass index (BMI), a "Western Diet" (WD) high in refined sugars and saturated fats contributes to poor metabolic health. Maternal WD is associated with adverse pregnancy outcomes—including altered placental development. Studies investigating the impact of WD in normal-weight pregnant populations are limited, despite the increasing prevalence of metabolically unhealthy normal-weight persons.

To elucidate the BMI-independent effects of WD on fetoplacental development, we utilized a guinea pig model in which sows fed lifelong WD do not become obese, but do become metabolically unhealthy. We hypothesized that lifelong maternal WD would impair placental vascularization and fetal development—independent of maternal body weight.

**Methods:** Female Dunkin-Hartley guinea pigs were weaned onto control diet (CD) or WD and mated to control males at six months of age, then necropsied at 36, 42, or 63 days (term ~68 days) and fetoplacental growth outcomes were recorded. Longitudinal placenta cross-sections were examined by immunofluorescence microscopy to analyze fetal capillaries with anti-vimentin staining, and maternal lacunae with anti-cytokeratin staining. Preliminary data are presented for the 63-day cohort (CD n=19 (6 pregnancies), WD n=25 (14 pregnancies), assessed by linear mixed model emmeans pairwise analysis with litter-ID fixed effect and Hedge's g effect size analysis.

**Results:** WD pregnancies had significantly decreased fetal-placental weight ratios ($p<0.001$) and 16.8% lower fetal brain-liver weight ratios ($p=0.086$, $g=1.041$), relative to CD. In placental labyrinths, maternal lacunae to fetal capillary area ratio was significantly increased in WD placentae, relative to CD ($p<0.01$). Fetal capillary diameters were significantly reduced in WD placentae, relative to CD ($p<0.001$).

**Discussion:** Our current findings indicate that impaired placental hemodynamics may contribute to adverse gestational outcomes associated with WD pregnancies. We will explore the timing of impaired fetoplacental development with maternal WD, by comparing our mid-gestational cohorts to our current late-term findings. Our findings could help to refine pregnancy risk assessments in clinical settings, as we highlight the importance of evaluating maternal lifestyle and metabolic health—rather than BMI alone.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Pan, Nachuan (Harrison)

**Additional Author(s):** Wang E, Wang H, Chakrabarti S, Chen S, Feng B

**Abstract Title:** The role of miR-9 in diabetic cardiomyopathy

**Abstract:**
**Introduction:** Diabetes mellitus is a major global health issue, and diabetic patients can develop many complications, including diabetic cardiomyopathy (DCM). One of the clinical manifestations of DCM is cardiac fibrosis which is regulated by TGF-βsignalling and endothelial-to-mesenchymal transition (EndMT). Therefore, TGF-βsignalling pathway is considered a promising therapeutic target for cardiac fibrosis in the context of DCM. microRNA-9(miR-9) is a family of miRNAs that target TGF-β receptor 1& 2. However, the role of miR-9 in DCM remains unclear.

**Methods:** We used human cardiac microvascular endothelial cells (HCMEC) to test whether high glucose will trigger EndMT by measuring the expressions of mesenchymal cell marker FSP-1 and endothelial cell marker VE-cadherin (VE) via RT-PCR. To identify the in vivo effects of miR-9, we used transgenic miR-9 over-expressing and wild-type C57BL/6 mouse models to compare the expressions of FSP-1 and VE, and fibrosis markers (Fibronectin, FN; Collagen 1, COL1A1; Collagen 4, COL4A1) in healthy and diabetic mouse cardiac tissues via RT-PCR. Mouse heart tissue staining was performed, followed by a histological analysis to compare the patterns of cardiac fibrosis.

**Results:** The in vitro experiments showed that the relative mRNA level of FSP-1 had a statistically significant increase in the high glucose-treated group compared to the control. However, the relative mRNA levels of VE were not significantly different. The data from the in vivo experiments suggested that high glucose increased the expressions of FSP-1, FN and COL1A1, and decreased the expression of VE in the hearts of diabetic mice compared to the control group, and these changes were prevented by miR-9 over-expression. However, there was no statistically significant difference observed in the expression of COL4A1 due to miR-9 over-expression. The histological analysis demonstrated fewer patterns of fibrosis in diabetic miR-9 transgenic mice than in diabetic wild-type mice.

**Discussion:** Our findings support that high glucose can induce EndMT in HCMECs and mouse hearts, which leads to cardiac fibrosis. miR-9 over-expression can inhibit EndMT and reduce fibrosis in diabetic mouse hearts. These findings suggest that miR-9 has therapeutic potential and can be incorporated into future RNA-based therapy for cardiac fibrosis in DCM.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Panjwani, Samina

**Additional Author(s):** Princz-Lebel O, Saksida L, Bussey T.

**Abstract Title:** Exploring the neurocircuitry mechanisms underlying stimulus-response learning in mice, and its relevance to Parkinson's disease

**Abstract:**
**Introduction:** Parkinson's disease (PD) is a neurodegenerative disorder classically characterized by motor impairments such as bradykinesia, muscle tremors, rigidity, and involuntary muscle contractions. Although the exact etiology is unknown, these symptoms are believed to be due to the progressive degeneration of dopamine-producing neurons and subsequent loss of dopamine in key pathways throughout the brain, such as the mesolimbic and nigrostriatal pathways. However, it has recently come to light that patients can also present with cognitive impairments prior to the onset of motor symptoms. To understand these cognitive impairments, human studies have taken an interest in understanding how PD patients are impacted in learning tasks and indicated that patients performed abnormally on a specific task known as stimulus-response learning (SRL). However, researchers have not connected how dopamine pathways are involved in the acquisition of SRL. As such, this research project aims to manipulate key dopamine pathways to understand the roles the nigrostriatal and mesolimbic dopamine pathways play in the acquisition of SRL.

**Methods:** We are using chemogenetics to selectively inhibit the nigrostriatal and mesolimbic dopamine pathways in a transgenic line of DAT.Cre mice to enable the controlled manipulation of these pathways. Simultaneously, we are running the mice on the Visuomotor Conditional Learning (VMCL) task, a stimulus-response learning task, to assess their performance and learning. Dopamine and viral expression will be analyzed using immunohistochemistry.

**Results:** The results indicated that compared to control mice, the inhibition of the nigrostriatal and mesolimbic dopamine pathways impacted the acquisition of the VMCL task.

**Discussion:** These findings will allow for improvements in the development of future therapeutic interventions. The current treatment options for Parkinson's patients involve dopamine replacement therapy which has been shown to improve motor impairments but has the potential to cause cognitive decline. If we can gain a stronger understanding of how dopamine is involved in cognition and which dopamine pathways impact different cognitive functions, we can develop more effective treatment options to lessen the burden of PD on patients and our healthcare system.

**Research theme 1:** One Health
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Passos, Daniel

**Additional Author(s):** Perampalam P, Hassan H, Lilly G, Passos DT, Torchia J, Kiser PK, Bozovic A, Kulasingam V, Dick FA

**Abstract Title:** Disrupting the DREAM transcriptional repressor complex induces apolipoprotein overexpression and systemic amyloidosis in mice

**Abstract:**
DREAM (Dp, Rb-like, E2F, and MuvB) is a transcriptional repressor complex that regulates cell proliferation, and its loss causes neonatal lethality in mice. To investigate DREAM function in adult mice, we used an assembly-defective p107 protein and conditional deletion of its redundant family member p130. In the absence of DREAM assembly, mice displayed shortened survival characterized by systemic amyloidosis but no evidence of excessive cellular proliferation. Amyloid deposits were found in the heart, liver, spleen, and kidneys but not the brain or bone marrow. Using laser-capture microdissection followed
by mass spectrometry, we identified apolipoproteins as the most abundant components of amyloids. Intriguingly, apoA-IV was the most detected amyloidogenic protein in amyloid deposits, suggesting apoA-IV amyloidosis (AApoAIV). AApoAIV is a recently described form, whereby WT apoA-IV has been shown to predominate in amyloid plaques. We determined by ChIP that DREAM directly regulated Apoa4 and that the histone variant H2AZ was reduced from the Apoa4 gene body in DREAM's absence, leading to overexpression. Collectively, we describe a mechanism by which epigenetic misregulation causes
apolipoprotein overexpression and amyloidosis, potentially explaining the origins of nongenetic amyloid subtypes.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:** Epigenetics
**Research theme 3:**





**Presenter's Name:** Prasad, Kendra

**Additional Author(s):** McCord C

**Abstract Title:** Characterizing Human Papillomavirus Associated Oral Epithelial Dysplasia: An Evaluation of Biomarkers

**Abstract:**
**Introduction:** In the oral cavity, oral epithelial dysplasia (OED) is a potentially malignant condition that may progress to squamous cell carcinoma. A subset of these dysplasias has been found to be associated with high-risk strains of human papillomavirus (HPV). However, differences in behaviour between HPV OED and non-HPV OED have not been well studied. Currently, there is little research available evaluating biomarkers in HPV OED. Preliminary research conducted in cervical and head and neck carcinoma suggests that candidate biomarkers cyclin D1, retinoblastoma (Rb) and E-cadherin may show differences in expression levels between HPV and non-HPV associated cases. The objective of this study is to investigate the expression of the biomarkers cyclin D1, Rb and E-cadherin in HPV OED and non-HPV OED.

**Methods:** Cases of formalin-fixed paraffin-embedded high grade OED, from 2003-2019, demonstrating histopathological features for high-risk HPV infection and previously determined to be p16+ and HPV E6 mRNA+ by RT-PCR, were included in the HPV OED group, while sequential cases of p16- high grade OED from 2017-2019, without histopathologic features of HPV, were included in the non-HPV OED group. All cases were stained with Rb and E-cadherin by immunohistochemistry (IHC). Staining with cyclin D1 is in progress. Stains will be evaluated quantitatively using QuPath.

**Results:** 31 cases of HPV OED and 33 cases of sequential non-HPV OED met the inclusion criteria for this study. The majority of HPV OED and non-HPV cases occurred in males (87% vs 58%, respectively). The mean age of the HPV group was 55 years (ranging 36-72 years), while the mean age of the non-HPV group was 60 years (ranging 33-76 years). The most commonly affected anatomic site was the floor of the mouth for the HPV group (51.6%) and the lateral tongue for the non-HPV group (51.5%). Quantification of IHC for Rb and E-cadherin is in progress.

**Discussion:** While both OED groups show a male predominance, the relative proportion of females in the non-HPV group is much higher than in the HPV group. The most commonly affected oral subsites, the floor of the mouth for the HPV OED group, and the lateral tongue, for the non-HPV OED group, are consistent with previous reports in the literature. Results from IHC evaluation of cyclin D1, Rb and E-cadherin may highlight differences in behaviour between the two groups and provide additional support for their use as surrogate markers of high-risk HPV infection.

**Research theme 1:** Oral Biology and Medicine
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Raina, Neha

**Additional Author(s):** de Chickera S, Sidahmed AM

**Abstract Title:** Identifying non-HLA antibodies and their role in kidney transplantation outcomes

**Abstract:**
**Introduction:** The long-term success of kidney transplants is limited by the immunological barrier. The pre-transplant matching process attempts to minimize this using a HLA-centric approach. Allograft rejection, however, has been observed in patients without detectable HLA-DSAs, suggesting another player may be involved. Non-HLA antibodies may be the answer. They target cryptic antigens and are often produced in the context of injury. Despite research on this topic beginning more than a decade ago, the link between non-HLA antibodies and kidney transplant outcomes is still weak and debated. Through this preliminary study, we hope to elucidate the relationship. We hypothesize that broad sensitization against non-HLA targets is associated with poor kidney transplant outcomes with antibodies against AT1R, LG3, Vimentin, and Agrin being of particular interest.

**Methods:** To test this hypothesis, we randomly sampled 15 control patients, 15 patients with DGF post-transplant, and 15 patients with rejection post-transplant from a pool of adults who received a deceased donor kidney transplant at LHSC University Hospital between January 1, 1985, and August 31, 2021. Pre-transplant non-HLA antibody positivity against 40 targets was determined using ELISA and Multiplex Luminex assays. Data was analyzed using the Kruskal-Wallis test with post-hoc Dunn's test and Fisher's Exact test.

**Results:** The Kruskal Wallis H-test indicated that broadness of non-HLA antibody profile is associated with kidney transplant outcomes ($H(2)=7.75$, $p=0.021$). Pairwise comparisons using Dunn's test revealed that the rejection group is more broadly sensitized against non-HLA targets relative to the control group ($p=0.018$) and DGF group ($p=0.014$). Also, Fisher's exact test indicated that pre-transplant antibody positivity against Vimentin ($p=0.00144$), PECR ($p=0.0035$), Agrin ($p=0.033$), PLA2R ($p=0.00737$), IFNG ($p=0.034$), GDNF ($p=0.026$), and Fibronectin ($p=0.00737$) are associated with kidney transplant outcomes. Pairwise comparisons using Fisher's exact test with a Bonferroni-adjusted alpha level of 0.017 revealed that the rejection group was significantly more likely to test positive for anti-Vimentin antibodies pre-transplant relative to the control group ($p=0.0078$) and DGF group ($p=0.0025$).

**Discussion:** The results of this preliminary study support that pre-transplant non-HLA antibodies are associated with kidney transplant outcomes and may have predictive value.

**Research theme 1:** Regenerative and Transplantation Medicine
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Ramnarine, Jordan

**Additional Author(s):** Williams L

**Abstract Title:** Who Speaks for the River?: An Indigenous Feminist Approach to the One Health Impacts of Climate Colonialism on Two-Spirit Peoples in Deshkan Ziibi

**Abstract:**
**Introduction:** The impending climate emergency is bringing about environmental change across the globe. In Southwestern Ontario, this crisis is impacting the health of all beings that dwell along the Deshkan Ziibi. Indigenous communities, in particular, have increased vulnerability to adverse health outcomes due to the legacies of colonialism, with climate change exacerbating these harms. Two-Spirit (2S) peoples within these communities can be theorized to have disproportionate climate health impacts, due to their unique connections to the land. However, 2S peoples can also be positioned at the axes of racial and queer oppression to equitably address the climate crisis. Thus, the main objective of this project is to explore how the climate crisis is impacting the health of 2S peoples in the Deshkan Ziibi. In doing so, it also seeks to address how queer and Indigenous knowledge can be used to counteract this emergency.

**Methods:** This project takes a multi-methods approach through an Etuaptmumk lens. First, a rapid literature review will be conducted to obtain preliminary data on relevant literature and create a stakeholder map. Indigenous creation stories will also be analyzed to demonstrate the possibilities of 2S agency in the climate crisis. Next, RStudio will be used to conduct a comparative analysis between Indigenous and non-Indigenous health data. Lastly, interviews and sharing circles will be conducted with 2S participants to understand their lived experiences of health within the crisis. Indigenous principles will guide this project to ensure culturally-safe health data is being collected and used.

**Results:** The data analysis demonstrates stark health inequities between Indigenous and non-Indigenous populations. The preliminary results from the literature review show that 2S peoples are vulnerable to ecosystem disturbance and more closely feel the embodied impacts of the climate crisis on their ecosystems. The results from the interviews and sharing circles are not yet available, but will be readily shared at the Pathology and Laboratory Medicine Research Day.

**Discussion:** The findings from this project shed light on the significance of taking a One Health approach to addressing 2S health issues arising due to ecosystem disturbance. It also understands the roles that stakeholders may play in climate mitigation strategies around Deshkan Ziibi. In addition, it exemplifies the importance of amplifying 2S voices within the climate crisis.

**Research theme 1:** One Health
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Rastin, Cassandra

**Additional Author(s):** Schenkel L, Sadikovic B

**Abstract Title:** Utility of NGS Testing in Epilepsy Patients: A Two-Year Review of the LHSC Experience

**Abstract:**
**Introduction:** Epilepsy is one of the most common neurological disorders, with a global prevalence of 5-8 per 1000 people and an individual lifetime risk of up to 3%. While there are many different etiologies of epilepsy, genetic epilepsies specifically affect more than 0.4% of the general population and are estimated to be causative for approximately 30% of all epilepsies. In October 2020, the Molecular Diagnostics Program at LHSC implemented a 167 gene targeted Next Generation Sequencing (NGS) panel with copy number detection for epilepsy testing based on the recommendations of the Epilepsy Genetic Testing Program (OEGTP). Inclusion criteria for panel testing includes the completion of pre- and post-testing questionnaires, and the responses of which are stored in an internally curated database at LHSC.

**Methods:** NGS test results and questionnaire responses were reviewed (n=1290) for all samples reported from October 1, 2020 to January 31, 2023. A molecular diagnosis was defined as presence of 1 or 2 pathogenic or likely pathogenic (P/LP) variants in a single gene, depending on the mode of inheritance of the associated disorder. A possible diagnosis was defined as 2 variants of unknown significance in a clinically related autosomal recessive (AR) gene, or 1LP/1P variant in an AR gene, or the presence of a confirmed de novo variant in an AR gene. Either NGS trio testing or follow-up familial Sanger was used to confirm de novo status.

**Results:** Our findings were consistent with what has been reported by other panel-based testing in the literature with ~20% of patients receiving either a molecular diagnosis or possible molecular diagnosis, though this yield was higher in some subpopulations (ex: patients with an earlier age of seizure onset). We also identified genes that had either a high- or low-diagnostic yield.

**Discussion:** Even though genetic testing is not always part of the routine clinical workup for some patients, it has demonstrated enormous potential not only to confirm diagnosis but also to guide clinical management and treatment. These results highlight the utility of targeted NGS panel testing in patients with epilepsy, particularly in patients with an earlier age of onset. As this targeted NGS panel was also able to detect copy number variants (CNVs), later confirmed by microarray, it may lead to a reduction in the length of the diagnostic odyssey for some patients.

**Research theme 1:** Test Utilization, Optimization and Quality Assurance
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Ratushny, Liam

**Additional Author(s):** Passos DT, Howlett C, Dick FA.

**Abstract Title:** Investigation of molecular mechanisms of the cancer cell cycle and their impact on treatment resistance and disease progression

**Abstract:**
**Introduction:** With breast cancer the world's most prevalent cancer, limiting the advancement of this disease is a significant clinical issue. This is difficult since mechanisms that allow tumor cells to survive and proliferate at secondary sites are unclear. Experimental models have confirmed disseminated tumor cells (DTCs) can enter dormancy and resist chemotherapy. This dormancy implies a counter-intuitive growth arrest to enhance survival. These findings suggest dormant DTCs are critical to tumor recurrence in breast cancer.

Impaired DREAM assembly in ovarian cancer cell lines compromises cell viability under dormant conditions. The DREAM complex contains DP, Rb-like protein (p130, p107), E2F, and MuvB. This multi-protein complex represses gene promoters and maintains cellular quiescence in dormancy. DYRK1A phosphorylates the MuvB core that binds to p130/p107 to mediate DREAM assembly. DYRK1A deletion/inhibition or p130 deletion causes a loss of cell cycle dependent gene repression, loss of cellular quiescence, and cell death in dormant culture conditions.

I hypothesize the loss of DREAM assembly in breast cancer cells will impair survival of DTCs and reduce development of secondary tumors.

**Methods:** To test if DREAM deficiency disrupts dormancy and diminishes TNBC spread, a xenograft mouse model will be used to recapitulate pulmonary spread of TNBC. Mice will receive tail vein injections of p130-KO, DYRK1A-KO, or unmodified breast cancer cells. One control group will receive CX-4945 treatments, a kinase inhibitor with DYRK1A inhibitory capabilities. Investigating DYRK1A inhibition/loss and comparing metastatic spread will offer valuable insights into the role of DYRK1A inhibitors as a potential treatment to minimize metastatic spread.

**Results:** Preliminary xenograft experiments identified that mice that received xenografts of p130-KO breast cancer cells exhibited lower rates of metastasis as well as smaller metastatic nodules when compared to those that received unmodified cells.

**Discussion:** Identifying a potential mechanism through which circulating breast cancer cells can enter a dormant state to enhance survival, is an exciting new therapeutic target. These findings will elucidate molecular mechanisms disseminated tumor cells use to enhance survival and potentially identify novel therapeutic targets that can limit metastatic spread and improve overall patient outcomes.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Ravichandran, Sevanthi

**Additional Author(s):** Bhattacharjee R

**Abstract Title:** Efficacy of repositioned drugs in the management of renal ischemia reperfusion injury using sIRI-cold and sIRI-RT in vitro models

**Abstract:**
**Introduction:** During kidney transplantation, the organ undergoes ischemia reperfusion injury (IRI) which is a result of the loss of oxygen followed by reintroduction of oxygen and is characterized by the release of a cytokine storm, multiple inflammatory pathways, and reactive oxygen species. This ultimately leads to advanced cell death and blood clotting, resulting in decreased graft function. While research has shown that oxygenated perfusion at 22°C is superior to the current clinical standard, static cold storage, there is still significant room for improvement. In addition to oxygenated perfusion, pharmacological agents may be used during perfusion to further reduce the effects of IRI. As there are currently no in vitro models that accurately represent the events during a transplant, the use of animal or human models for drug screening can be both costly and time-consuming. Therefore, our lab aims to develop and characterize a cold and room temperature injury model that can be used for large-scale drug screening to identify pharmacological agents that can be used in conjunction with machine perfusion at room temperature.

**Methods:** 1) Established and contrasted an in vitro hypoxia-anoxia-reoxygenation (HAR) injury model using human tubular epithelial cells at both 4°C and room temperature, 2) Characterized the levels of cell death, inflammation, and innate immune activity under conditions of HAR injury, and 3) Compare the expression of the aforementioned factors following treatment of 20 selected drugs on the in vitro HAR models.

**Results:** Successfully developed room temperature model demonstrated to be superior to previously developed cold model in terms of cell death, inflammation, and innate immune activity. To validate the effectiveness of the room temperature model, several techniques were used, which generated consistent and strong results. Findings suggest that the room temperature model is effective in reducing the damage caused by IRI during kidney transplantation. In addition, preliminary screenings of six drugs on the model already indicate one drug that may have a protective effect against IRI.

**Discussion:** The development of a successful drug screening model could have significant implications for the field of transplantation and the medical community. By reducing the effects of IRI, we can increase the number of viable donor kidneys available for transplantation and improve the long-term outcomes for patients.

**Research theme 1:** nfection, Immunity, and Inflammation
**Research theme 2:** Regenerative and Transplantation Medicine
**Research theme 3:**





**Presenter's Name:** Richmond, Julie

**Additional Author(s):** Cecchini MJ

**Abstract Title:** Malignant mesothelioma of the omentum: a case report

**Abstract:**
**Introduction:** Malignant mesothelioma develops commonly in the pleura and can rarely occur in the peritoneum. Mesothelioma arises from the mesothelial cells that line the pleura and peritoneum. The omentum, a fold of peritoneum, is subjected to this malignancy despite its rarity.

**Case History:** The patient of 36 years presented with persistent abdominal pain since February 2021. The CT scans revealed scarring of the omentum and polyps within the gallbladder. Following this discovery, a cholecystectomy was performed, and omental biopsies were taken for lymphoma protocol. These biopsies showed inflammation with no underlying cause. The abdominal pain persisted. This warranted an omentectomy for diagnostic and therapeutic effect.

**Discussion:** The gross appearance was limited to a slight inflammation of the omentum with areas of nodularity. No distinct mass could be seen. Representative sections of the nodules were submitted after consultation. The differential diagnosis for this case relied heavily on the histological examination with specific staining, making the selection of tissue submitted a crucial part of the gross. This case report highlights a rare form of malignancy with minimal gross findings to contribute to the final diagnosis.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Rooney, Kathleen

**Additional Author(s):** van der Laan L, Trajkova S, Haghshenas S, Relator R, Lauffer P, Vos P, Levy MA, Brunetti-Pierri N, Terrone G, Mignot C, Keren B, de Villemeur TB, Volker-Touw CML, Verbeek N, van der Smagt JJ, Oegema R, Brusco A, Ferrero GB, Misra-Isrie M, Hochst

**Abstract Title:** DNA methylation episignature and comparative epigenomic profiling of HNRNPU-related neurodevelopmental disorder.

**Abstract:**
**Introduction:** HNRNPU haploinsufficiency is associated with a neurodevelopmental disorder (NDD) referred to as Developmental and Epileptic Encephalopathy 54. This neurodevelopmental disorder is characterized by developmental delay, moderate to severe intellectual disability, speech impairment, and early onset epilepsy often refractory to treatment. We performed genome-wide DNA methylation analysis in a cohort of individuals to develop a clinical diagnostic biomarker and gain functional insights into the molecular pathophysiology of HNRNPU-related disorder.

**Methods:** DNA methylation profiles of individuals carrying pathogenic HNRNPU variants, identified through an international multi-center collaboration, were assessed using Infinium Methylation EPIC BeadChip arrays. The episignature was validated using an independent set of cases with pathogenic and uncertain significance HNRNPU variants. Statistical and functional correlation analyses were performed comparing the HNRNPU cohort to 56 rare disorders with previously reported DNA methylation episignatures.

**Results:** A robust and reproducible DNA methylation episignature and a global DNA methylation profile were identified. Correlation analysis identified partial overlap and similarity of the global HNRNPU DNA methylation profile to several other rare disorders.

**Discussion:** This study demonstrates new evidence of a specific and sensitive DNA methylation episignature associated with pathogenic heterozygous HNRNPU-variants, establishing its utility as a clinical biomarker for the expansion of the EpiSignTM diagnostic test.

**Research theme 1:** Epigenetics
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Ryan, Sarah

**Additional Author(s):** Zeng PYF, Barrett JW, Nichols AC

**Abstract Title:** Two Steps Forward: A New Generation of Targeted Therapy in Anaplastic Thyroid Cancer

**Abstract:**
**Introduction:** Anaplastic Thyroid Cancer (ATC) is rare but highly lethal. There is a high level of macrophage infiltration in ATC, a negatively prognostic sign. ATC is typically inoperable and resistant to chemoradiation. Advancements in targeted therapy have increased 5-year survival. Prominent mutations in ATC can occur in the MAPK pathway, including BRAF and RAS. Patients with BRAFV600E positive tumors are eligible for treatment with a RAF inhibitor (RAFi), Dabrafenib. Not all BRAFV600E patients respond to Dabrafenib, and in responders' resistance and disease progression are inevitable. RAS mutant ATC lines experience paradoxical growth and MAPK activation following RAFi treatment, making some patients ineligible. Second generation RAFi have been developed with different BRAF binding dynamics. One showed great efficacy at attenuating cell proliferation in BRAF and RAS mutant ATC cell lines. We hypothesize our drug of interest (DOI) will attenuate cell and tumor growth further than Dabrafenib in both BRAF and RAS mutant ATC in-vitro and in-vivo models.

**Methods:** BRAF and RAS mutant human and BRAF mutant murine ATC cell lines were cultured. Human lines were treated with Dabrafenib or DOI. Cells were lysed and applied to phosphor-MAPK antibody arrays. Densitometry was performed on resulting images to quantify levels of phospho-MAPK protein expression. Results were verified using fluorescent microscopy using antibodies specific for downstream MAPK proteins MEK1/2 and phosphor-MEK1/2. Murine lines were treated with Dabrafenib and second-generation RAFi in a cell proliferation assay to compare 50% inhibitory concentration (IC50). A murine line was then selected for implantation into an immunocompetent mouse. 20 mice were allocated to 4 groups: control, DOI, macrophage depletion, macrophage depletion and DOI. Tumor volume will be measured.

**Results:** Antibody arrays and fluorescent microscopy both show greater attenuation of MAPK signaling in cells following DOI treatment compared to Dabrafenib. Our DOI had the lowest IC50 of all agents in all murine lines, similar to results in human lines. Syngeneic mouse experimentation is ongoing.

**Discussion:** These findings demonstrate the increased capacity of our DOI in inhibiting cell proliferation and MAPK signaling in both BRAF and RAS mutant ATC lines compared to Dabrafenib. Future work aims to explore DOI mechanisms through RNA sequencing and proteomic analysis of Dabrafenib and drug of interest treated cell lines.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Shaker, Nader

**Additional Author(s):** Darling M

**Abstract Title:** Expression of S100A7 in verrucous hyperplasia

**Abstract:**
**Introduction:** Verrucous hyperplasia (VH) is an oral potentially malignant disorder (OPMD). Common sites include buccal mucosa (48%), tongue (20%), palate (18%), gingiva (7%) and labial mucosa (7%). 5-year malignant transformation rate is 10%. Histological assessment of a biopsy of VH with evidence of dysplasia is considered the gold standard for determining the risk of malignant transformation. However, a common difficulty with dysplasia grading is that the three grades are not good predictors of cancer progression due to extensive overlaps between the mild, moderate and severe groups. There is a tremendous need to identify molecular biomarkers that can be used to predict progression of OPMD to oral squamous cell carcinoma (OSCC). Early diagnosis can improve patient survival and reduce the high mortality rates of OSCC. S100A7 is a promising biomarker in early detection for OSCC, it activates the p38 mitogen-activated protein kinase and RAB2A signaling pathway. Mcm-2 and geminin are DNA licensing proteins that are present in the cell cycle that can be used to predict malignant transformation of OPMD such as VH. Straticyte TM test is a method to quantify the expression of S100A7 and provide a quantitative model for prediction of risk of oral cancer from pre-malignant lesions

**Methods:** A retrospective review of the department of pathology and laboratory medicine's archives will be completed to examine patients 'histological slides with a diagnosed of VH from January 1st, 2006 until January 1st, 2016. Immunostaining of the formalin-fixed paraffin embedded tissues (FFPE) with antibodies against S100A7, Mcm-2 and geminin. Straticyte TM test will be used to quantify the expression of S100A7 and provide a quantitative model for prediction of risk of OSCC from VH.

**Results:** Results are to be determined. It is expected that S100A7 protein expression is elevated in VH that progressed to OSCC. Also, Straticyte TM test is a reliable predictor of the risk of VH transformation to OSCC.

**Discussion:** No studies have looked at S100A7 expression in VH. The data from this study will help guide future clinical decision making in the treatment of VH to help improve patient outcomes and reduce patient morbidity and mortality.

**Research theme 1:** Cancer Biology
**Research theme 2:** Oral Biology and Medicine
**Research theme 3:**





**Presenter's Name:** Sun, Gracie

**Additional Author(s):** Schonberger Z, Oloriegbe M, Frisbee S

**Abstract Title:** Evaluation of the gaps in the continuum of stroke care in southwestern Ontario across the three pillars of clinical care, advocacy, and research – A qualitative needs-assessment study

**Abstract:**
The three pillars of stroke care consist of clinical care, advocacy and research. Along these pillars coexists a continuum of stroke care ranging from acute care, rehabilitation, prevention, and community support. The South Western Ontario Stroke network currently consists of seven healthcare units which all operate independently from one another, but are united by a regional stroke centre which refers current and previous patients to regional services for only healthcare; thus, there are gaps in collaboration between the research and advocacy pillars despite serving the same communities. In comparison, model programs such as the Ottawa Stroke program integrate all three pillars in a centralized network address the full range of patients needs before, during, and after stroke care. In Southwestern Ontario, a fully integrated academic stroke centre seeks to fulfill the remaining two pillars and address the needs of key community stakeholders. The goal of the study is to improve stroke outcomes for patients in Southwestern Ontario by filling gaps in advocacy, research, education, and clinical care along the continuum of stroke care. As such, a qualitative interview study will be performed to assess the needs of healthcare providers, community programming providers, and researchers across five different Southwestern Ontario sites (Windsor, Stratford, Strathroy, St Thomas, Chatham, Sarnia). Interviews will be conducted both in-person and through Zoom and participants will be asked questions regarding their experiences in four major areas of care: research, advocacy and education, and prevention and rehabilitation. Questions seek to highlight what areas of strengths and weaknesses of current programming and identify spaces where an academic stroke centre can be well-integrated. To shape these spaces, interview transcripts will be coded by research team members using a phenomenological approach to understand the provision stroke care from those with lived experience and address the needs of service providers from a holistic level.

**Research theme 1:** Test Utilization, Optimization and Quality Assurance
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Taray-Matheson, Danielle

**Additional Author(s):** Diao H, Collings S, McLoughlin A, Zheng X, Gunaratnam L, Ronald J, Min W

**Abstract Title:** The role of TEX-derived circHUWE1 in prostate cancer migration and metastasis

**Abstract:**
**Introduction:** Tumour-derived exosomes (TEXs) display enhanced expression of tumour antigens, and can be used in cancer treatment, either directly or by stimulating dendritic cells (DCs) for DC-based cancer vaccines. Circular RNAs (circRNAs) exert their functions by acting as microRNA (miRNA) sponges or altering parental gene translation. We have previously shown that circHUWE1 is differentially expressed in highly metastatic (Met-high) prostate cancer (PCa) cells compared to low metastatic (Met-low) PCa cells. In the present study, we attempt to assess the role of TEXs in tumour metastasis, and elucidate the mechanisms by which circHUWE1 may modulate prostatic cancer pathogenesis. We hypothesize that circRNA in TEXs promotes tumour cell proliferation, migration, and invasion. Therefore, manipulating TEX-derived circRNA (ex. circHUWE1) should reduce tumour cell proliferation/migration/invasion, and metastasis.

**Methods:** Met-high (PC3) and Met-low (LNCaP) cells were cultured in RMPI-1640 medium supplemented with 10% fetal bovine serum at 37°C, 5% CO2. PCa cells were transfected with circHUWE1 siRNA, HUWE1 siRNA, and C-MYC siRNA using Endofectin transfection reagent. Exosomes from PC3 and LNCaP cells were isolated using ultracentrifugation. Exosomes were then characterized by detection of an exosomal marker, CD63, using Western blot. The cellular and exosomal expressions of circHUWE1, HUWE1, and C-MYC were analyzed using qPCR and Western Blot. A scratch assay was used to assess cell migration.

**Results:** Knockdown of circHUWE1, HUWE1, and C-MYC in PC3 cells using siRNA transfection significantly reduced the mRNA levels compared to control, as confirmed by qPCR. Exosomes were successfully isolated from both serum-free and normal cell culture supernatant of PCa cells, as confirmed by the presence of CD63 in the exosome protein samples. 600ng of exosomal RNA and 150□g of exosomal protein were isolated from 100mL of culture medium (approximately 60 million PC3 cells). circHUWE1, HUWE1, and C-MYC mRNA levels were detectable in both the PC3 cells and exosomes. Preliminary results from the scratch assay showed knockdown of HUWE1 and C-MYC inhibited migration of PC3 cells compared to untransfected controls.

**Discussion:** Understanding the contribution and mechanism of circHUWE1 in TEXs to PCa progression may allow for the development of targeted therapeutics. Modulated TEXs may be used to prevent tumour metastasis and improve anti-cancer therapy.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Trautrim, Erik

**Additional Author(s):** Hammond R.

**Abstract Title:** The value of genetic panels in a case of pediatric Spitzoid melanoma

**Abstract:**
**Introduction:** Pediatric melanoma is a rare malignancy. Normally associated with excessive ultraviolet (UV) light exposure in adults, melanoma occurs in children who have underlying genetic conditions. Determining the genetic and molecular bases for such pediatric occurrences requires immunohistochemical analysis and molecular examination of tumour genetics. Ruling out the various etiologies of pediatric melanoma is done by a hereditary cancer panel (HCP) that determines whether genes that predispose hereditary familial melanoma (HFM) are mutated. Further genetic analysis of possible germline mutations, like those on PTEN and BRAF are used to rule out Bannayan-Riley-Ruvalcaba syndrome, Parkinson's disease, Lhermitte-Duclos disease and Cowden syndrome.

**Case:** An 11-year-old patient presented with a subcutaneous mass at the dorsum of the left hand. The rate of growth of the subcutaneous mass was substantial in the months leading up to a partial left-hand amputation. Examination revealed the mass to be infiltrative and multinodular with extension into underlying fibrotendinous and soft tissues. Necrosis with large polygonal cells showed 27 mitoses per squared millimeter. Vascular invasion was identified given the presence of tumour cells within the lumen. Upon molecular examination, evidence of a TERT gene promoter mutation and CDKN2A gene homozygous deletion was revealed. More significantly, a nonsense PTEN mutation was found that is common in those with Cowden syndrome. HFM was also ruled out following the sequencing of 8 commonly associated genes.

**Discussion:** The diagnostic features of spitzoid melanoma are appreciated under histologic and molecular examination. Genetic screening is useful for determining prognosis, as well as for screening of family in the case of HFM. As the mutations underlying pediatric melanoma vary greatly, careful genetic assessment provides improved patient care and intervention.

**Research theme 1:** Epigenetics
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Twible, Carolyn

**Additional Author(s):** Zhang Q

**Abstract Title:** Characterizing the hippocampal dentate gyrus involvement in temporal lobe epilepsy

**Abstract:**
**Introduction:** Hippocampal sclerosis (HS) is the most common pathology finding for drug-resistant temporal lobe epilepsy (TLE). HS is diagnosed by identifying pyramidal neuronal loss and gliosis in Cornu Ammonis (CA). Dentate gyrus (DG) is the critical entry point to the hippocampus and is the only site with adult neurogenesis. However, changes in DG are not included in the current diagnostic criteria of HS. In this study, we will characterize the morphological and genomic features of the hippocampal DG in TLE patients and investigate the underlying epileptogenic mechanisms.

**Methods:** Twenty-one TLE surgical resection cases (14 HS, 7 no-HS) and 10 control cases (4 non-TLE epilepsy control, 6 non-epilepsy control) were included. QuPath software was used to perform morphometry analysis on the DG, including Delaunay mean, cellular density, nuclear size and circularity. The DG of 18 selected TLE cases were micro dissected and underwent gene expression profiling, using NanoString targeted panels (1400 genes, targeted Neuroinflammation and Glial profiling panels). Histopathological diagnosis and post-operative outcome were included for clinicopathological correlation.

**Results:** 1) HS patients show a significant increase in granule cell (GC) spacing and decrease in GC density within the DG compared to no-HS patients. 2) Regardless of the clinical diagnosis, patients achieved seizure freedom post-operatively (Engel outcome scale 1) demonstrated an increase in GC spacing and decrease in GC density in comparison to patients without significant seizure reduction. 3) The DG of HS patients demonstrated significant complement system activation, increased gliosis (both A1 & A2 astrocytes) and apoptosis; but decrease in neurogenesis and neuronal populations.

**Discussion:** Dentate gyrus has distinct morphometric features and gene expression in TLE patients, suggesting an important role in epileptogenesis.

**Research theme 1:** Digital Pathology
**Research theme 2:** Pathobiology of Neurologic Diseases
**Research theme 3:**





**Presenter's Name:** Wang, Andrew

**Additional Author(s):** Tran C, Wilsdon D, Walsh JC, Goebel EA, Sansano I, Sonawane S, Cockenpot V, Mukhopadhyay S, Homer RJ, Taskin T, Zahra N, Cima L, Semerci O, Ozamrak BG, Mishra P, Vennavalli S, Cecchini MJ.

**Abstract Title:** Assessment of Pathology Domain Specific Knowledge of ChatGPT and Comparison to Human Performance.

**Abstract:**
**Introduction:** Artificial intelligence algorithms hold the potential to fundamental change/disrupt many aspects of society. These algorithms, including the publicly available ChatGPT, have demonstrated impressive domain specific knowledge in many areas including medicine. Pathology training requires understanding and mastery of complex concepts across a large area of topics, which can be one of the most challenging aspects of residency training. We sought to understand the level of pathology domain specific knowledge for ChatGPT in pathology.

**Methods:** An international group of pathologists (n = 15) were recruited from around the world to generate pathology specific questions at similar level to those that could be seen on licencing (board) exams. The questions (n=15) were answered by both ChatGPT and a staff pathologist that has recently passed their licencing exams in Canada. The participants were asked to score answers out of five and predict which answer was written by ChatGPT.

**Results:** ChatGPT was able to perform at a similar level to a staff pathologist with no statistical difference between the two groups. The overall score for both was within the range of meeting expectations for a trainee writing licencing exams. In the interim analysis, ChatGPT scored higher in 9 (of 15 questions). In all but one question, the reviewers were able to correctly identify which answer was written by ChatGPT.

**Discussion:** ChatGPT is able to perform at similar levels to a trained pathologist in pathology domain specific knowledge. This highlights the potential of these tools to be transformative in this space. These tools can be used to enhance pathology resident training and highlights a future for advanced algorithms with increased domain specific knowledge that can assist pathologists.

**Research theme 1:** Interdisciplinary Research in Health and Education
**Research theme 2:** Test Utilization, Optimization and Quality Assurance
**Research theme 3:**

**Presenter's Name:** Wang, Tan Ze

**Additional Author(s):** Zheng X

**Abstract Title:** Role of circular RNA ASPH in macrophage polarization and response in sepsis

**Abstract:**
**Introduction:** Circular RNAs (circRNAs), a novel non-coding RNA species generated by back-splicing, has been shown to participate in gene regulation of leukocytes. We have previously identified circular RNA ASPH (circASPH) to be highly expressed in peripheral blood mononuclear cells of sepsis patients at the start of intensive care. Macrophages, as ubiquitous innate immune cells, are responsible for the recruitment of other immune cells at sepsis onset. Thus, we hypothesize that circASPH participates in the regulation of macrophage polarization and function in sepsis.

**Methods:** We treated PMA-differentiated THP-1 cells with IFNy+LPS, IL-4, or various concentrations of LPS for various durations, and measured circASPH expression through quantitative PCR. We also knocked down circASPH levels through siRNA transfection prior to IFNy+LPS or IL-4 stimulation, and measured cytokine and transcription factor expression through quantitative PCR.

**Results:** CircASPH expression in PMA-differentiated THP-1 cells were slightly increased by lower LPS concentrations and decreased by higher LPS concentrations or longer treatment times. Stimulation with IFNy+LPS and IL-4 for 24 h significantly increased circASPH expression. Knockdown of circASPH prior to IFNy+LPS stimulation resulted in reduction of M1 cytokines and transcription factor STAT1, while knockdown of circASPH prior to IL-4 stimulation resulted in upregulation of ALOX15 by 24 h and reduction of CCL17 by 48 h.

**Discussion:** These results suggest a proinflammatory role of circASPH in macrophage polarization, which agrees with our previous observation of elevated circASPH levels in septic PBMCs. These findings support the potential of circASPH as a novel biomarker or therapeutic target for sepsis.

**Research theme 1:** Infection, Immunity, and Inflammation
**Research theme 2:**
**Research theme 3:**





**Presenter's Name:** Zakirova, Komila

**Additional Author(s):** Zakirova K, Dick FA.

**Abstract Title:** Identification of molecular mechanisms of spheroid dormancy in epithelial ovarian cancer

**Abstract:**
Metastatic dissemination of cancer cells is the major contributor to the mortality in epithelial ovarian cancer (EOC). Advanced stage EOC is characterized by the accumulation of ascites where these cells aggregate to form multicellular clusters, or spheroids. EOC spheroids become dormant by exiting cell cycle and as a result insensitive to chemotherapy. The persistence of drug-resistant cancer cells remains a major challenge in successful treatment of EOC and highlights the importance of elucidating the molecular mechanisms required for the formation and viability of spheroids. To identify genes and pathways that contribute to spheroid dormancy, genome-wide CRISPR knockout screens were performed in three EOC cell lines, iOvCa147, OVCAR8 and TOV1946. Bioinformatic analysis of the screens revealed a list of approximately 2500 genes needed for survival in non-adherent conditions and shared among these three cell lines. Pathway analysis identified enrichment of canonical Wnt signaling genes. Canonical Wnt pathway is known to be implicated in various cancers, however its role in EOC pathogenesis is not well studied. In the current study, we investigate the functional role of Wnt signaling in the context of EOC spheroid formation and metastatic potential. Inhibition of Wnt signaling using Porcupine inhibitor was found to have a negative effect on spheroid viability in three-dimensional culture conditions. Also, we observed a downregulation of stem cell marker gene ALDH1A1 in response to canonical Wnt signaling inhibition, suggesting stemness and self-renewal capacity of ovarian cancer spheroids regulated by Wnt.

**Research theme 1:** Cancer Biology
**Research theme 2:**
**Research theme 3:**

**Presenter's Name:** Zeng, Peter

**Additional Author(s):** Lin RJ, Khan H, Elkadri L, MacNeil D, Fung K, Yoo J, Mendez A, Barrett JB, Nichols AC

**Abstract Title:** The clinical, transcriptomic, and cellular architecture of idiopathic subglottic stenosis

**Abstract:**
First described in 1972, idiopathic subglottic stenosis (iSGS) is a devastating orphan disease characterized by recurrent and progressive scarring of the lower laryngeal and upper tracheal airway. The scarring leads to narrowing of the breathing passage and potentially life-threatening dyspnea in otherwise healthy individuals. Current standard treatment for iSGS is surgical dilatation or resection of the stenotic airway, but surgery is rarely curative, and many patients require repeat treatments. Consequently, iSGS poses a significant burden on both the individual patient and the healthcare system. Clinical and molecular studies of iSGS is challenging due to the low incidence (1:400,00) of the disease. Through a nation-wide consortium, we prospectively enrolled a large number of iSGS patients and healthy controls. We performed bulk RNA sequencing (RNA-seq) analysis of a total of 71 matched epiglottic-subglottic tissue from 71 iSGS patients, 25 epiglottic-subglottic pairs from healthy control patients, and 1 pair of epiglottic-subglottic tissue from an intubation-induced SGS patient. Bulk RNA-seq identified several putative diagnostic biomarkers and are aiming to translate them into clinical use. Single cell RNA-seq identified a group of basal keratinocytes distinct from other basal keratinocytes that were enriched in the iSGS subglottis and a group of club cells that was enriched in both traumatic and iSGS subglottic tissue but not control epiglottic tissue. Interestingly, the club cells and to a lesser degree the basal keratinocytes expressed a high abundance of estrogen related transcript including ESRRG and ERBB4. Deconvolution of our bulk RNA-seq data revealed that iSGS tissues were enriched in total leukocytes, granulocytes, and fibroblasts, while healthy controls were enriched in club cells. The paucity of club cells in iSGS tissue relative to both healthy control and traumatic SGS is intriguing as they play important roles in the integrity and regeneration of the airway epithelium. Taken together, our integrative large-scale analyses of implicated important transcriptional programs and cell subsets that will springboard future molecular characterization and nominate potential targetable pathways in this challenging disease.

**Research theme 1:** Cardiovascular, Respiratory Health, and Metabolic Diseases
**Research theme 2:**
**Research theme 3:**

PATHOLOGY AND LABORATORY MEDICINE

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