PATHOLOGY AND LABORATORY MEDICINE

RESEARCH DAY 2026

ABSTRACTS

Platform & Posters

Abstract: 1

Presenter's Name: Hong, Megan

Additional Author(s): Hong MMY, Figueredo R, Cheung T, Davidson C, Maleki Vareki S

Abstract Title: Macrophages as drivers of immune checkpoint inhibitor response in immune-hot DNA mismatch repair-deficient tumours

Abstract:
Introduction: Immune checkpoint inhibitors (ICIs) such as anti-PD1 and anti-CTLA4 enhance patients' anti-tumour immune responses to eliminate cancer cells. Notably, response to anti-PD1 therapy is higher in patients with DNA mismatch repair-deficient (dMMR) tumours due to the increased presence of intratumoural T-cells than those with MMR-proficient (pMMR) tumours. However, more than half of these patients do not respond to anti-PD1 therapy, suggesting that T-cell abundance alone is not a reliable predictor of therapeutic success. Macrophages are the most abundant immune cell in solid tumours that can promote or suppress anti-tumour T-cell responses. Yet, their role in the therapeutic response to ICIs in dMMR cancers remains poorly understood. This study investigates how MMR deficiency in cancer cells alters macrophage function and its consequent impact on the response to anti-PD1 therapy.

Methods: MMR repair deficiency was induced in the murine neuro-2a, 4T1, and CT26 cell lines by knocking out Mlh1 expression using CRISPR/Cas9. pMMR or dMMR tumours were grown in immunocompetent syngeneic mice and treated with anti-PD1 once tumours became palpable. Macrophages were depleted with anti-CSF1R to assess their role in the response to ICIs. Tumour volumes were monitored longitudinally and immunophenotyped by flow cytometry.

Results: MMR deficiency sensitized 4T1 tumours to anti-PD1 therapy, whereas dMMR neuro-2a and CT26 tumours remain resistant, despite high T-cell infiltration. Anti-PD1-sensitive dMMR 4T1 tumours exhibited an enrichment of pro-inflammatory M1-like macrophages alongside activated CD8 T-cells, a characteristic absent in anti-PD1-resistant dMMR CT26 and neuro-2a tumours. This divergence suggests that specific macrophage populations may drive anti-PD-1 sensitivity by modulating T-cell activation. Reprogramming macrophages in anti-PD1-resistant dMMR tumours with anti-CSF1R expands tumour-specific cytotoxic CD8 T-cells and sensitizes tumours to anti-PD1 therapy.

Discussion: These findings identify macrophages as a critical determinant of anti-PD1 responsiveness in dMMR tumours, independent of T-cell abundance. Targeting macrophages in the tumour immune microenvironment may therefore represent a strategy to enhance response to ICI therapy in dMMR cancers.

Keywords: DNA mismatch repair, Immunotherapy, Immune checkpoint inhibitors, T-cells, Macrophages

PLATFORM SESSION 1

Abstract: 2

Presenter's Name: Houpt, Jacob A.

Additional Author(s): Ang LC

Abstract Title: Unusual Neuropathological Findings in Cases of Unexpected Death with No Apparent Anatomical Causes

Abstract: Sudden unexpected death caused by central nervous system (CNS) pathologies is rare when compared to cardiovascular causes, and includes acute vascular compromise (hemorrhage, infarct), mass effect/obstructive phenomena causing hydrocephalus/cerebral edema/herniation, traumatic injuries causing diffuse axonal injury/pontomedullary rent, and sudden unexpected death in epilepsy (SUDEP). Sudden death in the context of multiple system atrophy (MSA) and Parkinson's disease has also been described and, as several of the aforementioned etiologies are thought to involve injury to respiratory/autonomic centres, the potential for other neurological conditions to mediate similar dysfunction at these centres might be considered in cases of unexpected death with no apparent anatomical cause.

Adult autopsy cases referred to neuropathology at LHSC over the previous 20 years were investigated, screening for those with unexpected death without an apparent anatomical cause of death at time of autopsy. Cases with acute intracranial hemorrhages, infarcts, evidence of head trauma, diffuse vascular/axonal injury, pontomedullary rent, mass effect phenomena (such as brainstem herniation) were excluded, as were those with any history of seizures to account for SUDEP cases.

A total of 11 cases fulfilled the criteria, almost all of which involved considerable neurodegenerative disease findings. These included MSA, multiple sclerosis, and tauopathies such as progressive supranuclear palsy (PSP), Saito stage 3 argyrophilic grains disease (AGD), and high level (A3B3C3) Alzheimer's disease. One case of diffuse Lewy body disease and one with a diffuse high-grade glioma were also examined. All cases demonstrated marked involvement of either the hypothalamus (4/11), pontomedullary brainstem (5/11), or both (2/11) by the predominating neuropathological disease process.

Cases of unexpected death lacking an apparent anatomical cause of death were associated with myriad disease findings, but despite dissimilar pathological processes, all featured respiratory/autonomic centre involvement at sites thought to be implicated in sudden death in MSA and other diseases. Although rarely the sole possible consideration, the potential for CNS pathologies to cause sudden unexpected death, particularly due to severe hypothalamic/brainstem involvement by neurodegenerative disease or extensive tumour infiltration, should be entertained in the absence of an apparent anatomical cause of death.

Keywords: Sudden unexpected death in neurological disease, Forensic neuropathology, Mechanisms of CNS causes of sudden unexpected death, Hypothalamic compromise, Central hypoventilation

Abstract: 3

Presenter's Name: Derakhshan Nazari, Mohammad Hossein

Additional Author(s): Larsen FV, Derouet M, Shooshtari P, Asfaha S.

Abstract Title: Single-Cell Profiling Identifies an Aberrant Epithelial–Stromal Regenerative Niche Linked to Colitis-Associated Cancer

Abstract:
Background: Inflammatory bowel disease (IBD) comprises chronic, relapsing inflammatory conditions of the gastrointestinal tract. IBD, if not managed, can lead to colitis-associated cancer (CAC), a form of colorectal cancer. Mouse models are widely used to study IBD, yet they differ in how closely they reflect human disease. Notably, when treated with the carcinogen azoxymethane, only dextran sodium sulfate (DSS)–induced colitis progresses to CAC, whereas other commonly used models do not. The cellular and molecular basis for this difference remains unclear. Here, we used single-cell RNA sequencing (scRNAseq) to compare intestinal cell states across multiple colitis models and identify features that may underlie CAC susceptibility. Methods: Healthy controls alongside DSS-, TNBS-, oxazolone (Oxa)-, or Citrobacter rodentium (Cr)-induced Colitis were used (n = 16). Disease induction was confirmed by colon length, histology, and myeloperoxidase activity. Approximately 8,000 distal colon cells per mouse were profiled by scRNAseq. Data processing steps included removing ambient RNA, doublet cells and batch effects, followed by cell type identification using unsupervised clustering and marker-based annotation. Gene set enrichment analysis compared biological processes across models. Results: scRNAseq retained 39,662 epithelial and 19,744 stromal cells. DSS and Oxa showed marked loss of mature enterocytes, while Cr colitis showed epithelial hyperplasia. A distinct epithelial population emerged in DSS, TNBS, and Oxa, expressing pancreatic exocrine enzymes (Cela2a, Cpa1, Prss2, Cel, Pnlip) alongside embryonic regenerative markers (Reg3a, Reg2). GSEA indicated enrichment of proteolytic and metabolic pathways, consistent with an exocrine-like regenerative state. Stromal analysis revealed DSS-specific remodeling, including loss of homeostatic fibroblasts and expansion of inflammatory subsets: Cxcl13+ and Cxcl5+ interstitial fibroblasts, Cxcl5+Ptx3+ Trophocytes, and Cxcl13+Cxcl5+ Telocytes. Discussion: DSS colitis is uniquely characterized by coordinated epithelial and stromal changes. The emergence of exocrine-like regenerative epithelial cells suggests an injury-driven repair program. Concurrent expansion of fibroblast subsets expressing Cxcl13, Cxcl5, and Ptx3, genes involved in immune recruitment and tissue repair, points to a mesenchymal niche that supports regeneration. These interactions may promote aberrant repair and explain why CAC develops selectively in DSS.

Keywords: Inflammatory bowel disease (IBD), Colorectal cancer (CRC), Single-cell RNA sequencing (scRNAseq), Mouse models of colitis

PLATFORM SESSION 1

Abstract: 4

Presenter's Name: Li, Hao

Additional Author(s): Patel D, Zhang Q

Abstract Title: An internal audit of neuropathology consultation for forensic/coroner's autopsies at London Health Sciences Centre – a quality improvement project

Abstract:
Introduction: As Neuropathology involvement in autopsy is relatively resource-intensive, an organized system of practice management is beneficial. In this quality improvement initiative, we present the utility of a centralized neuropathology forensic/coroner's autopsy database as an internal audit for laboratory management purposes.

Methods: The database is a retrospective digital spreadsheet recording on all LHSC regional forensic pathology unit forensic/coroner's neuropathological autopsy consultations from 2018 to 2023 (based on availability of data, total 425 cases) the following parameters: in-house vs. externally-referred, reason for neuropathology consultation, specimens examined (eg. brain, spinal cord, eyes, muscle), entire organ vs. representative tissue retention, age at death, dates of autopsy / brain cut / sign-out, involvement of trainees, final diagnosis, and contribution of the neuropathological diagnosis to the overall forensic opinion / cause of death statement.

Results: Once established, the database is easy to utilize, and multiple laboratory management statistics can be mined using basic spreadsheet functions. These include reason for neuropathology consultation; approximately 13% of cases involved an assessment of neurodegeneration (which typically require the most extensive work-up). Data for both general autopsy and neuropathology was readily available for 207 cases to assess the contribution of neuropathology, and in 33% the neuropathological diagnosis was deemed to be the primary cause of death (COD) or a significant component of the COD (e.g. ruptured intracranial aneurysm), 14% an underlying contributor to death (e.g. severe Alzheimer's Disease leading to complications such as hypothermia or pneumonia), and 30% exclusion of a potential neurological COD. Turn-around times can also be calculated, with a median of 120 days (interquartile range 91 to 151 days) from the date of autopsy to neuropathology consultation sign-out.

Discussion: The practical applications of an institutional neuropathology autopsy database for internal audit and laboratory management are many, ranging from guidance on resource management to informing curriculum design in pathology education. Continuing prospective maintenance of the database would be an asset.

Keywords: Laboratory management, Quality improvement, Database, Autopsy, Forensic/Coroner, Education

Abstract: 1

Presenter's Name: Win, Phyo

Additional Author(s): Win PW, Nguyen J, Shin EH, Nagano TS, Selimi B, Hong K, Meybodi AM, Yates BP, Burke EV, Carter DE, Newby GA, Newcomb C, Arking DE, Castellani CA

Abstract Title: Mitochondrial DNA copy number reduction via in vitro TFAM knockout remodels the nuclear epigenome and transcriptome

Abstract:
Introduction: Mitochondrial DNA copy number (mtDNA-CN) is associated with several age-related complex diseases and is an independent predictor of all-cause mortality. Although mtDNA-CN is widely known as a biomarker of disease risk, the specific molecular mechanisms underlying risk remain poorly defined. mtDNA-CN also influences nuclear DNA (nDNA) regulation through nuclear epigenome remodeling. Here, we examine site-specific differential nDNA methylation and differential gene expression resulting from in-vitro reduction of mtDNA-CN to uncover shared methylation sites, genes and biological pathways mediating the effect of mtDNA-CN on disease.

Methods: Three independent human embryonic kidney cell lines with heterozygous knockout of the mitochondrial transcription factor A gene (TFAM) were generated using CRISPR-Cas9 (TFAMKO), alongside three control lines. TFAM knockout was confirmed at both the protein and mRNA levels via western blot and qPCR, respectively. Off-target knockout effects were assessed at the DNA level using in silico prediction and targeted sequencing analysis. Stable mtDNA-CN reduction was confirmed via qPCR. Epigenome wide nDNA methylation was measured using the Illumina Infinium Methylation EPIC BeadChip, and transcriptome-wide gene expression profiling was performed using RNA sequencing.

Results: mtDNA-CN reduction was associated with 2,924 differentially methylated sites, 67 differentially methylated regions, and 102 differentially expressed genes (FDR<0.05). Integrated analysis uncovered 24 Gene-CpG pairs (FDR<0.05). TFAM overexpression in TFAMKO lines restored mtDNA-CN levels and reversed the gene expression changes induced by mtDNA-CN reduction. Enrichment analysis identified GABAA receptor genes and related pathways, the neuroactive ligand signaling pathway, ABCD1/2 gene activity, and cell signaling processes to be overrepresented (FDR<0.05). The results also implicate chromatin state regulatory mechanisms as modulators of mtDNA-CN's effect on gene expression.

Discussion: Targeted reduction of mtDNA-CN signals to the nuclear genome and induces coordinated changes in DNA methylation and gene expression. Identification of specific pathways and regulatory mechanisms driving mitochondrial–nuclear crosstalk is expected to explain nuclear remodeling relevant to development, aging, and complex disease risk.

Keywords: Mitochondrial DNA, Mitochondrial DNA copy number, Epigenomics, Transcriptomics, CRISPR-Cas9

PLATFORM SESSION 2

Abstract: 2

Presenter's Name: Baranova, Katherina

Additional Author(s): Baranova K, Shirley B.C, Wang A, Lockau L, Zhan K, McDonald L, Rasmussen S, Wehrli B, Cecchini M, Arking D, Castellani C.A.

Abstract Title: Characterizing mitochondrial alterations and molecular changes in oncocytic and tall cell variant papillary thyroid carcinoma

Abstract:
Objective: The oncocytic and tall cell variants of papillary thyroid cancer (PTC) are rare types of thyroid cancer, and the tall cell variant is considered aggressive. There is limited understanding regarding the molecular basis of these subtypes of PTC, however previous studies have demonstrated that both have abnormal mitochondria.

Methods: To better characterize these lesions, we reviewed 489 cases of PTC available through The Cancer Genome Atlas (TCGA). TCGA RNA-seq expression data and whole genome sequencing data was analyzed to contrast the molecular basis of these tumours with other cases of PTC. MitoHPC was run on all genome sequencing files to estimate mitochondrial DNA copy number and call mitochondrial mutations. To validate these findings, we have collected and isolated DNA from 50 PTC cases from patients at LHSC, diagnosed in house, as a second cohort to confirm the TCGA findings. This set comprises oncocytic (n=17), tall cell (n=20), and classical (n=8) or follicular variant (n=4) PTC as controls. Mitochondrial sequencing and mitochondrial DNA copy number analysis is underway on the samples.

Data and Results: We identified 23 cases of PTC with oncocytic histology in the TCGA digital slide archive and 33 cases of tall cell. The oncocytic cases had a distinct mutational profile with a lower frequency of BRAF mutations (p=0.001) and increased frequency of RAS driver mutations (p=0.002), whereas the tall cell group was uniformly BRAF mutant (p<0.001). Both groups showed increased mitochondrial copy number (p<0.001). Gene expression analysis identified overexpression of mitochondrial biogenesis genes and electron transport genes in the oncocytic group. The tall cell group demonstrated a high burden of deleterious mitochondrial heteroplasmies and a high Mitochondrial Local Constraint Score Sum (MSS) (p=0.035), demonstrating evidence of mitochondrial dysfunction.

Conclusions: This increased understanding of the genomics of the oncocytic and tall cell variants of PTC is expected to support the development of novel diagnostic and therapeutic avenues for further study.

Keywords: Thyroid carcinoma, Mitochondria, Molecular pathology, Cancer genomics

Abstract: 3

Presenter's Name: Magbor, Paula

Additional Author(s): Poon AFY

Abstract Title: Beyond Components: Using Community Detection to Resolve Transmission Risk Structure in HIV-1 Genetic Clusters

Abstract:
Introduction: For rapidly evolving viruses, clusters of genetically similar infections can reveal underlying transmission dynamics. Clusters are often generated by linking infections with genetic distances below some threshold. By convention, clusters are extracted from the induced graph as connected components: distinct subgraphs of nodes that are not connected to nodes outside the group. However, this approach leaves many infections unclustered at typical genetic distance thresholds, and may fail to resolve the transmission risk structure within large components. We used simulated and real HIV-1 sequences to evaluate the utility of community detection (CD) methods in extending the component clustering (CC) framework for molecular epidemiology.

Methods: We implemented multi-deme compartmental models in TiPS, and used Pyvolve to simulate HIV-like sequences along the resulting trees. Additionally, we retrieved 12,556 HIV-1 pol sequences from GenBank that were collected in China, along with associated metadata. We aligned these sequences with ViralMSA and removed non-overlapping sequences, leaving 8,593 sequences. Pairwise distances were computed for these alignments with TN93, and graphs were constructed at thresholds ranging from 0.005 to 0.045 substitutions/site. Using NetworkX and CDlib, we applied CC and seven CD algorithms to these graphs, and used adjusted mutual information (AMI) to measure concordance between clusters and putative risk factors.

Results: Among replicate simulations with assortative mixing among demes, we obtained higher AMI maxima for CD methods (0.271-0.297) than CC (AMI=0.165). These maxima were obtained at higher thresholds for CD (0.035) than for CC (0.025), indicating a benefit of partitioning large components. Similarly, for actual HIV-1 data, AMI maxima were higher for CD (0.137-0.145) than CC (0.042), and favoured higher thresholds (0.03-0.04 versus 0.02). CD also improved the concordance between genetic clusters and sampling locations by province.

Discussion: These findings demonstrate the utility of CD in detecting latent transmission structure. Future work will explore permutation tests and regression analyses to assess the significance of overlapping communities and multi-membership nodes.

Keywords: Molecular epidemiology, genetic clustering, transmission, HIV-1

PLATFORM SESSION 2

Abstract: 4

Presenter's Name: Del Papa, Josh

Additional Author(s): Del Papa, J., McDonald, L., Trifoi, F., Otukoya, D., Meshram, F., and Cecchini, MJ.

Abstract Title: Edge-Integrated, In-Line AI for Frozen Section Margin Assessment of Basal Cell Carcinoma: A Prospective Feasibility Study of the FROST Pipeline

Abstract:
Frozen section diagnosis of basal cell carcinoma (BCC) presents challenges for pathologists due to time constraints and the need for rapid, accurate intraoperative assessment in critical tissues of the head and neck. Objective: To develop and validate FROST, a deep learning-based classifier optimized for high sensitivity for automated detection of BCC in frozen section whole-slide images. Methods: A search was performed in our local database for frozen sections with a diagnosis of basal cell carcinoma. Positive cases and negative controls were identified within 403 individual slides from 41 cases and scanned using a portable digital slide scanner (Grundium Ocus®, Finland). WSIs were processed by extracting 224x224 pixel tiles at 20x magnification, and the Virchow 1.0 model was used to generate 2560-dimensional embeddings. These were used to train a 27.7 million-parameter classifier featuring a local transformer attention module that applies 8-head self-attention across 3x3 spatial grids of neighboring tile embeddings. The model was trained on 30 BCC-positive slides, 30 normal frozen sections, and 10 hard-negative regions. Evaluation was performed on 211 slides spanning a 6-year archival period. Results: FROST achieved an AUC of 0.978. At the optimized operating point, it demonstrated 100% sensitivity (58/58 positive cases) and 86.3% specificity (132/153 negative cases). Outputs are delivered as interactive HTML reports with tumor prediction overlays and adjustable thresholds for sensitivity-specificity trade-offs. Conclusions: We successfully developed and validated FROST, a screening tool optimized for high sensitivity. FROST serves as a safety net that works alongside the pathologist, boosting diagnostic confidence without compromising expert oversight.

Keywords: Neural Network, Digital Pathology, Dermatopathology, Edge-compute

Session Abstract: 1

Presenter's Name: Abdo, Rober

Additional Author(s): Rober Abdo, Qi Zhang, Shawn Li

Abstract Title: High-Resolution Spatial Mapping of Breast Cancer Brain Metastasis

Abstract:
Introduction: Breast cancer brain metastases (BCBrM) exhibit marked spatial heterogeneity, but the cellular architecture and neighborhood organization of the metastatic niche remain incompletely defined. We used high-resolution spatial transcriptomics to map cellular states and ecosystem organization within BCBrM.

Methods: We applied Xenium high-resolution spatial transcriptomics to BCBrM tissue sections to quantify RNA expression at single-cell/subcellular resolution and to enable spatially aware cell-state annotation across metastatic tumor cells and diverse microenvironmental compartments. We integrated cell-state mapping with spatial neighborhood analysis and signature/pathway scoring to stratify samples into three ecosystems and to localize ecosystem-associated programs in situ. Where applicable, we compared ecosystem-level patterns to region-level spatial profiling for cross-platform concordance.

Results: Xenium resolved three reproducible BCBrM ecosystems that differed in microenvironmental composition, spatial neighborhood structure, and pathway/signature activity. Ecosystem-associated programs were not uniformly distributed across tissue; instead, they localized to discrete tumor-adjacent, perivascular, and parenchymal neighborhoods. High-resolution mapping refined the localization of ecosystem programs to specific cell states and clarified spatial relationships among tumor regions and microenvironmental compartments. Cross-platform comparisons supported concordant ecosystem-level differences while Xenium provided cellular-resolution validation and spatial context.

Discussion: High-resolution spatial transcriptomics supports a three-ecosystem framework for BCBrM and enables localization of ecosystem-associated programs to defined cellular neighborhoods. This atlas-like resource provides a foundation for ecosystem-guided biomarker development and for prioritizing spatially defined tumor–microenvironment interactions for downstream mechanistic testing and therapeutic exploration.

Keywords: Brain Metastasis, Breast Cancer, Breast Cancer Brain Metastasis, Spatial Transcriptomic Profiling of Breast Cancer Brain Metastasis, Tumor Microenvironment in Metastatic Brain, Xenium Spatial Transcriptomic

POSTER SESSION 1

Session Abstract: 2

Presenter's Name: Wang, Jonathan

Additional Author(s): Shooshtari, P

Abstract Title: Extending RegSCOUT to Map Dysfunctional Non-Coding Elements in Pancreatic Cancer by Integrating Whole-Genome Sequencing with Single-Cell Multi-Omics

Abstract: Epigenetic dysregulation is a hallmark of many cancers, reshaping gene expression programs that drive tumor initiation, progression, and treatment resistance. A large fraction of regulatory control resides in the non-coding genome, yet connecting non-coding variants and altered regulatory elements to their downstream gene targets remains challenging, especially in heterogeneous tumors such as pancreatic ductal adenocarcinoma (PDAC).

To address this, we extend RegSCOUT, a computational framework that integrates genetic variation with single-cell chromatin accessibility and transcriptional state to nominate cell-type-specific regulatory mechanisms, to natively support whole-genome sequencing (WGS)-derived variant sets. RegSCOUT previously prioritized candidate regulatory networks using disease-associated loci from germline genome-wide association studies (GWAS) and integrated scATAC-seq, scRNA-seq, chromatin interaction data (e.g., Hi-C), and expression quantitative trait loci (eQTL) resources to link variants to regulatory elements, transcription factor binding, and putative target genes.

While GWAS has been highly successful for many traits and some cancers, it predominantly captures common germline variation and typically implicates loci rather than pinpointing causal regulatory mutations without additional fine-mapping and functional evidence. Moreover, for cancers with limited cohort sizes or strong subtype heterogeneity—common in PDAC—detecting subtype-specific germline signals can be difficult. Critically, GWAS does not capture the somatic mutational landscape that drives tumor evolution within individual patients.

In contrast, tumor–normal WGS enables base-pair resolution detection of rare germline variants as well as somatic alterations (including noncoding SNVs/indels and structural variants) that may disrupt cis-regulatory elements in a patient- and subtype-specific manner. By enabling RegSCOUT to ingest WGS-derived germline and somatic variants and prioritize them through single-cell chromatin accessibility, motif context, and 3D chromatin connectivity, this extension supports systematic identification of candidate non-coding regulatory disruptions and their downstream gene targets across tumor cell states. This integrated approach aims to improve mechanistic interpretation of regulatory variation in cancer and to generate testable hypotheses linking patient- or subtype-specific genomic alterations to tumor biology and clinical outcomes.

Keywords: Bioinformatics, epigenetics, whole-Genome Sequencing, single-cell multi-omics, pancreatic ductal adenocarcinoma, cancer

Session Abstract: 3

Presenter's Name: Greasley, Adam

Additional Author(s): Vytlingam K, Peng T, Zheng X

Abstract Title: Circular RNA CRIM1 Regulates Cardiac Cell Injury during Heart Transplantation

Abstract:
Introduction: Heart transplantation (HTx) is the gold-standard treatment for end-stage heart disease. Primary graft failure is the leading cause of early death following transplantation and are often at risk due to ischemia reperfusion injury (IRI). Circular RNA CRIM1 (circCRIM1) has not been studied in cardiac IRI but can influence cell death in other diseases. We previously showed that circCRIM1 responds to IRI injury, but now we wanted to investigate how this expression decides cell fate. Circular RNAs can regulate signaling pathways by binding to proteins, but so far, no protein-circCRIM1 interactions have been reported. Based on our previous work, we hypothesize that circCRIM1s response to cardiac IRI is crucial and that it can be used as a target to improve graft survival.

Methods: We used an in vitro cardiac IRI model using HL-1 cells and a murine heterotopic heart transplant model. HL-1 cells were subjected to cold ischemia (4°C) for 24h followed by warm reperfusion (37°C). We performed both knock-down (KD) and over-expression (OE) studies prior to IRI then quantified cell death using Annexin V/PI staining. To understand how circCRIM1 elicits its effect, we conducted an RNA-pulldown for circCRIM1 coupled with mass spectrometry to identify bound proteins. In vivo, we infused donor grafts with purified circCRIM1 at time of donor preservation and subjected transplanted grafts to ultrasound for functional assessment 24h post op and harvested grafts for pathological analysis.

Results: Our results show circCRIM1 is crucial for cell survival where KD leads to increased cell death while OE is protective. We found infusion of hearts using circCRIM1 at preservation leads to increased circCRIM1 in heart tissue. Infusion of circCRIM1 lead to an increase in contraction of heart grafts despite no significant changes in TUNEL or H&E scoring. We identified that circCRIM1 binds to IFI204, which can control NFkB. KD of circCRIM1 leads to increased IFI204 expression and increased IL-6 and TNFa expression which is consistent with NFkB signaling.

Conclusion: Our results show that circCRIM1 is crucial for cardiac cell survival during HTx. One-way circCRIM1 elicits this function is through binding to IFI204, which regulates TNFa which can induce cardiomyocyte apoptosis. Finally, our preliminary animal data shows that circCRIM1 can be used to increase graft function post preservation however, more studies on its utility in transplantation are needed.

Keywords: Circular RNA, Heart Transplantation, Ischemia Reperfusion Injury, Cardiomyocytes

POSTER SESSION 1

Session Abstract: 4

Presenter's Name: Huq, Eesa

Additional Author(s): Ambtman-Smith V

Abstract Title: Urban Indigenous Land Relations: Mapping Canadian Traditional Medicine and Food Sovereignty Programs

Abstract:
Introduction: Indigenous peoples in Canada experience persistent health inequities rooted in colonization, environmental dispossession, and disruptions to land-based practices. Most Indigenous people now live in urban settings, yet research and programming remain focused on reserve-based or rural models, leaving a gap in evidence to guide urban land-based health initiatives. Urban Indigenous health centres are increasingly braiding traditional medicine, food sovereignty, and land-based programming, but no Indigenous-centred critical appraisal of these models exists to inform program design. This study aims to critically appraise urban Indigenous food sovereignty and traditional medicine programs in Canada, to inform the development of the Southwest Ontario Aboriginal Health Access Centre (SOAHAC) Urban Medicine Nursery.

Methods: This scoping review involves a structured search of peer-reviewed and grey literature on Canadian urban Indigenous programs. Academic sources are identified through Medline (Ovid) and Indigenous-specific databases (Native Health Database, I-Portal, Arctic Discovery). Grey literature is identified via Google, screening the first 50 results for multiple relevant search strings. Program reports are appraised using an adapted Aboriginal and Torres Strait Islander Quality Appraisal Tool (QAT), modified for the Canadian context using Chapter 9 of the Tri-Council Policy Statement (TCPS2) on research involving First Nations, Inuit, and Métis peoples. The adapted framework assesses community leadership and governance, engagement processes, respect for community protocols and data sovereignty, use of Indigenous research paradigms, strength-based approaches, and documented benefits.

Results: Extracted data will map land-based and clinical components, relationships to local health systems, and reported health, cultural, and community outcomes. Data collection and analysis are ongoing; results will be presented on poster day.

Discussion: By mapping how urban Indigenous programs integrate traditional medicine, food sovereignty, and land-based practices, or implement them separately, this review will identify promising implementation approaches to inform the SOAHAC Urban Medicine Nursery and future urban Indigenous health initiatives in Canada.

Keywords: Indigenous Health, Urban Indigenous, Food sovereignty, Traditional medicine, Traditional healing, Land-based activity

Session Abstract: 5

Presenter's Name: Trinh, Kyla

Additional Author(s): Black M, Lin S, Jeong WD, Brown A, Wasserman JK, Cecchini MJ

Abstract Title: Understanding Patient Pathology Information Needs Through Qualitative Content Analysis of Real-World Patient Questions (INSIGHT)

Abstract:
Introduction: As patient access to electronic medical records expands, patients are increasingly reviewing complex pathology reports that were primarily designed for clinical expert communication. Despite the availability of educational resources such as MyPathologyReport.com, minimal empirical work has systematically characterized what patients ask when seeking clarification of their pathology findings. This study aims to generate a structured, clinically meaningful taxonomy of patient information needs and comprehension gaps using real-world patient-submitted questions.

Methods: We are conducting a qualitative descriptive study using content analysis of anonymized questions submitted to MyPathologyReport.com. The full dataset (approximately 500-1,000+ questions) will be analyzed descriptively to characterize patterns of patient engagement, including question length, language, and submission categories. A purposive maximum-variation subset (approximately 100-200 questions) will then be selected for in-depth analysis. Two reviewers will independently perform inductive coding focused on manifest content, with iterative codebook refinement, consensus resolution of discrepancies, and adjudication by a third reviewer as needed. Coded data will be grouped into higher-order categories to generate a structured taxonomy of patient information needs.

Results: Preliminary descriptive analysis demonstrated heterogeneity in patient question characteristics and topic focus. Content analysis of the purposive subset is ongoing with recurring domains of information need, including terminology clarification, report interpretation, staging and prognosis concerns, and emotionally driven reassurance-seeking observed to date.

Discussion: This structured analysis of real-world patient pathology questions highlights persistent gaps in pathology comprehension and aims to define priority domains for patient-centered educational support. The resulting taxonomy will provide an empirical foundation to inform targeted resource development, pathology communication strategies, and future AI-enabled patient support tools (e.g. Osler on MyPathologyReport.com). Future prospective studies are needed to evaluate interventions informed by these findings.

Keywords: Pathology communication, Content analysis, Patient education, Health literacy

POSTER SESSION 1

Session Abstract: 6

Presenter's Name: Smith, Sophie

Additional Author(s): Sophie X.Y. Smith[1], Cody P. Hird[1], Paula D. Segura[1], Yuxin Hu[2], Lawrence D. Goodridge[2], Miguel E. Quiñones-Mateu[1]

Abstract Title: Surveillance of SARS-CoV-2 Within the Fecal Virome of White-Tailed Deer in Southeastern Quebec

Abstract:
Introduction: The COVID-19 pandemic highlighted the importance of wildlife reservoirs in cross-species viral transmission. Evidence of reverse zoonosis suggests that animals may sustain viral evolution even as human transmission declines. White-tailed deer (Odocoileus virginianus), which frequently interact with humans, have emerged as a prominent host for zoonotic viruses. While previous studies have confirmed infection through nasal and serological sampling, limited research has examined fecal shedding despite evidence that SARS-CoV-2 is detectable in wastewater. This study investigates whether the fecal virome of white-tailed deer in Quebec contains RNA homologous to viruses with zoonotic potential.

Methods: RNA was extracted from 64 deer fecal samples at Gault Nature Reserve using the RNeasy PowerFecal kit. RNA purity was assessed using NanoDrop and the high-quality samples underwent rRNA depletion followed by Illumina sequencing. FASTQ files were subjected to quality control with FastQC, adapter trimming with Trimmomatic, de novo assembly using MEGAHIT, and read alignment with Bowtie2. Viral identification was performed through nucleotide homology searches against NCBI and protein-level classification using DIAMOND-BLASTx, with results cross-validated using Chan Zuckerberg ID and Genome Detective pipelines. In parallel, SARS-CoV-2 RNA detection was conducted using TaqMan-based qRT-PCR targeting the nucleocapsid gene. Samples were run in triplicate, and viral loads were quantified using cycle threshold values relative to a standard curve.

Results: We expect to identify diverse populations within the deer fecal virome, including CoVs and other zoonotic viruses. Detection of SARS-CoV-2 RNA would indicate ongoing environmental shedding and support the hypothesis that repeated spillover contributes to sustained viral circulation. Comparative genomic analyses may reveal similarities between CoVs and hCoVs, suggesting potential recombination within cervid reservoirs.

Discussion: By characterizing the fecal virome, we aim to address a critical gap in wildlife surveillance and expand our current understanding of SARS-CoV-2 transmission. Evidence of persistent viral shedding would highlight the role of cervids as reservoirs enabling spillover of chimeras into human populations. Although limited to Quebec, the findings may inform broader surveillance strategies across Canada and pandemic preparedness.

Keywords: SARS-CoV-2, Coronaviruses, White-tailed Deer,, Zoonosis, Metagenomics, Virome

Session Abstract: 7

Presenter's Name: Yoshida, Michael

Additional Author(s): Kum J, Poon A

Abstract Title: Investigating Gender Bias in Multiple-Choice Questions in an Undergraduate Pathology Course

Abstract: Multiple-choice question (MCQ) based assessments constitute the majority of students' final grades in many undergraduate courses. In this context, concerns about gender bias have increased; bias is defined as any statistical advantage favouring a particular gender after accounting for overall proficiency. While other subject areas have statistically analyzed their exam data for gender bias, this study represents one of the first systematic analyses of de-identified gender data in undergraduate pathology education. Eight years of student and exam question data were analyzed at the individual question (item), topic, and exam levels to evaluate whether performance differences varied by gender and question characteristics. Item-level logistic regression models were used to examine question characteristics. Bloom's taxonomy provides a framework for classifying MCQs based on the cognitive level required. K1 questions assess recall or basic comprehension, while K2 questions typically involve longer stems, data interpretation, and application. Since K2 questions are often longer and context-heavy, they introduce more opportunities for bias in phrasing, such as readability, ambiguity, and the inclusion of extraneous details versus shorter K1 items. After controlling for exam and academic year, females had lower odds of correctly answering K2 items (OR = 0.89, p = 2.49 x 10-14). At the exam level, gender differences were generally small and inconsistent across years, with statistically significant differences (FDR-adjusted) only detected in 2024-25 (p = 0.00192). Notably, this coincided with a curricular change in which application-based (K2) questions were standardized to comprise approximately 50% of exam items. Topic-level analyses revealed greater differences. After false discovery rate (FDR) correction, seven of twenty-three topics exhibited statistically significant gender-associated differences in performance (FDR <0.05). Overall, gender-associated performance differences were most evident at the item and topic levels, particularly in K2 questions. The significant gender effects in K2 items, together with topic-specific patterns and the emergence of exam-level differences only after K2 standardization, suggest that question composition and cognitive demand may contribute to observed gender differences. These factors should be explicitly considered when evaluating undergraduate pathology examinations for gender bias, especially in the design of K2 MCQs.

Keywords: Assessment equity, Gender bias, Multiple-choice questions, Pathology education, Undergraduate education, Item-level logistic regression

POSTER SESSION 1

Session Abstract: 8

Presenter's Name: Burr, Melanie

Additional Author(s): Mohseni Meybodi A, Schenkel L

Abstract Title: Optimizing Genomic Testing Strategies for Patients with Epilepsy and Intellectual Disability: A Comparative Analysis of Chromosomal Microarray and Next-Generation Sequencing

Abstract:

Introduction: Intellectual disability (ID) is defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), as lifelong impairments in intellectual and adaptive functioning with onset during childhood. Epilepsy and ID frequently co-occur, with approximately 25% of individuals with epilepsy also meeting criteria for ID. Although epilepsy is etiologically heterogeneous, an estimated 30% of cases are attributed to genetic causes. Identification of pathogenic variants in epilepsy-associated genes can elucidate the underlying molecular basis of disease and directly inform clinical management. Therefore, it is essential to select a genetic testing method with the highest likelihood of achieving a molecular diagnosis.

Methods: This study draws on a dataset comprising molecular diagnostic results from individuals referred for genomic evaluation of epilepsy. The cohort includes patients both with and without ID, representing a heterogeneous population who underwent both chromosomal microarray analysis (CMA) and next-generation sequencing (NGS)-based targeted epilepsy panel testing. To evaluate the performance of these diagnostic modalities, we contrasted their diagnostic yield, characterized the frequency of pathogenic and likely pathogenic variants identified by each approach, and examined the capacity of each method to detect specific classes of genomic alterations.

Results: Among 101 patients with intellectual disability, pathogenic or likely pathogenic variants were identified in 12 cases by NGS and in 10 cases by CMA, corresponding to diagnostic yields of 11.88% and 9.90%, respectively. Across the full cohort of 198 individuals referred for genomic evaluation of epilepsy, NGS detected pathogenic or likely pathogenic variants in 26 cases, whereas CMA identified such variants in 16 cases. These results correspond to overall diagnostic yields of 13.13% for NGS and 8.08% for CMA.

Discussion: No statistically significant difference was observed between the diagnostic yields of CMA and NGS in this cohort. Accordingly, the findings do not support the prioritization of one test over the other based on diagnostic yield alone. Rather, the limited overlap in pathogenic findings between the two approaches highlights their complementary diagnostic value. These results suggest that the combined application of NGS epilepsy panels and CMA may enhance overall diagnostic yield and improve the likelihood of establishing a molecular diagnosis.

Keywords: Intellectual disability, epilepsy, Chromosomal Microarray, Next-Generation Sequencing

Session Abstract: 9

Presenter's Name: Wang, Annie

Additional Author(s): Castellani CA, Min W

Abstract Title: Investigating DLC1β as a Cardioprotective Target in Cardiac Ischemia

Abstract: Cardiac ischemia, defined as inadequate oxygen supply to cardiac muscle, is an inevitable consequence during heart transplantation (HTx), and its severity is a major determinant of patient prognosis following the procedure. Ischemia-induced cell death is primarily uncontrolled (necrosis) or programmed (apoptosis). Prior research elucidated the RhoA/ROCK/PTEN pathway as a pro-apoptotic pathway initiated in ischemic conditions. Deleted-in-liver-cancer 1 (DLC1) is a protein found to inhibit RhoA activity, with the beta-isoform (DLC1β) as the predominant isoform only in the heart but has limited characterization. Therefore, we hypothesize that DLC1β overexpression (OE) confers anti-apoptotic protection against cardiac ischemia. H9c2 cells (rat cardiomyocytes) were maintained under normoxic conditions or were transfected with control/DLC1β plasmid for 48 hours and underwent 24 hours of hypoxia (N=24). Afterwards, the cells were collected for apoptosis detection using flow cytometry with propidium iodide staining, RNA isolation using Qiazol lysis reagent (Qiagen), and transfection confirmation via RT-qPCR. Upon confirmation of decreased apoptosis in the DLC1β condition, RNA-sequencing (RNAseq) will be performed to characterize transcriptomic changes. Transcriptomic analysis will be expected to identify differentially expressed genes (DEGs) between the three conditions; functional enrichment analyses will be performed using Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) databases. Preliminary results support this approach, with flow cytometry analysis demonstrating decreased apoptosis in the DLC1β-transfected condition. Current work involves protocol optimization to maximize apoptotic differences between the hypoxic conditions prior to RNAseq analysis. Concurrent cross-analysis has been performed to compare overlapping DEGs using the publicly available GSE254950 dataset: an H9c2 RNAseq dataset comparing differential expression between normoxia and 12h hypoxia/6h reoxygenation (H/R) groups (n=3 per group). Analysis of the GSE254950 dataset found 6450 DEGs (FDR < 0.05). Further gene set enrichment analysis will be performed to compare affected pathways in ischemia and the cardioprotective mechanisms of DLC1β If the role of DLC1β in cardiac ischemia is successfully characterized, future research will validate the in vitro findings within in vivo animal models and assess translational potential of the results across additional species.

Keywords: DLC1β, ischemia, transcriptomics, cardiovascular research

POSTER SESSION 1

Session Abstract: 10

Presenter's Name: Babasola, Favour

Additional Author(s): Ardakani FB, Shooshtari P, Pin CL

Abstract Title: Benchmarking Methods that Identify Gene Regulatory Sites from Chromatin Accessibility Profiles in Cancer Datasets

Abstract:
Background: Regulatory elements of the genome play a crucial role in gene expression by mediating and controlling interactions between transcriptional machinery and genomic sequences. Yet, accurately linking regulatory sites to their specific genes remains challenging due to the inherent complexity of the mechanism, which often includes long-range interactions and context-specific behaviour. This is especially true in cancer cells, where their heterogeneity makes studying oncogenes, tumour suppressor genes, and their regulation increasingly complex.

Methods and Results: The Shooshtari Lab has recently developed a machine learning based computational approach for predicting gene expression data (RNA-seq) using chromatin accessibility data (ATAC-seq) with the outcome of identifying candidate genomic regulatory sites of target genes from individuals with cancer. This study aims to systematically benchmark this new computational method against three existing machine learning models (RandomForest, XGBoost, and Elastic net linear regression). The methods are to be compared across five cancer multiome datasets from bladder cancer, breast cancer, pancreatic cancer, Ewing sarcoma, and leukemia. The results will be assessed based on standardized metrics that evaluate overall accuracy, reproducibility, and precision while using corresponding Hi-C data as ground truth. For each cancer type, we have used standardized preprocessing pipelines to process raw sequencing files (FASTQ format) of bulk RNA-seq and ATAC-seq data, and we have obtained aligned sequencing data in the BAM format. This project is a work in progress, and we will have more data to present by PaLM Research Day.

Conclusion: The results of this study will contribute to improved evidence-based method selection in regulatory genomics workflows, specifically when working with cancer data, improving future cancer and regulatory genomics research.

Keywords: Cancer, Bioinformatics, Epigenetics, Benchmarking, Machine Learning, Gene Regulation

Session Abstract: 11

Presenter's Name: Wang, Eric

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

Abstract Title: Topical treatment for diabetic retinopathy via silencing of lncRNA HOTAIR

Abstract:
Introduction: Diabetic retinopathy (DR), a leading cause of blindness in working-age adults, is driven by vascular dysfunction mediated by various angiogenic regulators, primarily VEGF. Although current anti-VEGF therapies reduce vision impairment, their efficacy is limited by a single-target approach and the clinical burden of frequent intravitreal injections. The long non-coding RNA (lncRNA) HOTAIR is upregulated in the diabetic retina and acts as a master regulator of several pathogenic factors, including VEGF. We investigated whether silencing HOTAIR using N-acetylgalactosamine (GalNAc)-conjugated siRNA could provide a robust, non-invasive therapeutic strategy for DR.

Methods: GalNAc-modified siHOTAIR was initially evaluated in vitro using human retinal endothelial cells (HRECs) under high-glucose conditions. In vivo localization to the retina following topical delivery was assessed using FAM-tagged GalNAc-siRNA. The functional efficacy of GalNAc-siHOTAIR was tested in streptozotocin (STZ)-induced diabetic mice and rats. Treatments were administered via either topical eye drops or intravitreal injection, with outcomes measured through molecular, protein, and functional assessments of retinal pathology.

Results: In vitro, GalNAc-siHOTAIR effectively entered HRECs and inhibited glucose-induced endothelial dysfunction by blocking multiple factors, including VEGF-A. In vivo, topically administered GalNAc-siRNA successfully localized to the retina. GalNAc-siHOTAIR delivered via eye drops prevented diabetes-induced pathological retinal changes and inhibited vascular cell recruitment with efficacy comparable to traditional intravitreal injections.

Discussion: These findings demonstrate that GalNAc-modified siHOTAIR is a potent inhibitor of retinal vascular dysfunction. By targeting a lncRNA that regulates a broad suite of pathogenic mediators, this approach may offer superior efficacy compared to anti-VEGF monotherapy. Importantly, the success of topical delivery suggests a transformative, non-invasive treatment paradigm that circumvents the complications associated with intravitreal injections. GalNAc-siHOTAIR represents a promising advancement for the comprehensive management of diabetic retinopathy.

Keywords: Long non-coding RNA, HOTAIR, diabetic retinopathy, siRNA, Treatment, GalNAc

POSTER SESSION 1

Session Abstract: 12

Presenter's Name: Ye, Daniel

Additional Author(s): Truscott E

Abstract Title: Chemical Contraceptive Efficacy in the Common Marmoset

Abstract: The common marmoset (Callithrix jacchus) is an increasingly utilized non-human primate model in biomedical research due to its rapid reproductive capacity, small size, and translational relevance to human disease. However, frequent twin births, postpartum estrus, and the absence of lactational anoestrus create significant challenges for colony population control. Ethical and regulatory standards require controlled breeding practices to prevent overpopulation and ensure responsible animal use. Although multiple chemical contraceptives are employed in captive marmosets, there is no standardized comparative evaluation of their contraceptive efficacy, reversibility, and clinical outcomes.

This study aims to determine which of three commonly used chemical contraceptives - etonogestrel implant (Nexplanon), medroxyprogesterone acetate (Depo-Provera), or cloprostenol (Estrumate) - demonstrates the greatest overall contraceptive effectiveness in captive common marmosets. A retrospective analysis will be conducted using clinical health records and contraceptive logs from approximately 43 breeding female marmosets. Extracted variables will include contraceptive type, dosage, administration frequency, pregnancy occurrence, parturition outcomes following contraceptive failure, and reproductive recovery after discontinuation. Data will be compiled into a standardized dataset and analyzed using appropriate statistical methods to compare efficacy rates and reversibility among treatments.

It is hypothesized that the long-acting Nexplanon implant will demonstrate higher contraceptive reliability and consistent reversibility relative to Depo-Provera and Estrumate, which may exhibit greater variability due to dosing frequency and cycle dependence. This study will provide a unified comparative analysis of real-world chemical contraceptive outcomes in captive marmosets, addressing a critical knowledge gap in husbandry practices. The findings will inform evidence-based recommendations for colony management, improve animal welfare, and support ethical breeding practices in research institutions and other captive settings.

Keywords: Common marmoset, Chemical contraception, Contraceptive efficacy, Reproductive management, Animal welfare, Retrospective analysis

Session Abstract: 13

Presenter's Name: Nosrati, Sepehrdad

Additional Author(s): Kim S.

Abstract Title: Evolutionary and Epigenetic Analysis of the Emergence of Adaptive Immunity Across Caenorhabditis elegans, Drosophila melanogaster Homo sapiens, and Petromyzon marinus.

Abstract:
Introduction: Adaptive immunity is restricted to vertebrates, yet key regulators of vertebrate immune development have recognizable homologs in invertebrates that lack adaptive immunity, most notably the ETS transcription factor Spi1/PU.1. This demonstrates a gap between conserved DNA-binding domains and the emergence of vertebrate immune lineage differentiation. This study tests the hypothesis that adaptive immunity arose through the evolution of regulatory features, including increased enhancer density, chromatin accessibility, and binding-network complexity of these transcription factors.

Methods: ETS homologs and vertebrate Spi1/PU.1 sequences will be retrieved from NCBI and UniProt, aligned with Clustal Omega to assess ETS-domain conservation and divergence in flanking regions, and analyzed phylogenetically in MEGA to compare invertebrate and vertebrate lineages. Where available, synteny will be examined to evaluate genomic context. Published PU.1 ChIP-seq and ATAC-seq datasets from vertebrate immune cells will be used to identify PU.1-bound enhancers and accessible chromatin, with peaks annotated to nearby genes. In invertebrates, available epigenomic data will be used when possible; otherwise, ETS motifs and published target sets will be used to infer regulatory scope.

Results: This study is currently ongoing with results still being investigated. Strong conservation of the ETS DNA-binding domain across all four species is anticipated, paired with the phylogenetic separation of vertebrate Spi1/PU.1 from invertebrate ETS factors, along with increased enhancer density and PU.1 occupancy at loci implicated in macrophage differentiation, antigen presentation, and adaptive-immune gene regulation in vertebrate datasets relative to invertebrate homologs.

Discussion: This study frames the emergence of adaptive immunity as an outcome of expanded regulatory networks enabling PU.1 to cooperate with lineage-defining partners (e.g., IRF4/8) and coordinate vertebrate immune cell differentiation. Within the One Health framework, these differences in immune regulation across species help explain why many invertebrates function as long-tem reservoirs or vectors for pathogens that circulate between animals and humans. Thus by linking ETS/PU.1-centered regulatory systems to differences in host immune control, this study aims to connect molecular immunology with ecological transmission dynamics and public health risks for zoonotic diseases.

Keywords: ETS transcription factors, PU.1 (Spi1), Adaptive immunity, Evolutionary immunology, Epigenetic regulation, One Health

POSTER SESSION 1

Session Abstract: 14

Presenter's Name: Le, Quinn

Additional Author(s): Pemberton J[2,3], Castellani CA[1,3,4]

Abstract Title: Effect of Mitochondrial Transplantation on Nuclear Epigenome Remodeling

Abstract: Mitochondrial DNA copy number (mtDNA-CN) serves as a widely accepted indicator of mitochondrial quantity and cellular health. Reductions in mtDNA-CN are frequently linked to mitochondrial dysfunction and altered nuclear gene regulation. Mito-nuclear crosstalk refers to the bidirectional communication between mitochondria and the nucleus, which connects mitochondrial state to nuclear regulatory programs. However, the mechanisms by which mitochondrial dysfunction leads to nuclear epigenomic remodeling remain poorly understood. Mitochondrial transplantation, involving the transfer of mitochondria from healthy donor cells into recipient cells, provides a practical approach to experimentally increase mtDNA-CN and assess the extent and mechanisms by which altered mitochondrial input induces changes in nuclear DNA methylation and gene expression. Using a TFAM-knockout (TFAM-KO) HEK293T model of mtDNA depletion, we isolated mitochondria from wild-type (WT) HEK293T donor cells, quantified by BCA protein assay, and transplanted donor mitochondria into TFAM-KO and WT recipient cells by co-centrifugation under sham, low-, medium-, and high-dose conditions. Uptake and localization were assessed 24 hours post-transplant by live-cell confocal microscopy, and mtDNA-CN was quantified by qPCR (D-loop relative to nuclear albumin). Following confirmation of mtDNA-CN dose modulation, nuclear DNA methylation will be profiled using Illumina MethylationEPIC arrays, and transcriptomic changes will be assessed by RNA-seq, with integrated methylation-expression analyses and pathway enrichment. Preliminary experiments confirmed uptake by confocal imaging and, transplantation of 40 µg of donor mitochondria led to a 3.84-fold increase in mtDNA-CN ($p=0.019$). A pilot dosing series revealed mtDNA-CN increases compared to sham ($p=0.001$) and differences between high and medium doses ($p=0.030$). Ongoing work aims to determine whether controlled mitochondrial dosing produces reproducible, dose-dependent shifts in nuclear methylation and gene expression relative to sham-treated TFAM-KO controls. Alongside this work, analysis of public GSE267826 RNA-seq data comparing co-cultured fibroblasts with high vs low MitoTracker signal (proxy for mitochondria uptake/transfer) identified 135 differentially expressed genes (FDR<0.05; fold change>2) with enrichment for muscle system process ($FDR=1.31\times10^{-4}$) and muscle contraction ($FDR=1.48\times10^{-4}$).

Keywords: Mitochondria, mitochondrial transplantation, mitochondrial DNA, nuclear epigenome, nuclear transcriptome, mito-nuclear crosstalk

Session Abstract: 15

Presenter's Name: Chang, XingJian

Abstract Title: In Vitro Generation and Validation of Scarless Circular ZMIZ1 RNA Using a Modified Permuted Intron-Exon System

Abstract:
Introduction: Circular RNAs (circRNAs) are covalently closed RNA molecules with exceptional stability and emerging therapeutic potential. The Permuted Intron–Exon (PIE) system, which utilizes self-splicing Group I introns, enables precise in vitro circRNA generation but leaves non-native "scar" sequences in the final product—a significant limitation for therapeutic applications. ZMIZ1 is a transcriptional coactivator central to developmental and oncogenic pathways, where precise dosage is critical. We hypothesized that the sequence flexibility of Group I introns would allow the terminal nucleotides of the native ZMIZ1 transcript to function as exon guides, enabling scarless circularization.

Methods: We engineered a PIE construct wherein the ZMIZ1 coding sequence was positioned directly between permuted intron fragments, embedding exon-identifying sequences within the transcript itself. Following in vitro transcription, we optimized electrophoretic analysis using 2% sodium hypochlorite-agarose gels with SYBR Green II staining to resolve RNA species. Circularization was assessed through RNase R exonuclease resistance, DNase I insensitivity, and RT-PCR with divergent primers targeting the backsplice junction. Gel-purified putative circRNA was transfected into HEK293 and B16 cells, and the backsplice junction was confirmed by Sanger sequencing.

Results: We identified an RNase R-resistant RNA species that was insensitive to DNase I digestion, consistent with circular topology. Systematic variation of splicing conditions—including buffer additives and 55°C GTP incubation—failed to alter circRNA yield, and the resistant band was present even when the splicing step was omitted entirely, indicating circularization occurred co-transcriptionally. Transfection of gel-purified RNA into HEK293 and B16 cells yielded 20-fold and 70-fold increases in circRNA-specific qPCR signal, respectively. Sanger sequencing of the amplified product confirmed the precise head-to-tail backsplice junction unique to circZMIZ1.

Discussion: These findings demonstrate successful generation of scarless endogenous circZMIZ1 RNA by exploiting the sequence flexibility of the Group I intron PIE system. Circularization occurred efficiently without a dedicated in vitro splicing reaction, simplifying production. From biochemical characterization to cellular delivery and junction sequencing, this work provides a streamlined framework for producing therapeutically relevant scarless circRNAs.

Keywords: Circular RNA, Group I intron, PIE system, scarless RNA

Session Abstract: 16

Presenter's Name: Chahal, Serina

Additional Author(s): Vytlingam K, Greasley A, Zheng X

Abstract Title: Circular RNA ZMIZ1 Overexpression Drives Melanoma Progression and Anti-tumour Immune Dysregulation

Abstract:
Introduction: Melanoma is a skin cancer that originates in melanocytes and is becoming increasingly prevalent in adults, including young adults aged 15-29. Despite an increased push for UV-protective measures over the past decade, the non-responsiveness and resistance to standard treatments have resulted in an increased incidence of melanoma world-wide. There is an urgent need to develop new therapeutic approaches and determine new targets to study melanoma activity. Recently, circular RNA's have emerged as key regulators of cancer cell activity, and growing evidence supports their involvement in tumorigenesis, metastasis, and immune evasion. Our study examines the role of circular RNA ZMIZ1 (circZMIZ1) in immune regulation in a melanoma cancer context.

Methods: To determine its role in melanoma, a B16-F10 murine melanoma stable cell line over-expressing circZMIZ1was generated by plasmid transfection and fluorescent cell sorting. CircZMIZ1 over-expression cells were subject to various treatments to measure cell proliferation, migration, and death, in addition to co-culture with C57BL/6 syngeneic immune cells to determine their immunosuppressive effect. Finally, the effect of circZMIZ1 over-expression on anti-tumour immunity was tested in vivo using a C57BL/6 melanoma model.

Results: In vitro, circZMIZ1 over-expression increased melanoma cell proliferation and migration, as well as reduced cell death in response to chemotherapeutic treatment compared to control B16-F10 cells. Looking at immune regulation, co-culture with circZMIZ1 over-expressing melanoma cells retained dendritic cells in an immature state and promoted T cell exhaustion. In vivo, circZMIZ1 over-expressing tumours showed increased tumour burden and CD8+ T cell apoptosis. Ex vivo, reduced T cell responses during antigen re-challenge were also observed in conjunction with the retention of dendritic cells in an immature state.

Discussion: Together, these findings suggest that circZMIZ1 is a novel regulator of oncogenic activity and immune regulation in melanoma, highlighting its potential as a therapeutic target, and as both a diagnostic and prognostic biomarker.

Keywords: Melanoma, Circular RNA, Cancer, Dendritic Cell, T cell exhaustion, Anti-tumour Immunity

Session Abstract: 17

Presenter's Name: Mgbiri, Chukwubuikem

Additional Author(s): Darling M, Cecchini M.

Abstract Title: Proliferation Marker Expression in Chronic Hyperplastic Candidiasis and Its Malignant Transformation

Abstract:

Introduction: Oral Squamous Cell Carcinoma (OSCC) accounts for approximately 90% of oral malignancies and continues to pose a significant clinical burden, with rising incidence among younger individuals lacking traditional risk factors. Chronic hyperplastic candidiasis (CHC) is a Candida-associated oral lesion historically considered to possess malignant potential, yet no validated biomarkers currently exist to identify CHC lesions at high risk of transformation. Proliferation markers including MCM2, Ki-67, and Geminin demonstrate progressive overexpression from normal oral mucosa to OSCC, suggesting their utility in detecting early cell cycle dysregulation. However, quantitative comparisons of these markers in CHC lesions that undergo malignant transformation to OSCC versus those that remain benign are lacking.

Methods: FFPE tissue images immunohistochemically stained for MCM2, Ki-67, or Geminin using DAB chromogen with hematoxylin counterstain will be analyzed. Whole-slide images will be imported into QuPath, where epithelial regions of interest (ROI) will be manually annotated using a standardized protocol, blinded to transformation status. Positive cell detection will be applied to quantify marker-positive and marker-negative nuclei, from which ROI-level percent positivity will be calculated. Mechanistic ratios (MCM2/Ki-67 and Geminin/Ki-67) will be derived as secondary analyses to explore replication licensing and cell cycle phase distribution. Differences in marker expression and ratios across normal oral mucosa, non-transformed CHC, and CHC lesions that transformed to OSCC will be evaluated using ANOVA with post-hoc comparisons.

Expected Outcomes: It is hypothesized that CHC lesions that undergo malignant transformation will demonstrate increased expression of MCM2, Ki-67, and Geminin relative to non-transformed CHC and normal oral epithelium. Elevated MCM2/Ki-67 ratios may reflect increased replication licensing, while higher Geminin/Ki-67 ratios may indicate shortened G1 and accelerated cell cycle progression.

Discussion: This study aims to generate the first quantitative comparison of proliferation marker expression in transformed versus non-transformed CHC lesions. Identification of candidate biomarkers reflecting early malignant potential may support improved risk stratification of CHC and inform biomarker-based assessment across other oral potentially malignant disorders.

Keywords: Chronic hyperplastic candidiasis, Oral squamous cell carcinoma, Proliferation markers, Digital pathology, QuPath, Malignant transformation

POSTER SESSION 1

Session Abstract: 18

Presenter's Name: Limo, Luis

Additional Author(s): Suljak J[(1)], Ogilvie J[(3)], Da Silva K[(1)], Wilk P[(4)], Duerden E[(3,5,6)], Gomaa N[(1,2,4,6)]

Abstract Title: Family Socioeconomic Profiles and Children's Oral and Developmental Health: A Latent Class Analysis with Effect Modification by Access to Dental Care

Abstract:

Introduction: Children's oral and developmental health are shaped by interconnected social and material family conditions. Analyses based on single socioeconomic indicators may overlook the cumulative nature of disadvantage. We applied a person-centered approach to identify family socioeconomic profiles and examined their associations with children's oral and developmental health, including potential modification by access to dental care.

Methods: We analyzed baseline data from CHiMES cohort study in Southwestern Ontario, Canada (n=504). Latent class analysis identified family socioeconomic profiles using six socio-structural and economic/material indicators. Outcomes included caries experience, clinical consequences of untreated decay teeth, gingivitis, and caregiver-reported developmental health and functioning using age-specific, standardized PROMIS® instruments. Associations were examined using regression models appropriate to outcome distributions, stratified by age group and sex. Effect modification by dental insurance status and dental care utilization in the past year was assessed using interaction terms. All models adjusted for child age, sex, race/ethnicity, and birth history where appropriate.

Results: Three family socioeconomic profiles were identified. Compared with the most advantaged group, the most constrained profile was associated with higher caries experience in children younger than 6 years (IRR=1.30, 95% CI 1.06, 1.59) and those aged 6 years or older (IRR=1.41, 95% CI 1.20, 1.66), higher gingivitis prevalence (PR=2.33, 95% CI 1.36, 4), and, among younger children, more clinical consequences of untreated caries (IRR=2.66, 95% CI 1.48, 4.79). Children in this profile also had higher odds of adverse developmental functioning across age groups (younger: OR=2.21, 95% CI 1.43, 3.41; older: OR=1.78, 95% CI 1.13, 2.79). Access to dental care modified several associations: among younger children in the most constrained profile, lack of dental insurance (OR=3.59, 95% CI 1.38, 8.20) and no recent dental visit (OR=2.39, 95% CI 1.03, 5) were linked to higher odds of adverse developmental health.

Discussion: Family socioeconomic disadvantage clusters into distinct profiles that are differentially associated with children's oral and developmental health. Limited access to dental care amplifies these inequalities, underscoring the importance of integrated, equity-oriented oral health and early childhood policies.

Keywords: Latent class analysis, Early childhood caries, Cohort study, Child development, Social class

Session Abstract: 19

Presenter's Name: Limo, Luis

Additional Author(s): Le Q, Crosara K, Duerden E, Castellani C, Gomaa N

Abstract Title: Higher buccal-epithelial mitochondrial DNA copy number is associated with early childhood caries and adverse developmental health and functioning

Abstract:
Introduction: Variation in mitochondrial DNA copy number (mtDNA-CN), a biomarker of cellular stress and mitochondrial function, has been linked to cardiometabolic and immune-related disorders, but its role in early childhood oral and developmental health remains unclear. We examined associations between mtDNA-CN, early childhood oral disease, and adverse developmental health and functioning, and assessed whether these associations differed by sex and/or were modified by oral disease status.

Methods: We analyzed a sub-sample (children < 6 years of age) from CHiMES, an ongoing population-based cohort in Southwestern Ontario. mtDNA-CN was quantified from buccal epithelial cells collected using OC-175 DNA-Genotek® kits and adjusted for age and sex. Calibrated clinical examinations assessed untreated caries, clinical consequences, and gingivitis. Developmental health and functioning were measured using age-specific PROMIS® instruments. Stratified multivariable regression models were used to identify associations, adjusted for age, sex, race/ethnicity, family socioeconomic position, and birth history. Interaction terms by oral disease status were constructed to assess effect modification.

Results: The sample included 101 children (49% female). Half of the children had ≤4 untreated decayed teeth (IQR=0-8) and the overall mean standardized mtDNA-CN was 2.36 (SD±1). Higher buccal-epithelial mtDNA-CN was associated with a greater number of untreated decayed teeth (IRR=1.17; 95% CI 1.01, 1.39) and 46% higher odds of adverse developmental health and functioning (OR=1.46; 95% CI 1.01, 2.11). Among females, mtDNA-CN was associated with 25% increased number of decayed teeth, and more than twice the odds of adverse developmental health (OR=2.13; 95% CI 1.23, 3.1). In sex-stratified analyses, a strong modifying effect was observed among females, whereby the association between mtDNA-CN and adverse developmental health and functioning was significantly stronger in the presence of oral diseases.

Discussion: Higher buccal-epithelial mitochondrial DNA copy number is associated with early childhood caries and adverse developmental health and functioning. Results from our stratified analysis were consistent with emerging evidence of sex-specific mitochondrial regulation during early development. The association was stronger in the presence of oral disease, particularly among females, highlighting early oral health as a potential modifier of biological stress pathways.

Keywords: Oral diseases, Child development, Mitochondrial genes, Cohort study

POSTER SESSION 1

Session Abstract: 20

Presenter's Name: Kawa, Daniel

Additional Author(s): Tobias IC, Bell GI, Hess DA, Kiser PK, Betts DH

Abstract Title: Characterizing p66Shc-Dependent Effects on Pluripotent Stem Cell Fate Using Teratomas and Single Cell Transcriptomics for Comparative in vivo Multi-Lineage Differentiation Modeling

Abstract: When stem cell regulation is disrupted during early ontogenesis, defects in developmental timing and synchrony often lead to maturational delay and arrest. As key drivers of stem cell fate and state decisions, mitochondrial homeostasis, metabolism, and redox state are interconnected through the adaptor protein p66Shc. Our lab previously generated p66Shc knockout (KO) mouse embryonic stem cells (mESCs) and demonstrated that acclimation to a defined feeder-free cell culture (2i/LIF) abrogated phenotypic differences with wildtype (WT) mESCs in the naïve pluripotency state; the resulting murine allograft teratomas exhibited immature development. While teratomas enable developmental potential modeling, heterogeneity poses challenges for distinguishing p66Shc-dependent effects across distinct cell types. Here, advances in single-cell RNA sequencing show promise. In this study, we acclimated a WT and two p66Shc KO mESC clones to 2i/LIF conditions, and generated teratomas in female NOD-scid IL2rγ-null mice. Alongside cells of all three germ layers in WT (n = 11) and p66Shc KO (n = 13) teratomas, histological analysis revealed enrichment of uniform populations of putative early developmental stage cells in KO, which were associated with well-differentiated structures when present in WT. To capture intra-teratoma heterogeneity, we validated a tissue fixation and nuclei isolation protocol from OCT-embedded tissue that incorporates sections across intra-tumor regions, yielding 112,000 nuclei/mg on average, complemented by parallel serial histological assessment of these regions. After rigorous quality control, 303,613 nuclei from eight teratomas were profiled. Among non-host nuclei by Y Chromosome gene expression, p66Shc KO teratomas exhibited enrichment (–log10P = 12.03) of WP1763: mechanisms associated with pluripotency. Among 29 mESC- and ten host-derived manually annotated populations, p66Shc KO enrichment of primordial germ cells is particularly evident. After ongoing per-cluster pseudo-bulk analyses, we will construct differentiation trajectories. Our work aims to provide a robust, representative evaluation of p66ShcKO-induced effects on developmental cell fate decisions, thereby helping elucidate the mechanisms underpinning mitochondrial control of this fundamental process.

Keywords: Embryonic Stem Cells, Pluripotent Stem Cell Fate, Teratoma, p66Shc, Multi-Lineage Development Modeling, Single-Cell RNA Sequencing (scRNA-seq)

Session Abstract: 21

Presenter's Name: McDonald, Leah

Additional Author(s): McDonaldLJJ, Lopes A, Otukoya D, Trinh K, Keller BA, Cecchini MJ

Abstract Title: Assessing Efficacy of a Digital Denominator approach to PD-L1 Combined Positive Score Reporting

Abstract: Immunotherapy has revolutionized the treatment of many cancer types and pathologist assessment of PD-L1 immunohistochemistry (IHC) is a critical feature to determine treatment eligibility for immune checkpoint inhibitors. For most tumours, the Combined Positive Score (CPS) is utilized, which is calculated as the number of PD-L1-staining tumour cells, lymphocytes, and macrophages divided by the total number of viable tumour cells, multiplied by 100. This method introduces practical challenges. A single slide may contain thousands to hundreds of thousands of tumour and immune cells, and staining is often heterogeneous. This means that complete enumeration is impractical. Consequently, pathologists visually estimate PD-L1–positive cells across multiple 20× fields, scoring each field within seconds. This approach contributes to substantial interobserver variability, yet specific CPS cut-offs, such as <1, 1–4, 5–9, and ≥10 in upper gastrointestinal cancers, directly guide treatment decisions.

We hypothesize that providing a digitally derived tumour-cell denominator will improve interobserver agreement and scoring consistency in PD-L1 CPS assessment. We propose an observer study evaluating whether a denominator-derived digital tool enhances agreement amongst pathologists. Archived slides from the Department of Pathology at LHSC will be used. Tumour types will include adenocarcinoma and squamous cell carcinoma from the cervix, upper gastrointestinal tract (esophagus, gastroesophageal junction, stomach), breast, and head and neck sites. Three cases per site (12 total) will be selected around established CPS thresholds, with corresponding H&E slides available.

Slides will be digitized at 40× magnification. Using QuPath, a cell segmentation model and classifier will estimate total tumour cell counts. For each field, the tool will display the estimated denominator and the minimum number of PD-L1 positive cells required to reach common CPS cut points. 10 fully certified pathologists who routinely report PD-L1 will score each case twice: once by viewing the slide digitally without the digital tool and once using the digital tool, with a minimum three-week washout period. We will compare interobserver agreement, concordance at clinically relevant cut-offs, and scoring time between workflows to determine whether denominator guidance improves reliability in PD-L1 CPS assessment.

Keywords: Adenocarcinoma, Squamous Cell Carcinoma, PD-L1, Digital Pathology

POSTER SESSION 1

Session Abstract: 22

Presenter's Name: Moersch, Alexander

Additional Author(s): Minuk J, Quiñones IC, Quiñones-Mateu ME, Kus J, Delport J, Shahmirzadi MR, AlMutawa F.

Abstract Title: Patient and sample specific factors that predict a positive 16S ribosomal RNA gene PCR test

Abstract:
Background: In diagnostic microbiology laboratories, amplification and sequence analysis of the 16S Ribosomal RNA (16S rRNA) gene can identify fastidious bacteria. We sought to determine patient and specimen factors associated with a positive 16S rRNA gene PCR result in a tertiary care center.

Methods: Specimens submitted for 16S rRNA gene testing at London Health Sciences Centre (London, Ontario, Canada) from January 2018 to December 2023 were reviewed. We recorded demographics, specimen type/source, Gram stain, histopathology, operative note, C reactive protein (CRP), white blood cell count, and recent antibiotic exposure. Categorical variables were analyzed with χ^2 testing and predictors of a positive 16S rRNA gene result were assessed with binary logistic regression.

Results: Among 215 entries (261 total samples) from 175 patients (58.2% male; mean age 45.5 years), 45/215 (20.9%) entries were 16S rRNA gene positive. χ^2 analysis demonstrated that a positive Gram stain was significantly associated with a positive 16S rRNA gene result ($p < 0.001$). The multivariable model ($\chi^2 = 19.67$, $p = 0.006$; Nagelkerke $R^2 = 0.207$) retained two independent predictors: Positive Gram stain (adjusted OR 7.5, 95 % CI 2.1–26.9;$p = 0.002$) and CRP (adjusted OR 1.004 per mg L^{-1}, 95 % CI 1.000–1.010; $p = 0.027$).

Conclusions: Observation of bacteria on Gram stain increased the odds of a positive 16S rRNA gene PCR test by greater than 7 times. Per unit increase in CRP, the odds of a positive 16S rRNA gene PCR test increased by 0.4. Incorporating Gram stain and CRP into diagnostic algorithms could conserve laboratory resources and improve pre-test probability.

Keywords: Clinical Microbiology, Chronic Infection, Fastidious Bacteria, Ribosoma RNA PCR, Diagnostic Stewardship, Antibiotic Stewardship

Session Abstract: 23

Presenter's Name: Quan, Trinity

Additional Author(s): Kiser PK, Kum JY

Abstract Title: A Comparative Evaluation of Hematoxylin and Eosin and Movat Pentachrome Staining in Diabetic and Non-Diabetic Mouse Tissues

Abstract:
Background: Hematoxylin and eosin (H&E) staining is the gold standard for routine histological evaluation due to its efficiency and ability to clearly visualize cellular morphology. In contrast, special stains such as the Movat pentachrome stain provide enhanced differentiation of specific structures such as extracellular matrix and vascular components but are less commonly used.
Objective: This study aimed to compare the histological utility of H&E and Movat pentachrome staining in diabetic and non-diabetic mouse tissues to assess their relative effectiveness in visualizing cellular and structural features across multiple organs for clinical use.

Methods: Male C57BL/6 mice were divided into diabetic and non-diabetic groups, with diabetes induced using streptozotocin (STZ). Tissues, including the eye, heart, lung, liver, kidney, pancreas, femur, tibia, and white adipose tissue, were harvested and stained using both H&E and Movat pentachrome protocols. A standardized quantitative scoring system was applied by three independent reviewers to assess nuclear clarity, cytoplasmic definition, and overall tissue architecture. Scores were analyzed separately for control and diabetic tissues, and representative annotated images were used to support comparative interpretation.

Results: Across tissues, H&E staining consistently provided superior nuclear and cellular interpretative value in both control and diabetic mice, particularly in highly cellular organs such as heart and pancreas. In contrast, the pentachrome preferentially enhanced visualization of extracellular matrix components, including collagen, elastin, and vascular structures, and performed best in matrix-rich tissues such as bone, lung, and adipose tissue. While overall staining performance was largely consistent between control and diabetic conditions, diabetes-associated structural changes influenced the stain interpretability in select tissues, highlighting the complementary, tissue-specific strengths of each stain.

Conclusion: H&E remains the most practical and reliable stain for routine histopathological evaluation. However, the pentachrome stain offers meaningful value for highlighting fibrosis, vasculature, and stromal architecture in specific tissues and can provide critical structural insight that complements conventional histology and deepens interpretation of tissue remodeling and disease-associated architectural change.

Keywords: Special stains, histopathology, mouse models, pentachrome stain, mouse tissues

POSTER SESSION 1

Session Abstract: 24

Presenter's Name: Wei, Rilla

Additional Author(s): Chan N, Kum JY.

Abstract Title: Preparing Pathologists' Assistants for Practice: Graduate Outcomes and Training Experiences in a Canadian Master's Program

Abstract: As Pathologists' Assistants (PathAs) become more standardized and in-demand in Canada, programs are expected to prepare graduates for complex, time-sensitive clinical work while also meeting academic and accreditation expectations. Yet there is limited published evidence describing which program elements most strongly support entry-to-practice readiness and professional identity development. We conducted a focused program evaluation to generate actionable quality-improvement signals for curriculum and distributed clinical training, and to add empirical data to the emerging literature on PathA education.

We analyzed past quality-assurance data from a Canadian Master's PathA program accredited by NAACLS, including an alumni survey of 2015–2020 graduates and aggregated exit surveys (2015–2021; 37 responses). Quantitative data including Likert-scaled responses were summarized descriptively. Open-text responses underwent semantic thematic analysis informed by Communities of Practice and Professional Identity Formation.

Findings showed a strongly practice-forward trajectory. Most alumni obtained employment before completing the community rotation, and 87% reported the program met overall expectations. Starting salaries most commonly fell in the CAD $70,000–$80,000 range. Early roles were predominantly clinical, with all respondents reporting grossing of large specimens (100%), while research duties were uncommon (9%). Graduates favored scholarship that aligns with practice, with 58% preferring a mandatory case report and an optional research project. Among respondents who had written or intended to write certification exams, 67% felt prepared for ASCP-BOC and 79% for CCCPA.

Themes clarified what drove confidence and what created friction. Strengths clustered around workforce readiness and employability, skill and knowledge development, extensive clinical exposure, and credentialing that reinforced legitimacy and professional identity within pathology teams. Improvement targets were consistent across narratives: uneven clinical support affecting trust and belonging, perceived misalignment between academic requirements and workplace and credentialing needs (especially scholarly expectations), and variable supervision with delayed, non-actionable feedback across placements. These findings add to the emerging evidence base for PathA education and offer a transferable framework for programs seeking to improve distributed clinical training.

Keywords: Surgical pathology, Pathologists' Assistant, Pathology education, anatomical pathology

Session Abstract: 25

Presenter's Name: Gu, Yuanyuan

Additional Author(s): Bret Wehrli

Abstract Title: Intradural Extramedullary Capillary Hemangioma of the Spinal Canal: A Report of Two Cases

Abstract: Decalcification of trephine bone marrow biopsies and other calcified hematopathology specimens is necessary to prepare histological sections. Strong acids, such as hydrochloric acid (HCl), are typically used for tissue decalcification due to their rapid action. However, their use may significantly decrease the ability to detect diagnostic, prognostic, and predictive markers, as detected by immunohistochemistry (IHC), due to denaturation of proteins. HCl is used routinely for decalcification at LHSC. In contrast, ethylenediaminetetraacetic acid (EDTA), a chelating agent, has been shown to better preserve cellular morphology and protein antigenicity.

This pilot study examines and compares the effects of EDTA and HCl decalcification on the IHC results of selected key diagnostic hematopathology markers. Lymph nodes were obtained from five, non-neoplastic colectomy specimens and used as surrogate bone marrow tissue. The lymph nodes were fixed in 10% neutral buffered formalin for periods ranging from 24 hours to 2 weeks. Matched tissue sections of lymph nodes were submitted to EDTA or HCl decalcification for 1, 2, 6, and 24 hours, with non-decalcified tissue from each case serving as baseline levels of expression controls. Following decalcification, all specimens were routinely processed, paraffin-embedded, and subjected to IHC to semi-quantitively determine the expression of the following proteins: CD20, PAX5, CD3, CD5, CD4, CD8, CD10, CD43, CD138, BCL2, BCL6, Cyclin D1, Lambda light chain, MPO, CD45, CD117 and Ki67. The staining results will be independently evaluated by multiple pathologists (hematopathologists and director of IHC).

We hypothesize that EDTA-based decalcification will demonstrate superior preservation of protein antigenicity and overall staining quality compared to HCl, supporting its preferential use for accurate immunophenotypic assessment of decalcified hematopathology specimens.

Keywords: Decalcification, bone marrow, immunohistochemistry, ethylenediaminetetraacetic acid (EDTA)

POSTER SESSION 1

Session Abstract: 26

Presenter's Name: Pyne, Hayley

Abstract Title: Investigating HNRNP F's Role in Melanoma Development & Progression

Abstract:
Introduction: Melanoma, a highly aggressive and immunogenic skin cancer, continues to rise in global incidence despite public health efforts and advances in early detection strategies. Patient relapse and therapeutic resistance highlight the urgent need to identify novel molecular drivers of melanoma progression. Heterogeneous nuclear ribonucleoprotein F (HNRNP F) is an RNA-binding protein that regulates mRNA stabilization, alternative splicing, polyadenylation and other aspects of RNA metabolism. While HNRNP F has been implicated in several types of cancer, its role in melanoma remains unknown.

This project aims to investigate the functional role of HNRNP F in melanoma progression, metastasis, and immune interactions within the tumour microenvironment.

Methods: HnRNP F expression will be silenced in B16-F10 murine melanoma cells, where a series of cell-based functional assays will be performed to investigate how HNRNPF influences the key hallmarks of cancer. We will assess how HNRNP F affects cell proliferation, cell cycle progression, migration, and invasion using live-cell imaging, flow cytometry, wound-healing assays and matrix-coated Boyden invasion assays. To identify RNA networks underlying these phenotypes, we will perform RNA-seq, mRNA stability assays, and HNRNP F immunoprecipitation. The effect of HNRNP F on dendritic cell phenotype and functioning will be determined through ex vivo-cultures DC and splenocyte co-cultures followed by flow cytometry. In vivo studies using C57Bl/6 mice will assess tumour onset, growth and changes within the tumour microenvironment. We will assess the impact of HNRNP F on tumour initiation, growth and immune responses within the tumour microenvironment using n B16-F10 syngeneic mouse models.

Results: We hypothesize that silencing HNRNP F will reduce cell proliferation, migration, and melanoma cell survival while promoting a more immunogenic dendritic cell phenotype, leading to delayed tumour onset and reduced cell growth.

Discussion: This study will help elucidate HNRNP F's role in melanoma growth, metastasis, tumour growth and immune regulation. Targeting HNRNP F may represent a novel therapeutic strategy or provide a biomarker for disease progression in melanoma.

Keywords: Melanoma, Cancer biology and immunology, Heterogenous Nuclear Ribonucleoproteins, Therapy resistance

Session Abstract: 27

Presenter's Name: Baysah, Francis

Additional Author(s): Baysah F, Chan NG, Stefanovski S, Zhang A

Abstract Title: Comparative Evaluation of Pathological Inks for Surgical Margin Assessment

Abstract:
Introduction: In surgical pathology, tissue inking is the primary method used to delineate specimen margins and ensure complete excision of malignant or high-risk lesions. Accurate margin identification directly impacts diagnosis and patient management. Variability in ink quality may influence clarity, bleed, and overall slide interpretation. This study aimed to compare the performance and cost-effectiveness of currently used pathological inks with a newer, more expensive ink set.

Methods: Renal tissue specimens were inked by students using six standard colors, each with two variants: the existing laboratory ink and a newer formulation. Two additional colors—purple and India ink—were included from the newer set. Following routine processing, embedding, sectioning, and hematoxylin and eosin (H&E) staining, slides were digitally scanned using an Aperio system. A blinded survey was conducted among five pathologists representing multiple subspecialties. Slides were evaluated for surface consistency, degree of tissue bleed, color clarity, and overall visibility.

Results: Pathologists demonstrated an overall preference for the newer ink formulations. The existing black and blue inks were frequently described as lighter or weaker compared to their newer counterparts. The older yellow ink was considered thicker and slightly more orange in appearance and was preferred by some evaluators. The older orange and green inks were darker, with minimal perceived difference between green variants. Purple ink was acceptable but may pose challenges in cases involving small blue round cell tumors due to reduced contrast on H&E staining. The India ink was consistently rated as the clearest and most prominent and was preferred over prior formulations.

Discussion: Newer ink formulations, particularly India ink, may improve margin visualization and slide quality. Despite limitations including small sample size and potential variability in inking technique, these findings support further large-scale evaluation, including assessment across special stains and frozen sections, to optimize laboratory practice and enhance diagnostic accuracy.

Keywords: Surgical pathology, margin assessment, pathological ink, quality improvement, H&E staining

POSTER SESSION 1

Session Abstract: 28

Presenter's Name: Brar, Sukhman

Additional Author(s): Zeman-Pocrnich C, Goebel E

Abstract Title: Evaluation of Breast Carcinomas with HER2 IHC 2+ Expression and Associated FISH Amplification Rates

Abstract:
Introduction: Human epidermal growth factor receptor 2 (HER2) amplification occurs in 15–20% of invasive breast carcinomas and is associated with aggressive tumor behavior. Immunohistochemistry (IHC) is the first-line test, with 2+ scores considered equivocal and requiring reflex fluorescence in situ hybridization (FISH). FISH testing is resource-intensive and may prolong turnaround times and delay treatment. Variable FISH positivity rates among HER2 IHC 2+ tumors have been reported in literature. These rates may differ by tumor grade, histologic subtype, nodal status, and hormone receptor status. This study aimed to assess institutional HER2 IHC 2+ cases and their concordance with FISH results.

Methods: We conducted a retrospective review of invasive breast carcinoma cases with reported HER2 IHC 2+ scores at London Health Sciences Center from January–December 2025. Data collected included histologic subtype, tumor grade, nodal status, estrogen receptor (ER)/progesterone receptor (PR) status, interpreting pathologist, FISH results, and FISH turnaround time. Associations with FISH positivity were analyzed using Fisher's exact tests, chi-square tests, and the Cochran–Armitage trend test.

Results: 18.2% of HER2 IHC 2+ cases (95% CI, 13.0–24.4%, n =187) were HER2 amplified by FISH. Mean FISH turnaround time was 22.4 ± 9.5 days (95% CI, 21.0–23.8; n = 183). FISH positivity rates varied among pathologists (6.7%–29.2%) without significant difference ($p = 0.32$). FISH positivity increased significantly with tumor grade (Grade 1: 5.4%, Grade 2: 13.4%, Grade 3: 43.9%; $p < 0.0001$). Although not statistically significant, node-positive cases had higher FISH positivity than node-negative cases (34.9% vs 13.0%, $p = 0.085$). HER2 amplification rate was 15.6% in ER+PR+ (n=135), 23.8% in ER+PR− (n=21), 27.8% in ER−PR− (n=18), and 100% in ER−PR+ (n=1), with no significant difference across groups ($p=0.10$). HER2 amplification rates between invasive carcinoma of no special type and invasive lobular carcinoma were not significantly different (19.1% vs 18.8%; $p = 1.00$).

Discussion: HER2 amplification rate by FISH among HER2 IHC 2+ tumors was consistent with published data. Tumor grade was the strongest predictor of HER2 amplification. Histologic subtype, nodal status, hormone receptor status, and pathologist-level variation showed non-significant results. These findings establish an institutional benchmark and support optimized use of FISH testing to improve turnaround times

Keywords: Invasive breast carcinoma, FISH, HER2, IHC

Session Abstract: 29

Presenter's Name: Ennema, Grace

Additional Author(s): Cameron L, Shooshtari P

Abstract Title: Sex-Specific Gene Regulatory Mechanisms in Asthma Identified Through Integrative Genomic and Epigenomic Analyses

Abstract:
Background: Asthma affects 4.6 million Canadians and over 300 million people globally, representing a significant public health and economic burden. Its development reflects interactions between genetic and environmental factors, with well-documented sex differences in disease prevalence and severity. Immune cell-type-specific gene regulation is critical to asthma pathogenesis, yet the extent that genetic variations shape regulatory processes in a sex-dependent manner remains unclear. The predominance of asthma-associated variants in non-coding regions highlights the need to decode their functional regulatory roles.

Objective: To identify immune cell-type-specific gene regulatory mechanisms in asthma across biological sex.

Methods: A computational pipeline, RegSCOUT, developed in the Shooshtari Lab, was applied to multi-omic data for the identification of asthma-associated regulatory mechanisms. Sex-stratified genome-wide association study summary statistics from the UK Biobank (45,253 cases; 363,004 controls) were analyzed. These data were integrated with single-cell chromatin accessibility profiles from 17 immune cell types to map asthma-associated genetic variants to putative regulatory elements. Regulatory elements were linked to target genes using complementary approaches, including Cicero, Hi-C, and expression quantitative trait loci analyses. Network and gene set enrichment analyses were used to identify implicated biological pathways

Results: Sex-stratified analyses identified distinct regulatory features associated with asthma in males and females. Male-associated regulatory elements were enriched near histone gene clusters and involved in innate immune pathways such as Toll-like receptor signaling (TLR1 and TLR6). Female-associated regulatory elements were enriched for interleukin signaling genes (IL13 and IL2) and markers of T-cell activation, indicating a greater representation of adaptive immune and inflammatory pathways. Regulatory associations shared between sexes included genes related to airway structure and T-cell function, reflecting common mechanisms contributing to asthma susceptibility.

Discussion: This novel sex-stratified analysis reveals how noncoding variants differentially shape immune regulatory programs in males and females with asthma. Identification of shared and sex-specific regulatory mechanisms refines the genetic architecture of asthma and highlights targets for functional validation and sex-aware precision medicine.

Keywords: Asthma, Genetics, Epigenetics, Chromatin accessibility, Inflammatory condition, Bioinformatics

POSTER SESSION 1

Session Abstract: 30

Presenter's Name: Wang, Xuan

Additional Author(s): Xuan Wang, Rober Abdo, Carolyn Twible, Chelsey Zhao, Ali R Khan, Qi Zhang

Abstract Title: Transcriptomic profiling reveals hippocampal white matter inflammation as potential epileptogenic focus in temporal lobe epilepsy

Abstract: Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures and affects millions worldwide. Surgical resection is the preferred treatment for drug-resistant temporal lobe epilepsy (TLE). While hippocampal sclerosis (HS) defined by pyramidal neuronal loss in the Cornu Ammonis (CA) sectors is the most common pathology. However approximately 20% of TLE patients show no significant neuronal loss, leading to a diagnosis of "no hippocampal sclerosis" (no-HS). Despite the absence of classical histopathological findings, nearly 40% of no-HS patients become seizure-free following hippocampectomy. This suggests that molecular alterations, undetectable by routine pathology, may contribute to epileptogenesis in no-HS TLE.

We hypothesized that transcriptomic changes within no-HS hippocampi underlie disease mechanisms and are associated with surgical outcomes. To investigate this, we pursued two aims: (1) spatial transcriptomic profiling of no-HS hippocampi, and (2) validation of identified molecular signatures. From 66 no-HS cases at LHSC, ten were selected based on outcome (five Engel 1A seizure-free; five Engel 2–4 non-seizure-free) and RNA quality. Spatial transcriptomics was performed using 10x Genomics Visium, and gene expression patterns were analyzed using Loupe Browser and R/Bioconductor (FDR < 0.05). Validation was conducted using immunohistochemistry (IHC) and semi-automated cell quantification in QuPath.

Unsupervised clustering (BayesSpace) closely matched manual histological annotations and successfully distinguished the Prosubiculum from CA1. Differential expression analysis revealed upregulated neuroinflammatory pathways in seizure-free patients, particularly within hippocampal molecular layers. Trajectory analysis suggested disease progression originating in these layers and extending into CA sectors and the dentate gyrus. IHC confirmed increased CD68 and HLA-DR, alongside more activated microglial morphologies, in seizure-free tissue(TMEM119,IBA1).

The study reveals molecular heterogeneity between the Prosubiculum and CA1 and suggests a significant neuroinflammatory signature in patients with better post-surgical outcomes. These findings could help develop prognostic biomarkers and targeted therapies for no-HS TLE patients.

Keywords: Temporal lobe epilepsy, drug resistant, no hippocampal sclerosis, Spatial transcriptomic, post-surgical, IHC

Session Abstract: 31

Presenter's Name: Lockau, Laura

Additional Author(s): Goebel E, Tran C

Abstract Title: Simulation-based medical education in postgraduate pathology training: A scoping review

Abstract:
Introduction: Simulation-based medical education (SBME) is a form of experiential learning that uses simulation aids in place of real patients to replicate clinical scenarios. Literature on SBME in postgraduate training has largely focused on clinical specialties, where these techniques have been used to build procedural skills. To date, no study has comprehensively reviewed SBME applications in postgraduate pathology training.

Methods: We searched six databases (Medline, Embase, Cochrane library, Web of Science, ERIC, and Scopus) from inception to July 2023. Inclusion and exclusion criteria were applied during title and abstract screening and subsequent full text review by two independent reviewers.

Results: We included 25 studies focusing on SBME in pathology postgraduate training. Most studies were published as conference abstracts (n=15), with fewer primary research articles (n=8) and review articles or book chapters (n=2). Common areas of focus included microscopic examination (n=10), clinician-pathologist communication (n=5), frozen section examination (n=4), grossing (n=4), quality assurance (n=2), molecular pathology (n=1), and on-call responsibilities (n=1). No study explicitly defined the term "simulation," and interventions varied widely from the use of online modules with whole-slide images, to communication role-play scenarios, to physical specimen models. Only one study examined a Canadian context.

Conclusions: SBME has been used to enhance teaching in multiple areas of postgraduate pathology training. Available literature on the use of simulation in pathology education is, however, limited by the small number of studies, the variable application and lack of standardized definition of "simulation," and the predominance of conference abstracts containing limited detail on the interventions used and outcome data produced.

Keywords: Medical education, Simulation, Experiential learning, Postgraduate education

POSTER SESSION 1

Session Abstract: 32

Presenter's Name: Ortiz, Angelica

Additional Author(s): Cecchini MJ

Abstract Title: Evaluating the Quality of AI-Generated Visual Educational Content for Pathology Training

Abstract:
Introduction: Pathology residents have access to a wide range of printed and digital educational resources throughout their training and routinely synthesize information from these materials, alongside knowledge gained through daily clinical work and interactions with peers and staff. Despite pathology being a highly visual discipline, resident-created study notes remain predominantly text-based. This likely reflects both the impracticality of producing visual representations for the breadth of material covered during residency and variability in residents' artistic skills. Artificial intelligence (AI) has the potential to be an infinite source of illustrated educational content for pathology trainees; however, concerns remain regarding spelling or labeling errors, factual inaccuracies, and potentially misleading design choices in AI-generated materials.

Methods: In this study, we compared two AI models (Google Gemini Pro and ChatGPT Pro) in their ability to generate accurate and efficient pathology educational infographics. Each model was given the same prompt on three occasions, with the second and third prompts restricting the model to use either PathologyOutlines.com or the World Health Organization (WHO) website as the sole reference.

Results: Generated images were scored using a standardized rubric assessing orthography, accuracy, content thoroughness, and overall design, with each category rated as poor (1), adequate (2), or good (3). Content produced by Gemini scored significantly higher than ChatGPT in both accuracy and overall score ($p < 0.01$), regardless of whether a specific source was provided. Notably, restricting models to a specific source did not significantly improve performance in most scenarios.

Discussion: These findings suggest that Google Gemini has potential to generate accurate visual educational materials for pathology trainees, even without reliance on paid resources such as the WHO database. Given the rapidly evolving nature of AI, continued evaluation is essential, particularly for image-based pathology content where high-quality visual representations may substantially enhance trainee learning.

Keywords: Education, AI, Visualization, Pathology

Session Abstract: 33

Presenter's Name: Thirukumar, Sahanah

Additional Author(s): Ni R, Zhang J, Peng T

Abstract Title: Targeting Cardiac Necroptotic Cell Death in Diabetic Cardiomyopathy with Murine Cytomegalovirus M45

Abstract:
Introduction: Diabetic cardiomyopathy (DCM) is defined by diabetes-induced structural, functional, and metabolic abnormalities in the myocardium, possibly leading to heart failure. We and others have reported that cardiac cell necroptosis contributes to DCM. Murine cytomegalovirus encodes M45, a protein that disrupts necroptotic signalling via its N-terminal RIP homotypic interaction motif (RHIM). We hypothesize that delivery of the RHIM-encoding, N-terminal 1-90 residues (N90) of M45 can inhibit necroptosis and reduce diabetes-related cardiac damage.

Methods: Mouse cardiac endothelial cells (MCECs) were exposed to high glucose and BSA-conjugated palmitate (HG-Pal) to establish diabetic conditions in vitro. Cytotoxicity and necroptotic activity were assessed by LDH release and Western blot analyses, respectively. MCECs were then transfected with a plasmid expressing DDK-tagged N90 and EGFP and treated with HG-Pal to measure changes in cell injury and death. Mechanisms underlying HG-Pal-induced necroptosis were investigated in vitro via CRISPR/Cas9-mediated knockout of ZBP1 and pharmacological inhibition of RIPK3 with GSK'872. An in vivo approach explored the cardioprotective effect of N90 on Akita mice, modelling type 1 diabetes, using serum analysis, echocardiography, and tissue collection.

Results: Under HG-Pal conditions, MCECs displayed elevated cytotoxicity and necroptotic protein expression with increased ZBP1, pMLKL, and pRIPK3 levels. N90 delivery reduced the cell injury and necroptotic death of MCECs, demonstrating notable protective capacity. Genetic knockout of ZBP1 and GSK'872-mediated RIPK3 inhibition each diminished the cytotoxic effects of HG-Pal, validating the ZBP1-RIPK3-MLKL axis as a potential target of N90 in suppressing necroptosis in vitro. N90-transfected Akita mice showed decreased pRIPK3 expression, RIPK1-to-RIPK3 interactions, and cardiac troponin I levels, indicating reduced myocardial injury in vivo. Echocardiographic analyses revealed preserved ventricular function in N90-expressing mice four weeks following dosage administration.

Discussion: With rising diabetes prevalence, cardiovascular complications pose increasing risks. Our preliminary findings demonstrate the protective potential of N90 against cardiac damage, serving as a novel therapeutic approach while providing mechanistic insight for alternative applications.

Keywords: Diabetic cardiomyopathy, necroptosis, RIP homotypic interaction motif (RHIM), murine cytomegalovirus M45, gene therapy, cardioprotection

POSTER SESSION 1

Session Abstract: 34

Presenter's Name: Zhang, Mimi

Additional Author(s): Wang R, White M, Megyesi J, Zhang Q

Abstract Title: The Brain Tumour Tissue Bank at LHSC: A Digital Pathology Resource

Abstract: Central nervous system (CNS) malignancies remain challenging to treat and are associated with significant morbidity and mortality. Despite recent technological advances in sequencing and the emergence of new diagnostic tools, the identification of morphological features in resected tissues remains a core component of clinical diagnosis. Deep learning models are an emerging tool that can be trained to systemically and accurately identify morphological features; however, training requires large numbers of annotated slide images. Currently, there are limited number of datasets available to train such models, especially those with brain metastases (BrM), where morphology can present heterogeneously based on the primary tumour. The Brain Tumour Tissue Bank (BTTB) at London Health Sciences Center (LHSC) has archived over 2400 CNS malignancies since 1991. Here, we catalogue the current contents of the BTTB and present a collection of high-quality slide images with corresponding clinical information. The BTTB contains over 600 glioblastomas, 400 BrMs, 370 meningiomas, 250 oligodendrogliomas, and 260 pediatric cases. Additionally, 100 cases of the most recent BrMs, collected between 2015-2024, were scanned at 40x magnification to yield 250 high quality slide images, many of which have genomic profiling. Notably, this subset contains rare sources of BrMs, including gynecological, testicular, neuroendocrine, and urothelial malignancies. The integration of morphological features, molecular landscape, and genomic profiling can contribute to and strengthen the training of deep learning models for diagnostic and prognostic purposes. Future efforts will focus on digitizing the remaining slides from the BTTB to establish a comprehensive, open-access digital brain tumour atlas, creating a platform for quantitative pathology research and multi-institutional collaboration.

Keywords: Brain Tumour, Brain Metastasis, Digital Slide Images, Data Curation

Session Abstract: 35

Presenter's Name: Nakada-Sasaki, Yuto

Additional Author(s): Wang C, Liu Q, Passos D, Dick F, Peng T

Abstract Title: Suppression of Obesity by DDIT3-mediated Necroptosis Signaling

Abstract:
Introduction: Obesity is a major global health challenge associated with dysregulated adipocyte turnover, contributing to low-grade chronic inflammation and metabolic syndrome. Sustained endoplasmic reticulum stress induces DNA damage–inducible transcript 3 (DDIT3/CHOP), a key regulator of stress-induced cell death. While the C-terminal basic leucine zipper domain promotes apoptosis through transcriptional regulation, we identified a non-transcriptional N-terminal motif (Glu19–Val28) that mediates necroptosis. Although global DDIT3 knockout increases adiposity, the role of DDIT3-mediated necroptosis in adipose tissue homeostasis remains unclear. We hypothesize that deletion of this 10–amino acid necroptotic motif promotes obesity by impairing regulated cell death.

Methods: We generated DDIT3 ΔGlu19–Val28 knock-in mice (Ddit3-mt-TP) and monitored body weight in Ddit3-mt-TP and wild-type mice for 20 weeks. Serum free fatty acid levels were analyzed to determine whether the progressive weight gain observed in Ddit3-mt-TP mice was associated with metabolic dysfunction. Adipose tissue depots were harvested, weighted, and processed for histological analyses to assess changes in adipocyte number and cell size.

Results: Female Ddit3-mt-TP mice exhibited greater progressive weight gain compared to wild-type mice. Gonadal white adipose tissue showed a significant increase in depot weight normalized to body weight in Ddit3-mt-TP compared with wild-type mice. Serum free fatty acid levels showed no significant difference between Ddit3-mt-TP and wild-type mice. Adipose tissue from Ddit3-mt-TP mice revealed adipocyte hypertrophy and increased inflammatory cell infiltration.

Discussion: Our findings suggest that impaired necroptosis promotes obesity without metabolic dysfunction, providing insight into DDIT3-mediated necroptosis as a key mechanism regulating adipose tissue homeostasis. This study may provide a framework for targeting necroptotic signaling pathways to prevent or treat obesity and its associated complications.

Keywords: Obesity, DDIT3, Necroptosis, Adipose tissue

POSTER SESSION 1

Session Abstract: 36

Presenter's Name: Hird, Cody

Additional Author(s): Smith S, Lawley B, Allias M, Quiñones-Mateu ME.

Abstract Title: Assessing Spillback Risk: Coronavirus Entry Across Mammalian Hosts

Abstract:
Introduction: The COVID-19 pandemic highlighted the remarkable adaptability of coronaviruses (CoVs) and their capacity to cross species barriers. SARS-CoV-2 has since been detected in a growing number of domestic and wildlife species, raising concerns about reverse zoonosis and the establishment of new animal reservoirs. This broad host range is thought to be driven, in part, by conservation of the viral entry receptor, angiotensin-converting enzyme 2 (ACE2), across mammals. In this study, we evaluated the ability of diverse mammalian ACE2 orthologs to support SARS-CoV-2 entry and explored whether acquisition of SARS-CoV-2 spike domains could enhance ACE2-dependent entry of animal CoVs, modelling recombination events that may occur during coinfection.

Methods: ACE2 genes from ten mammalian species were stably expressed in HEK293 cells and validated by qRT-PCR and western blot analysis. Susceptibility to infection was assessed using live SARS-CoV-2 as well as a panel of pseudoviruses bearing divergent CoV spike proteins, with entry quantified via GFP and luciferase reporters. To investigate the impact of spike recombination, the receptor-binding domain (RBD) and N-terminal domain (NTD) of SARS-CoV-2 were exchanged with corresponding regions from selected animal CoV spike genes using Gibson assembly. Resulting chimeric spikes were incorporated into the pseudovirus system and functionally characterised.

Results: ACE2 orthologs from sheep, ferrets, possums, and bottlenose dolphins supported SARS-CoV-2 pseudovirus entry, further enhanced by co-expression of human TMPRSS2. The majority of chimeric spike constructs were successfully expressed. Notably, insertion of either the SARS-CoV-2 RBD or NTD into the spike backbone of certain animal CoVs, including bovine (BCoV) and canine (CCoV) CoVs, enabled entry via human ACE2.

Discussion: These findings demonstrate that multiple mammalian ACE2 orthologs could facilitate SARS-CoV-2 entry, supporting the possibility of spillback into diverse animal hosts. In addition, the gain of human ACE2 usage by chimeric animal CoV spikes underscores the potential for recombination to expand host range and zoonotic risk. Together, this emphasises the importance of ongoing surveillance in animal populations to identify emerging recombinant CoVs and to anticipate future cross-species transmission events.

Keywords: Reverse zoonosis, Coronavirus spike protein, ACE2 receptor, Viral recombination

Session Abstract: 37

Presenter's Name: Wong, Delicia

Additional Author(s): Wang W, Poon AFY

Abstract Title: Assessing the Impact of Superinfection and Recombination on Phylodynamic Inference by Multi-Level Simulation

Abstract:
Introduction: Phylodynamic methods estimate key epidemiological parameters, such as the basic reproduction number (R_0), from viral sequence data by linking phylogenetic tree structure to transmission dynamics. In practice, one generally assumes that sequences are related by a single phylogenetic tree. Superinfection allows divergent viral lineages to coexist within the same host and undergo recombination — the exchange of genetic material between lineages that is common in many viruses. When recombination occurs in the context of superinfection, different genomic regions can have discordant evolutionary histories that cannot be accurately represented by a single tree, potentially biasing phylodynamic inference.

Methods: Here, we quantify how superinfection and recombination affect phylodynamic estimates of R_0 using a multi-level simulation framework. Viral transmission trees and nested within-host phylogenies were simulated under a susceptible–infected–removed (SIR) model. Phylodynamic inference was performed using the birth–death SIR (BDSIR) model implemented in BEAST2. Simulations without recombination were used to establish a baseline level of accuracy. Recombination and superinfection were then introduced by generating ancestral recombination graphs, which were resolved into phylogenies on intervals between breakpoints. Sequence data were simulated along phylogenies with 100 tips using pyvolve and analyzed with BDSIR. Inferred R_0 values were compared to known simulation parameters (R_0=1.96, HIV-1; 3.38, SARS-CoV-2) to measure accuracy and bias.

Results: Baseline simulations accurately recovered R_0 in the absence of recombination (RMSE=0.06 HIV, 0.12 COV). With increasing recombination, trees reconstructed from full alignments became increasingly star-like, i.e., with shorter internal branches. Estimates of R_0 were significantly biased upwards with increasing recombination — +0.012 (95% CI 0.007–0.016) per 10 breakpoints for HIV; +0.041 (0.030–0.053) for COV — with diminishing returns at extreme rates of recombination.

Discussion: These results demonstrate that superinfection can substantially bias phylodynamic inference and highlight important limitations of standard tree-based methods when applied to viruses with high rates of recombination.

Keywords: Phylodynamics, Basic reproduction number, Recombination, Superinfection

POSTER SESSION 1

Session Abstract: 38

Presenter's Name: Lin, Yiming

Additional Author(s): Zia S

Abstract Title: Correlation of C4d Staining with Donor-Specific Antibodies and Clinical Outcomes in Post–Liver Transplant Rejection: A retrospective Single-Center Study

Abstract:
Introduction: Antibody-mediated rejection (AMR) is an important cause of liver allograft dysfunction and failure, driven by donor-specific antibodies (DSA) targeting donor human leukocyte antigens. Complement activation, reflected by C4d deposition, is commonly used to support the diagnosis of AMR in kidney transplantation but remains variably interpreted in liver allografts due to the liver's unique immune tolerance and lack of standardized diagnostic thresholds. This study aims to address this gap by evaluating the relationship between C4d deposition, DSA levels and clinical parameters in post-liver transplant biopsies.

Cases: We retrospectively analyzed liver biopsies from 30 post-transplant patients (ages 6-74): 10 with suspected or diagnosed AMR based on Banff criteria and clinical correlation, 10 with cellular rejection, and 10 with chronic hepatitis. C4d immunostaining was performed and graded using Banff criteria with positivity defined by the extent and distribution of portal and capillary staining. Histopathologic features including portal eosinophilia, endothelial cell hypertrophy, and venulitis severity will be assessed. C4d results were correlated with DSA levels and liver function tests.

Results (Anticipated): We hypothesize that AMR cases will demonstrate strong portal and capillary C4d staining associated with elevated DSA levels. Cellular rejection is expected to show weak or absent C4d staining, while chronic hepatitis cases are anticipated to display minimal or nonspecific C4d labeling.

Discussion and Conclusion: This study aims to clarify the diagnostic utility of C4d staining in liver transplantation by integrating histologic findings with serologic and clinical data. Improved interpretation of C4d in conjunction with DSA levels may enhance recognition of AMR and support more targeted therapeutic decision-making in liver transplant recipients. Although limited by sample size, this study may provide foundation for future multicenter validation.

Keywords: Liver transplant, Antibody-mediated rejection, donor-specific antibodies, C4d, cellular rejection, diagnostic criteria

Session Abstract: 39

Presenter's Name: Searle, Taylor

Additional Author(s): Dick F. A.

Abstract Title: Mechanistic investigation of Trametinib-Mediated Cell Death in High Grade Serous Ovarian Carcinoma Spheroids

Abstract:
Inroduction: High grade serous ovarian carcinoma (HGSOC) is the ninth most common, and fifth most deadly malignancy in Canadian women. The disproportionate mortality of this disease indicates an urgent need for novel treatments. Disease recurrence is a characteristic challenge in treatment of HGSOC as it has the ability to form dormant spheroids. Spheroids undergo unique metabolic processes that make them resistant to growth arresting chemotherapeutics. Previous studies indicate that the MAPK pathway is critical in spheroid survival, and its inhibition via the MEK inhibitor trametinib has been shown to be toxic in spheroids. Thus, further research is warranted to elucidate trametinib's mechanism of action in treatment of dormant spheroids in HGSOC. We hypothesize that trametinib kills spheroids by a controlled non-apoptotic death mechanism.

Methods: To elucidate the mechanism of cell death in spheroids triggered by trametinib treatment, a series of Western blot analyses will be performed. Different protein targets have been selected for the 5 mechanisms of cell death to be explored. They include cleaved caspase 3 (apoptosis), N-terminal gasdermin D (canonical and noncanonical pyroptosis), N-terminal gasdermin E (gasdermin E-dependent pyroptosis), phosphorylated MLKL (necroptosis), and SLC7A11 (ferroptosis). Cells will be treated with selected chemicals to induce each particular cell death pathway for comparison to trametinib treated cells as a positive control. Western blots for target proteins and an alpha tubulin loading control will be analysed via densitometry to investigate protein level differences to determine the mechanism of trametinib-mediated cell death.

Results: In preliminary western blots the absence of cleaved caspase 3 in trametinib-treated OVCAR8 spheroids indicates that apoptosis is unlikely to be the mechanism of cell death. Determined by lack of cleaved caspase 3 protein. However, an observed decrease in SLC7A11 in trametinib treated cells relative to an untreated control suggest that ferroptosis may represent the drug's mechanism of action.

Discussion: This investigation will contribute to a better understanding of Trametinib's mechanism of action. This may additionally allow for expanded Trametinib use and provide the opportunity to investigate how it could be used in a more clinical scenario.

Keywords: High Grade Serous Ovarian Carcinoma, MAPK, MEK, Trametinib, Spheroid, Dormancy

POSTER SESSION 1

Session Abstract: 40

Presenter's Name: Hadj Hassine, Ikbel

Additional Author(s): Jennifer S. Lin, Annelise E. Barron, Miguel E. Quiñones-Mateu

Abstract Title: Natural Host Defense Peptides as Broad-Spectrum Antivirals Targeting Viral Envelopes

Abstract:
Background: The constant threat of known and novel enveloped viruses highlights the urgent need for new and broad-spectrum antiviral strategies. Natural host defense peptides, such as the human cathelicidin LL-37 and amyloid-β (Aβ) are promising candidates since they can directly target viral envelopes, potentially blocking virus entry and replication.

Methods and Results: Here we tested LL-37 and an Aβ-derivates alone and in combination, using cell-based infection assays against different RNA enveloped viruses. Both peptides showed strong antiviral activity, most likely associated to a virucidal (direct) effect without causing noticeable harm to host cells. Targeting viral envelopes provides a mutation-resistant mechanism that is distinct from conventional virus-specific inhibitors.

Conclusions: Inspired by broad-spectrum antibiotics, antivirals with wide-ranging activity could be deployed immediately to reduce the impact of newly emerging viral threats. LL-37 and Aβ demonstrate potential as broad-spectrum antiviral candidates for rapid-response strategies against enveloped viruses.

Keywords: Broad-spectrum antivirals, Host defense peptides, Viral envelopes, Enveloped viruses, Antiviral peptides, Innate immunity

Session Abstract: 41

Presenter's Name: Karimi, Amir Hossein

Additional Author(s): Harrison Pan, Peter Zeng, Sarah EB Ryan, Senyang Wei, Wessam Al Jawhri, Shengjie Ying, Nhi Le, Halema Khan, Krista Joris, Joe S Mymryk, John W Barrett, Anthony C Nichols

Abstract Title: Efficacy, Functional Consequences, and Immunomodulatory Effects of Treatment with a Type II RAF Inhibitor in Anaplastic Thyroid Carcinoma

Abstract: With a historical median overall survival of less than 6 months, anaplastic thyroid cancer (ATC) is the most aggressive type of thyroid malignancy. The improvements in patient outcomes with the addition of RAF inhibitors (RAFis) and MEK inhibitors (MEKi) to the standard of care are marred by the restriction of the efficacy of these treatments to the BRAFV600E-mutant tumours and the rapid development of treatment resistance. These limitations are attributed to the inability of the conventional RAFis to inhibit RAF dimers. Type II RAFis, which are active against RAF dimers, may circumvent treatment resistance in this setting. Here, we investigated the efficacy, functional consequences, and immunomodulatory effects of treatment with the type II RAFi naporafenib, alone or combined with the MEKi trametinib (NT). Using two PDXs and an immunocompetent mouse model of ATC, we have shown that NT can effectively suppress the growth of the tumours resistant to the clinically used combination of dabrafenib and trametinib (DT). Moreover, while monotherapy with anti-PD1 antibodies (αPD1) does not suppress the tumour growth in the immunocompetent model, treatment with the combination of NT and αPD1 demonstrates a more durable response compared to NT alone. Our molecular characterizations have shown that 1) unlike dabrafenib, naporafenib suppresses the MAPK signalling in ATC cells regardless of the MAPK-activating alteration, and this effect is generalizable to the different stages of the disease, 2) naporafenib exerts its effect by concurrent downregulation of the MAPK and PI3K pathways, rendering it more effective against advanced tumours with oncogenic bypass, 3) treatment with naporafenib enhances the expression of interferon-stimulated genes and the MHC complex assembly in cancer cells, promoting their immunogenicity, 4) NT-treated tumours show a higher proportion of lymphocytes in their microenvironment, and the combination of αPD1 with NT significantly increases this proportion, contributing to a more prolonged response, and 5) resistance is primarily achieved through reactivation of the MAPK pathway, and this is accompanied by the depletion of the lymphocytes in the microenvironment. Overall, we have shown that NT can overcome the resistance to DT and is more effective against advanced ATC tumours, combining NT with immunotherapy can lead to a more prolonged response, and resistance primarily recurs via reactivation of the MAPK pathway and enhanced immune evasion.

Keywords: Anaplastic thyroid cancer, Targeted therapy, Immunotherapy, RAF Inhibition

POSTER SESSION 1

Session Abstract: 42

Presenter's Name: Tadepalli, Lakshmi Suchitra

Additional Author(s): Tadepalli LS, Janbahan KS, Gupta R

Abstract Title: Shifting ecology and early resistance signals in Candidemia across Southwestern Ontario, Canada (2020-2024): a multicenter laboratory driven surveillance study

Abstract: Candidemia remains a leading cause of healthcare-associated bloodstream infection with substantial mortality. Local species ecology and antifungal susceptibility patterns determine empiric therapy and vary by region. We performed multisite laboratory-driven surveillance across Southwestern Ontario to quantify trends (2020–2024), define species ecology by age and care setting, and detect early resistance signals to inform stewardship.Retrospective multicenter analysis of routine blood-culture data (Jan 2020–Dec 2024). Episode-level deduplication defined distinct candidemia events. Isolate-level analyses characterized species distribution by age group, hospital unit, and care setting. Antifungal susceptibility testing (AFST) was summarized as categorical interpretations and MIC distributions by species, agent, and year; emergent MIC shifts were examined for early resistance signals.Among 28,847 bloodstream infection episodes, 1,039 were candidemia (3.6%). Non-albicans Candida (61%) exceeded C. albicans (39%). C. glabrata 314 (30%) and C. parapsilosis 185 (18%) were the most frequent NAC. Episodes rose from 160 (2020) to 264 (2023) and declined to 201 (2024); C. glabrata proportion increased from 25% to 36%. Older adults (≥65) had similar C. glabrata (39%) and C. albicans (41%). Adults 40–64 were dominated by C. glabrata (316, 24%) and C. parapsilosis (235, 18%). Pediatric isolates were dominated by C. parapsilosis (125); C. glabrata was rare (3, 2%); neonatal isolates were rare. Medicine wards and ICUs showed highest C. glabrata and C. parapsilosis; C. tropicalis was more common in emergency departments.C. parapsilosis remained fluconazole-susceptible (≈95.5%) but showed emergent resistance (≈1.5%) and SDD with modal MIC shift 2→4 µg/mL (2023–24), consistent with early MIC creep. Caspofungin retained activity (100% susceptible). C. glabrata showed rising micafungin non-susceptibility (~8.3% to ~10.3% from 2022) and fluconazole resistance (up to 16.7%) with increasing high-end MICs. C. tropicalis had rare fluconazole resistance (3.6%) but notable voriconazole intermediate results (~23.1%).Increasing non-albicans candidemia and early MIC shifts in C. parapsilosis and C. glabrata reflect echinocandin selection pressure, FKS-mediated resistance, and emerging fluconazole-resistant C. parapsilosis and heteroresistance that may undermine empiric azole therapy. Routine laboratory surveillance is essential to detect MIC creep and guide stewardship.

Keywords: Candidemia, Non-albicans Candida, Antifungal resistance, Micafungin non-susceptibility, MIC creep, Labratory surveillance

Session Abstract: 43

Presenter's Name: Kim, Ashlyn

Additional Author(s): Santos S, AlMutawa F

Abstract Title: Detection of Mycobacterium tuberculosis in Formalin-Fixed Paraffin-Embedded Tissue Using GeneXpert and BD MAX

Abstract:
Introduction: The diagnosis of tuberculosis (TB) from formalin-fixed, paraffin-embedded (FFPE) tissue samples remains a challenge as the formalin fixation process renders microorganisms non-viable, preventing culture-based methods from being performed. Consequently, there has been increasing interest in the application of nucleic acid amplification tests (NAATs), such as the GeneXpert and BD MAX assays, for TB diagnosis from FFPE samples. However, limited data exists regarding the diagnostic accuracy of NAATs on FFPE tissue, and no standardized DNA extraction protocol has been established. This study aimed to evaluate the performance of GeneXpert and BD MAX assays on the detection of Mycobacterium tuberculosis (Mtb) DNA in FFPE tissue using a simple, xylene-free extraction protocol given the lack of a standardized method.

Methods: FFPE tissue samples with histopathologic features suspicious for TB, such as granulomas or acid-fast bacilli, were analyzed. Specimen types included lymph node, lung, gastrointestinal, skin, and salivary gland tissue. All samples had previously undergone Mtb NAAT testing at a reference laboratory, and these results were used as the reference standard. A total of 12 FFPE samples were tested using GeneXpert and BD MAX following deparaffinization and DNA extraction. Of the 12 FFPE samples, 3 were Mtb-positive and 9 were Mtb-negative by reference lab testing.

Results: Among the 9 Mtb-negative samples, 3 had a presumed nontuberculous mycobacterial infection and 3 had a presumed non-mycobacterial infection. All Mtb-positive samples were from patients who were foreign born and have traveled to TB endemic countries, compared to 2 of 9 patients in the Mtb-negative group. Compared with the reference standard, both GeneXpert and BD MAX demonstrated a sensitivity of 66.7% (2/3) and a specificity of 100% (9/9). The same sample produced a false-negative on both platforms, which may be due to the heterogeneity of the distribution of Mtb in the tissue. As no tissue remained following initial testing, repeat analysis was not possible.

Discussion: Both GeneXpert and BD MAX demonstrated high specificity but moderate sensitivity for the detection of Mtb DNA in FFPE tissue using a simple extraction protocol. These findings support the potential use of NAATs for TB diagnosis in FFPE specimens when culture is not feasible, though further studies with larger sample sizes are needed to optimize extraction methods and improve sensitivity.

Keywords: Mycobacterium tuberculosis, FFPE tissue, GeneXpert, BD MAX

POSTER SESSION 1

Session Abstract: 44

Presenter's Name: Fang, Lisa

Additional Author(s): AlMutawa F, Khan ZA

Abstract Title: Cell-free long non-coding RNAs as mediators of endothelial activation: a novel biomarker and mechanistic link in bacterial sepsis

Abstract:
Introduction: Sepsis is a life-threatening condition characterized by acute organ dysfunction resulting from a dysregulated host response to infection. Current biomarkers often lack the sensitivity to detect sepsis in early stages, which is crucial for achieving optimal patient outcomes. Emerging evidence suggests that cell-free long non-coding RNAs (cf-lncRNAs) are stable, biologically active molecules in serum that may serve as early indicators of host immune response. However, their diagnostic potential and mechanistic relationship to endothelial activation, a key driver of sepsis progression, remain poorly defined. We hypothesize that bacterial sepsis induces a distinct circulating cf-lncRNA signature that is distinguishable from non-septic inflammatory states and correlates directly with vascular endothelial activation.

Methods: We will analyze blood samples from patients with bacterial sepsis and non-septic inflammatory controls, which will be cultured under both aerobic and anaerobic conditions. We will fractionate the samples using differential centrifugation and density gradient media to obtain cf-lncRNAs from cell-free serum and perform lncRNA profiling. To supplement these studies, we will apply filtered patient serum to human umbilical vein endothelial cells (HUVECs) and human dermal microvascular endothelial cells (HDMECs) in vitro; the subsequent expression of SELE, VCAM1, and ICAM1 markers will be measured to quantify endothelial activation.

Results: We expect to identify a reproducible cf-lncRNA signature that reliably distinguishes septic patients from non-septic inflammatory controls. We anticipate that exposure to septic serum will induce significant endothelial activation in both HUVEC and HDMEC models, characterized by the upregulation of and release of SELE, VCAM1 and ICAM1 into the media. Additionally, we expect that the magnitude of this endothelial activation will correlate with the specific cf-lncRNA signature identified, supporting a mechanistic link between the circulating RNA molecules and the endothelial dysfunction in sepsis.

Discussion: This study aims to address a critical gap in understanding the early molecular events underlying bacterial sepsis by linking cf-lncRNA signatures to endothelial activation. Our anticipated findings may support earlier sepsis detection for life-saving clinical intervention and provide a foundation for patient risk stratification and future therapeutic developments.

Keywords: Sepsis, Cell-free long non-coding RNAs, Endothelial dysfunction, Biomarkers, Diagnosis, Systemic inflammation

Session Abstract: 45

Presenter's Name: Patel, Darshil

Additional Author(s): Li H, Zhang Q

Abstract Title: Quality Assurance Analysis of Turn-Around-Times in Neuropathology Medical/Hospital and Biobank Autopsy Consultations at London Health Sciences Centre

Abstract:
Introduction: Neuropathology involvement in autopsy is a relatively complex and time-consuming process, oftentimes requiring tissue fixation, extensive tissue sampling, and a large battery of ancillary staining. This quality assurance (QA) project aims to analyze multiple turn-around-time (TAT) parameters, and the factors associated with them, for neuropathology consultations in medical/hospital and biobank autopsies performed at London Health Sciences Centre (LHSC).

Methods: Multiple parameters were collected for neuropathology consultations in medical/hospital cases from 2014 to 2024 (769 total cases). These included consultation reason (i.e., biobank, diagnostic, documentation), TAT checkpoints (i.e., date of autopsy, date of gross examination (brain cut), final case sign-out), specimen type(s) collected (i.e., brain, spinal cord, muscle, etc.), and involvement of trainees. The data was organized (599 cases; 170 cases were excluded due to an inability to acquire date of gross examination) to analyze the association of various parameters on TAT.

Results: From 2014 to 2024, the median TAT from the date of autopsy to neuropathology consultation sign-out (overall TAT) was 116 days with an interquartile range (IQR) of 60 days. The median TAT from the date of autopsy to specimen gross examination (brain cut) was 16 days (IQR 13 days). 64% of cases had a grossing TAT of greater than 14 days, and among these cases 69% were for biobanking or involved a question of neurodegenerative pathology, which typically require more extensive sampling. The inclusion of additional specimens beyond brain and spinal cord (e.g. eyes, muscle, nerve) was not associated with a longer grossing TAT, although assessment is limited by low case volumes and under-representation in this group. For more recent cases from 2022 to 2024, the median overall TAT remained stable at 117 and 116 days respectively (IQR - 60 days for both years); however, the average increased from 110 to 165 days. This was associated with an increase in grossing TAT from 15 to 36 days. The number of biobank cases per year remained relatively stable during this time.

Discussion: While the factors underlying turn-around-times in neuropathology autopsy consultations (including a noticeable increase in recent years) are multiple and complex, this analysis highlights certain parameters, such as reason for consultation and particular stages of specimen processing, which are worth further exploration.

Keywords: Neuropathology, Hospital/Medical autopsy, Quality Assurance, Lab Management

Session Abstract: 46

Presenter's Name: Gordon, Caroline

Additional Author(s): Olea-Popelka FJ

Abstract Title: Exploring the Relationship Between Antimicrobial Resistance and Biosecurity Practices in Swine Production Systems

Abstract: The misuse of antibiotics in both human and animal populations has accelerated the development of antimicrobial resistance (AMR), rendering many first-line lifesaving antibiotics ineffective against resistant bacteria. Swine production systems are one of the world's primary drivers of AMR development, particularly due to the consolidation and intensification of farms, as fewer facilities confine animals in increasingly dense populations. The subtherapeutic use of antibiotics in livestock feed to increase productivity has provided a major avenue for the selection of AMR, however, several studies discuss the persistence of AMR despite reduced or absent antimicrobial use (AMU) in livestock systems. Biosecurity practices—for example, disinfection routines, waste management, and limiting external farm access—traditionally implemented to reduce the spread of infectious disease, are considered a promising approach to reducing AMU and resistance. However, no research has synthesized the specific effects of biosecurity on AMR; thus, this scoping review maps available literature on this relationship. This scoping review follows the PRISMA-ScR framework, using PubMed, Scopus, and USDA NAL databases to retrieve publications and (1) determine which biosecurity factors have been studied in relation to AMR in swine, (2) describe how these practices are defined across available literature, (3) synthesize reported associations between AMR and biosecurity measures, and (4) report any gaps in the literature. By mapping the current evidence base and identifying knowledge gaps, this review assesses the potential role of biosecurity as a complementary strategy for AMR mitigation in swine systems. Findings aim to support more integrated One Health approaches by addressing underexplored links between animal husbandry and AMR development and spread.

Keywords: Antimicrobial Resistance, Biosecurity, Farm Management, Livestock Production, One Health

Session Abstract: 47

Presenter's Name: Wang, Xiaopu

Additional Author(s): McKinley G

Abstract Title: A Retrospective Review of an Adolescent Suicide Cluster among First Nations Communities in Northern Ontario using the Integrated Motivational-Volitional (IMV) Model

Abstract:
Introduction: Suicide clusters among adolescents are a significant public health concern and remain underexplored in First Nations populations in Northern Ontario. The Integrated Motivational-Volitional (IMV) model of suicidal behaviour provides a structured framework to examine progression from early life adversity and suicidal ideation to suicidal behaviour. This study retrospectively examined a First Nations adolescent suicide cluster in Northern Ontario using the IMV model.

Methods: A file review was conducted on suicide deaths among individuals aged 10-17 years in Ontario between January 2017 and August 2019. Coroner investigation files, police reports, and supporting documentation were reviewed. Initial screening identified five deaths occurring within nine months in nearby First Nations communities in Northern Ontario, with documented social connections between decedents. Case information was coded into the pre-motivational, motivational, and volitional phases of the IMV model. Past and recent non-suicidal self-injury (NSSI) were incorporated across all phases.

Results: All five decedents were female adolescents aged 11-13 years, and all deaths occurred by hanging. In the pre-motivational phase, four had substance misuse and a history of NSSI, and three had Children's Aid Society involvement. In the motivational phase, all demonstrated recent NSSI, and four expressed suicidal ideation or distress. Volitional moderators (VMs) were consistently identified, including exposure to suicide, access to means, and past or recent NSSI in all cases; suicide planning and prior attempts were present in three.

Discussion: Consistent factors were identified across the three IMV phases, suggesting that vulnerabilities were present at multiple stages across cases within this cluster. Shared VMs align with the IMV model, which emphasizes their role in the transition from ideation to behaviour. All decedents were exposed to the suicide of a friend, which may indicate social contagion. Additionally, the age and sex distribution observed in this First Nations suicide cluster differs from the national Canadian suicide trends: higher rates among older adolescents and males. In short, these findings highlight the value of the IMV model in understanding adolescent suicide clusters, emphasize the importance of considering multilevel risk factors, and underscore the need for community-specific prevention strategies.

Keywords: Suicide cluster, adolescent suicide, Integrated Motivational-Volitional (IMV) model, non-suicidal self-injury (NSSI)

POSTER SESSION 1

Session Abstract: 48

Presenter's Name: Sharobim, Michael

Additional Author(s): Darling M, Cecchini M

Abstract Title: Signaling Pathway Markers (E-cadherin, β-catenin, and BRAF) in Chronic Hyperplastic Candidiasis and Malignant Transformation Risk

Abstract:
Introduction: Oral squamous cell carcinoma (OSCC) is frequently preceded by oral potentially malignant disorders (OPMDs), yet current clinicopathologic tools such as histologic dysplasia grading do not reliably predict which lesions undergo malignant transformation. Chronic hyperplastic candidiasis (CHC) is a persistent, non-scrapable oral white plaque associated with Candida infection and remains clinically relevant because some lesions progress to OSCC, but transformation-specific biomarkers are lacking. E-cadherin, β-catenin, and BRAF are key components of epithelial adhesion and oncogenic signaling pathways implicated in early carcinogenesis, and quantifying their epithelial expression may improve risk stratification in CHC.

Hypothesis: CHC lesions that transform to OSCC will demonstrate reduced membranous E-cadherin, increased nuclear β-catenin, and increased epithelial BRAF V600E immunoreactivity compared with non-transforming CHC and normal tissue controls.

Methodology: This retrospective study will analyze immunohistochemistry (IHC) slides for E-cadherin, β-catenin, and BRAF from normal tissue controls (NTC) and CHC cases stratified by transformation outcome (non-transforming vs transforming CHC), using digitized slide images and QuPath-based quantitative bioimage analysis. For each marker, epithelium will be annotated and quantified using positive cell detection to generate intensity-based metrics (e.g., H-score, mean DAB optical density, percent positivity) and, where applicable, compartment metrics emphasizing membranous (E-cadherin) and nuclear localization (β-catenin). Group differences will be assessed using appropriate statistical testing (e.g., one-way ANOVA with post-hoc comparisons or non-parametric equivalents depending on distribution), with exploratory analyses evaluating associations with clinicopathologic variables (e.g., age, sex, site, dysplasia grade).

Results: We anticipate that pathway-disruptive staining patterns such as membranous E-cadherin loss and nuclear β-catenin accumulation will be most pronounced in CHC lesions that transform to OSCC, with increased BRAF V600E immunoreactivity in the transforming group.

Discussion: If confirmed, these findings would support a mechanistically grounded quantitative biomarker approach to complement routine histopathology, improve identification of higher-risk CHC lesions, and provide a rationale for future validation studies and pathway-informed risk models in CHC and related OPMDs.

Keywords: Chronic hyperplastic candidiasis, oral potentially malignant disorders, QuPath, E-cadherin, β-catenin, BRAF

Session Abstract: 49

Presenter's Name: Wang, Tracy

Additional Author(s): Houpt J, Eric L, Qi Z

Abstract Title: The Prognostic Value of Atypical Mitotic Figures in Meningiomas

Abstract:
Introduction: Meningiomas arise from the meninges and are the most common type of primary intracranial tumour. The WHO classifies meningiomas into three grades: grade 1 tumours are slow growing and benign, with 0-3 mitotic figures per 10 HPF. Grade 2 are more aggressive and have a higher risk of recurrence, with 4-19 mitotic figures per 10 HPF. Grade 3 are highly aggressive and malignant, with ≥20 mitotic figures per 10 HPF. Mitotic figures can also be classified as normal or atypical, with atypical mitotic figures representing abnormal, asymmetrical forms of cell division. These atypical mitoses have shown to be negative prognostic markers for certain tumours, such as pancreatic and breast cancers. This research aims to identify whether such an association exists for meningiomas as well.

Methods: 30 meningioma whole slide images were retrieved from the Digital Brain Tumour Atlas, with 10 from the meningothelial category, 10 atypical, and 10 anaplastic, representing grade 1-3 meningiomas respectively. Each slide was annotated for normal and atypical mitotic count, and the annotations were confirmed by an expert reviewer.

Results: Preliminary findings suggest that there are more atypical mitotic figures present in anaplastic/grade 3 meningiomas, with very few being identified in the atypical and meningothelial samples. Atypical mitoses were present to varying degrees in many, though not all, of the anaplastic samples.

Discussion: The current histopathological criteria to diagnose a grade 3 meningioma are either a mitotic rate ≥20 mitotic figures/10 HPF or frank anaplasia, the latter of which is up to individual judgement. Establishing a correlation between atypical mitosis score and tumour grade may provide another diagnostic criterion that is quantitative and notably does not rely on mitotic figure density. If a threshold score can be characterized, atypical mitoses would transform from simply an interesting observation to a prognostically significant marker in the management of meningiomas.

Keywords: Meningioma, mitotic figure, atypical mitosis, anaplastic, intracranial tumour

POSTER SESSION 1

Session Abstract: 50

Presenter's Name: Cheah, Lok In

Additional Author(s): Nichols M, Rutledge A, Stevic I

Abstract Title: Determining Pre-analytical Requirements for Testing Biogenic Amine Markers in Neuroendocrine Tumors

Abstract:
Introduction: Measurement of analytes in 24-hour urine specimens can be done for reasons such as assessing renal function, hormone levels, metabolic function, or toxin exposure. Another role is diagnosis of neuroendocrine tumors (NETs), a heterogeneous group of neoplasms arising from neuroendocrine cells. However, accurate results and diagnosis depend on maintaining integrity of the analytes in the specimens until testing is completed (i.e. during the 24-hour urine collection period, until the urine is delivered to the lab, and during storage within the lab). No guidelines exist with recommendations for standardized pre-analytical procedures; instead, inconsistent practices are followed between labs. This study aimed to evaluate the effects of pre-analytical factors such as temperature and acid preservatives on stability of key urinary biogenic amines used in specialized NET testing (5-hydroxyindoleacetic acid (5-HIAA), metanephrines (metanephrine, normetanephrine, and 3-methoxytyramine), homovanillic acid (HVA), vanillylmandelic acid (VMA), and serotonin), as well as analytes measured in more routine urine tests (calcium, creatinine, glucose, albumin, magnesium, phosphate, total protein, urea, and uric acid) that were felt to be potentially susceptible to pre-analytical factors.

Methods: Urine samples were stored at 4 °C or room temperature, with or without addition of hydrochloric acid, for up to four weeks. Analyte concentrations were measured periodically using automated chemistry analyzers or liquid chromatography–mass spectrometry for four weeks or until degradation exceeded acceptable stability criteria.

Results: Although prior studies generally report superior analyte stability with acid preservation, our findings showed that storage at 4 °C without acid provided the greatest stability for HVA, VMA, serotonin, and all routine analytes evaluated. Acidification conferred a modest stability advantage only for 5-HIAA, while significantly compromising albumin, total protein, and uric acid.

Discussion: By identifying optimal conditions for urinary biogenic amines and commonly tested analytes, this study will improve the accuracy and reliability of urine testing for neuroendocrine tumors and other conditions. These findings will support development of effective urine handling procedures at London Health Sciences Centre and will be published to assist other labs.

Keywords: Neuroendocrine tumor, Biogenic amine, Urinary biomarker, Urine stability, Pre-analytical, Acid

Session Abstract: 51

Presenter's Name: Romagnoli, Tommaso

Additional Author(s): Romagnoli T, Lin S, Bychkov A, Cima L, Munari E, Rasmussen S, Sharma A, Singh R, Ullah E, Wehrli, B, Cecchini M

Abstract Title: Evaluating the utility of large language models for cross-linguistic pathology reporting

Abstract:
Background and Objectives: Large language models (LLMs) demonstrate potential for improving pathology text translation, offering a tool for better cross-border collaboration. This study evaluates the translational capacity of LLMs in pathology compared to traditional methods.

Methods: Ten pathology cases were prepared in English and translated into Italian by two pathologists including diagnosis and commentary. These were then translated back into English using GPT-4, Gemini (1.0) and Google Translate. Five English-speaking pathologists evaluated the translations for medical terminology, report structure and contextual comprehension using a 5-point Likert scale. Their suitability for clinical use was also assessed.

Results: GPT-4 demonstrated significantly better performance in medical terminology and report structure compared to Gemini and Google Translate. Contextual understanding was similar across the three translation methods. The majority of pathologists rated GPT-4 translations as acceptable for clinical practice (62%), exceeding Gemini (40%) and Google Translate (36%). Notably, only 8% of GPT-4 translations were deemed unacceptable as compared to Gemini (38%) and Google Translate (26%).

Conclusion: This study offers preliminary insights into the potential of LLMs for improving pathology text translation. The ability of LLMs to grasp the nuanced medical context holds promise. As LLMs rapidly evolve, future studies with larger datasets and a wider range of languages will be needed to fully explore their capabilities. LLMs could play a role in breaking down language barriers in pathology thereby facilitating global collaboration and potentially driving standardization in reporting

Keywords: Machine learning, Pathology, Large language model, Translation

POSTER SESSION 1

Session Abstract: 52

Presenter's Name: Chen, Maggie

Additional Author(s): Jacques R

Abstract Title: Making Autopsy Pathology Green: A Quality Improvement Project

Abstract:
Introduction: Climate change is driving substantial increases in global morbidity and mortality, yet the contribution of healthcare systems to this problem remains under-recognised. Within the ethical framework of principlism, physicians have a responsibility to engage in climate-conscious practice to support the health of current and future patients. The largest opportunity for mitigation lies in Scope 3 emissions, which include all waste-related emissions. Preliminary observations in pathology at University Hospital (UH) have revealed substantial overclassification of biomedical waste, high volumes of formalin disposal, and preventable waste of plastic cassettes. Hence, this study aims to develop detailed, replicable quality improvement interventions in these areas to reduce Scope 3 emissions within autopsy pathology at UH.

Methods: Three initiatives will be piloted: (1) solid waste audit paired with a redesigned bin system, (2) formalin recycling circuit that repurposes clear formalin from surgical pathology for autopsy use, and (3) cassette-reduction strategy informed by usage-pattern analysis. Each intervention was developed collaboratively with waste management staff, pathology personnel, and housekeeping teams to ensure feasibility within existing workflows. Pre- and post-intervention comparisons quantified changes in biomedical waste diversion and formalin reuse, which were converted to carbon emission equivalents and cost savings. Cassette usage analysis was used to encourage reflective practice and reduce unnecessary plastic consumption.

Results: Preliminary findings demonstrate a significant shift in waste composition per autopsy, from 99% biomedical and 1% landfill waste to 25% biomedical waste, 63% landfill waste, and 12% recycling. The formalin recycling pilot implemented at a single workstation is projected to re-purpose approximately 360 kg of formalin waste annually, with greater reductions anticipated as the initiative expands.

Discussion: These interventions significantly reduced Scope 3 waste streams within autopsy pathology while generating standard operating procedures (SOPs) for sustainable practice that can be adopted at an institutional level. This quality improvement project establishes a foundation for sustained cultural change within pathology and highlights the importance and impact of integrating planetary health principles into everyday ethical healthcare practice.

Keywords: Sustainable healthcare, Autopsy pathology, Waste reduction, Quality improvement, Planetary Health

Session Abstract: 53

Presenter's Name: Zhang, Richard

Additional Author(s): Hosseini N, Bérubé NG, Shooshtari P

Abstract Title: Identifying cell type- and developmental stage-specific gene regulation driving schizophrenia risk using a comprehensive multi-omics approach.

Abstract:
Introduction: The prenatal period of neurodevelopment is considered an important susceptibility period where genetic and other risk factors can act to increase one's likelihood of developing schizophrenia (SZ) later in life. Genome-wide association studies (GWAS) have identified thousands of SZ-associated single nucleotide polymorphisms (SNPs), many located in regulatory regions of DNA where they may perturb gene expression. To date, the specific SNPs driving SZ risk and their gene regulatory effects, which may be restricted to specific brain cell types and/or developmental stages, remain unclear.

Methods: To pinpoint these SNPs and their context-specific regulatory effects, we utilized RegSCOUT (Regulatory Single-Cell Omics for Unraveling Trait-loci), a disease-agnostic computational pipeline developed in-house, which integrates GWAS with other omics datasets. RegSCOUT integrated 2 SZ GWAS with 5 scATAC-seq datasets. This provided context specificity over 1 adult and 4 prenatal timepoints across mouse and human neurodevelopment, with a median of 10 cell types per timepoint. This analysis identified developmental stage- and cell type-specific open chromatin regions, transcription factors (TFs), and SNPs putatively relevant to SZ etiopathogenesis. Results of this step were then coupled with 3 Hi-C and 2 eQTL datasets to prioritize context-specific SZ-relevant genes. The expression of TFs in their associated cell types and developmental timepoints was confirmed using 6 scRNA-seq datasets. EnrichR was used to conduct pathway enrichment analysis of prioritized genes.

Results: A total of 393 SNPs influencing the binding affinity of 415 TFs, 563 open chromatin regions, 86 genes, and 28 biological pathways were found relevant to SZ risk. Notably, the binding of the TFs DLX6 and NKX6-2 to their binding motifs, two TFs important for GABAergic interneuron development, were both impacted by an average of 12 SZ risk-associated SNPs. In addition, two genes, SATB2 and BCL11B, involved in excitatory neuron fate specification, were prioritized in neuronal progenitor cells at two prenatal timepoints.

Discussion: Our findings demonstrate the importance of SNP-mediated gene regulation in the prenatal susceptibility period of SZ. They underscore the need to account for cellular and developmental context when studying complex disease-associated SNPs. Overall, our results substantiate previous and generate novel mechanistic hypotheses into SZ etiopathogenesis.

Keywords: Schizophrenia, Prenatal neurodevelopment, Multi-omics analysis, GWAS, Gene regulation

POSTER SESSION 1

Session Abstract: 54

Presenter's Name: Zhang, Xuanning

Additional Author(s): Naghavi NH, Nazari MHD, Zhang R, Shooshtari P

Abstract Title: Uncovering Immune Cell-type- and Site-specific Gene Regulatory Mechanisms Underlying Osteoarthritis

Abstract:
Introduction: Osteoarthritis (OA) is the most common degenerative joint disease with a complex multi-factorial pathogenesis that is not fully understood. Immune processes are increasingly recognized as relevant to the disease; however, it remains largely unknown which specific immune cell subtypes contribute to OA and which gene regulatory mechanisms are disrupted within those cells. My research addresses these gaps through multi-omics data integration.

Methods: To develop a better understanding of the involvements of specific immune cell subtypes in OA, the computational pipeline RegSCOUT developed at Shooshtari Lab was applied to integrate OA GWAS statistics at commonly affected joints knee, hip, and hand with open chromatin regions in 17 immune cell subtypes determined by scATAC-seq. RegSCOUT identified OA risk variants located in cell-type specific chromatin accessible regions that can be accessed by transcription factors (TFs). Motif information was then used to pinpoint variants that alter the binding affinity of TFs. scRNA-seq data were incorporated to confirm the implicated TFs are expressed in the relevant cell type. The putative genes were prioritized using findings from Hi-C, eQTL, and chromatin co-accessibility using Cicero. Downstream analysis was performed using R to visualize and compare the findings from all the joints.

Results: 21 genes and 57 TFs were identified to be associated with knee OA, 35 genes and 97 TFs with hip OA, and 5 genes and 16 TFs with hand OA. Among all the genes, TGFA, which encodes transforming growth factor alpha, was the only gene prioritized to OA at all three sites (knee, hip, and hand) in adaptive natural killer cells and cytotoxic natural killer cells with evidence from eQTL and Cicero.

Discussion: The findings from my research revealed the putative immune cell-specific gene regulatory mechanisms that may contribute to the risks of OA across different joints. Although several prioritized genes have been studied in chondrocytes, their roles in immune cells remain unexplored. Our analysis also identified novel genes which have not been linked to OA before. This highlighted an important knowledge gap and direction for future research. As a next step, scATAC-seq and scRNA-seq data from immune cells in OA patients and healthy controls can be used to validate and further characterize the gene regulatory mechanisms identified in this study.

Keywords: Osteoarthritis, Gene regulation, Immune cells, Single-cell, Genome-wide association study, Chromatin accessibility

Session Abstract: 55

Presenter's Name: Wu, Christina

Additional Author(s): Chang X., Zheng X.

Abstract Title: Optimizing In Vitro Production of circZMIZ1 via the T4 Permuted Intron-Exon System

Abstract:
Introduction: Circular RNAs (circRNAs) are covalently closed RNA molecules generated through back-splicing and are characterized by high stability and diverse regulatory functions. Their durability and translational potential have driven interest in synthetic circRNAs for therapeutic applications, yet current in vitro synthesis methods often yield low circularization efficiency and substantial linear RNA contamination. This study aims to optimize the T4 Permuted Intron-Exon (PIE) system for efficient, high-purity synthesis of circZMIZ1-7354, and to assess its sustainment in vivo.

Methods: Using the DNA template of circZMIZ1-7354 (657 base pairs), linear precursor RNA was generated by in vitro transcription. Circularization was optimized by testing different combinations of cofactors, including $MgCl_2$, NH_4Cl, PEG8000, NaCl, HEPES, KCl, and GTP. RNA was extracted via the chloroform-isoamyl alcohol method, and RNase R digestion was conducted to remove linear RNA species. Next, the RNA products were separated by native agarose gel electrophoresis and visualized using different SYBR stains. To demonstrate sustainment, purified circZMIZ1 was transfected into B16 mouse melanoma cells, and circRNA levels were assessed after 6, 12, 24, and 48 hours by cDNA synthesis followed by qPCR.

Results: Optimized reaction conditions showed that inclusion of RNase OFF during in vitro transcription reduced RNA degradation and increased transcriptional yield. Addition of supplemental cofactors during circularization did not significantly increase circRNA yield, indicating that splicing primarily occurred during overnight transcription. RNase R titration identified optimal enrichment at 1U per 1µg RNA for thirty minutes to effectively remove linear RNA. Gel electrophoresis and visualization were enhanced by the incorporation of 2% sodium hypochlorite and SYBR Green II staining. Lastly, RT-qPCR is expected to demonstrate sustained circZMIZ1 levels across all time points, supporting post-transfection stability.

Discussion: These findings may enhance current approaches for synthetic circRNA production by establishing a more efficient, high-purity workflow. Improved optimization and validation methods could support broader applications of synthetic circRNAs in research and therapeutics, offering a scalable framework for generating durable RNA constructs.

Keywords: Circular RNA, circZMIZ1, T4 PIE system, RNA circularization, circularization efficiency

POSTER SESSION 1

Session Abstract: 56

Presenter's Name: Gupta, Ruchika

Additional Author(s): Delport, Johan

Abstract Title: An Explainable, Scalable, and Auditable AI Microscope for Clinical Gram-Stain Triage

Abstract:
Introduction: Rapid interpretation of Gram-stain microscopy remains a critical bottleneck in early sepsis management, where diagnostic delays directly affect patient outcomes. Gram stain images present unique machine learning challenges that make generalization difficult: wide variation in bacterial size and distribution (class imbalance), organisms occupy only a few pixels per field (pixel-wise imbalance), staining and scanner variability (domain shift), and the clinical requirement for localization and counts, not just a morphology label to support interpretable evidence.

Methods: We developed an integrated, audit-ready AI microscopy system that performs high-throughput screening, segmentation, and deterministic classification in a unified pipeline engineered for explainability and clinical reliability. The pipeline has five components: a binary screening classifier (filters 60–90% of empty patches), dual-headed segmentation-classification network (one forward pass, two outputs), explainability suite (attention-map CAM methods), multi-threshold tuning tool (to adjust sensitivity for active learning) and local batch inference engine (preserves directory structure, generates overlays and CSVs). The approach combines a joint segmentation–classification architecture with a multi-method explainability suite that explicitly visualizes model attention across the field of view. The system incorporates tunable thresholds, full traceability, and an active-learning loop designed to counter domain shift and class imbalance.

Results: Trained on 500K crops (256×256 pixels), the system achieves 99.5% classification accuracy and 97.7% segmentation accuracy while producing overlays with adjustable thresholds and complete audit trails. A cascade of lightweight convolutional networks and transformers enables high-throughput local inference approximately 1,000 images per minute on consumer-grade GPUs.

Conclusion: By prioritizing auditability, tunability, and operational robustness over raw accuracy, this work demonstrates a viable path toward deployable, trustworthy AI tools for microbiology and real-time sepsis triage.

Keywords: AI, Gram stain, Automation, Sepsis Triage

Session Abstract: 57

Presenter's Name: McConkey, Haley

Additional Author(s): van der Laan L, Ghosh S, Kleinendorst L, Levy MA, Rzasa J, van Hagen JM, Waisfisz Q, Biskup S, Schulz HL, Platzer K, Jamra RA, Marinakis N, Veltra D, Kosma K, Sofocleous C, Henneman P, van Haelst MM, Sadikovic B

Abstract Title: Discovery of a DNA methylation episignature for Weiss-Kruszka syndrome

Abstract: Weiss–Kruszka syndrome (WSKA; OMIM 618619) is a rare autosomal dominant neurodevelopmental disorder caused by haploinsufficiency of ZNF462, a zinc-finger transcription factor involved in chromatin regulation and early embryonic development. WSKA is characterized by craniofacial dysmorphism, developmental delay, hypotonia, and variable congenital anomalies. Genome-wide DNA methylation (DNAm) profiling was performed on peripheral blood DNA from individuals with pathogenic or likely pathogenic ZNF462 variants and matched controls to look for differential methylation. Analysis using the EpiSign pipeline identified a robust DNAm pattern, or episignature, specific to WSKA cases. Supervised machine-learning classification demonstrated high sensitivity and specificity, with reproducibility confirmed by leave-one-out cross-validation, as well as correctly classifying a validation case with a pathogenic ZNF462 variant. Comparative analysis revealed partial overlap of genome-wide DNA methylation changes between the WSKA episignature and other neurodevelopmental disorders involving epigenetic machinery. Functional annotation of differentially methylated probes and regions demonstrated enrichment for pathways related to neurodevelopment, neuron function, and cell adhesion. These findings define and validate a distinct DNAm episignature for WSKA, providing a valuable diagnostic biomarker to support variant classification, and offer insight into the epigenomic consequences of ZNF462 haploinsufficiency.

Keywords: Episignature, Diagnostic biomarker, DNA methylation, Chromatin-remodeling, Rare disease, Functional assay

POSTER SESSION 1

Session Abstract: 58

Presenter's Name: Reyes-Ballesteros, Bernardo

Additional Author(s): Reyes-Ballesteros B, Kang C.Y, Mason N.C, Lawley B, Hernandez L.C, Comoletti D, Connor L.M, Avis P, Arts E.J, Quiñones-Mateu M.E.

Abstract Title: Development of Pan-Vaccines for Pandemic Prevention.

Abstract:
Background: There are over 100 alpha (a)- and beta (b)- coronaviruses (CoVs) circulating in animals that have the potential to spill over into humans; thus, multiple groups across the globe are working on universal or Pan-CoV vaccines able to protect against one or more CoV lineages. Here we describe a proof-of-concept study aimed to characterize the ability of a SARS-like b-CoV spike consensus sequence to elicit broadly reactive antibodies against different b-CoVs.

Methods and Results: Forty-two SARS-like CoV spike amino acid sequences were aligned and used to generate a SARS-like b-CoV spike consensus sequence. We used AlphaFold3 to predict protein structure, showing a root-mean-square deviation of 5.15 and 6.94 Å when compared with the SARS-CoV-2 Wuhan (Wu) and SARS-CoV tor2 spike structures, respectively. Moreover, the SARS-like b-CoV spike consensus sequence showed in silico predicted B-cell epitope immune response. Next, we cloned the SARS-like b-CoV spike consensus -and SARS-CoV-2 Wu spike as control- into a proprietary rVSV-based vaccine system and used them to immunize BALB/c mice. Serum samples from mice immunized with the control VSV-SARS-CoV-2 Wu vaccine were able to neutralize autologous SARS-CoV-2 Wu spike pseudotyped viruses (median NT50 = 2,448) but failed to inhibit viruses pseudotyped with SARS-CoV spike (median NT50 = 138, $p < 0.001$). Interestingly, serum samples from mice immunized with our vaccine candidate VSV-SARS-like b-CoV spike consensus showed broader neutralization, inhibiting CoV-spike mediated entry of both SARS-CoV-2 Wu and SARS-CoV (median NT50 = 1,228 and 1,118, respectively, $p = 0.51$). Similar results were obtained with bat SARS-like CoV spike pseudotyped viruses, such as WIV1, LYRa11, and BANAL-20-236.

Conclusions: This successful proof-of-principle study, based on a SARS-like b-CoV spike consensus sequence, encouraged us to expand our universal vaccine program aimed to develop vaccine candidates against selected a- and/or b-CoV lineages. Ongoing promising studies with Sarbecovirus-specific constructions may led to the production of novel vaccines capable of conferring broad protection against disease by CoV lineages known to currently or potentially infect humans, and most likely to be responsible for the next zoonotic viral outbreak. This pan-vaccine approach could, be extended to other pathogen families/groups such as the influenza, Ebola, and Lassa virus, where broad-spectrum strategies are required.

Keywords: Pan-Vaccines, Pandemic Prevention, Viral Evolution, Coronavirus, AlphaFold3, Vaccine Development

Session Abstract: 1

Presenter's Name: Sutherland, Janice

Additional Author(s): McKinley, G.

Abstract Title: A Qualitative Examination into the Factors that Influence Dog Walking: A One Health Approach

Abstract: The factors impacting dog walking in London and surrounding area are not well documented. Research tells us that physical activity is associated with both positive physical and mental health outcomes. Lack of physical activity is known to be one of the main risk factors for non-communicable disease. In this study, a One Health perspective was used to explore what factors influence dog walking frequency and duration. Through qualitative interviews an examination is being done to identify the barriers and facilitators of dog walking. The interview data gathered is being examined through thematic analysis to determine the factors that impact dog walking. These factors are then being mapped onto the Dahlgren and Whitehead Model of the social determinants of health to identify areas where policy can be developed to address barriers to dog walking and to facilitate dog walking in London and Middlesex area.

Keywords: One Health, Dog walking, Health, Exercise, Social Determinants of Health

POSTER SESSION 2

Session Abstract: 2

Presenter's Name: Lu, Haitao

Abstract Title: ADAR1 and RIPK1 orchestrate the ZBP1-RIPK3 complex-mediated PANoptosis and heart transplant rejection

Abstract: Following heart transplantation, ischemia–reperfusion injury and graft stress promote the accumulation of Z-DNA within cardiac grafts, particularly in microvascular endothelial cells. ZBP1 functions as a cytosolic sensor of Z-DNA, triggering PANoptosis, an integrated inflammatory cell death program encompassing pyroptosis, apoptosis, and necroptosis.

At early stages of graft injury, ADAR1 interacts with ZBP1 to restrain PANoptotic signaling, limiting ZBP1–RIPK3 complex formation and protecting endothelial integrity. As injury progresses, RIPK1 promotes RIPK3 phosphorylation and stabilizes the ZBP1–RIPK3 complex, amplifying PANoptosis and propagating inflammatory graft damage.

In vivo heart transplantation models demonstrate marked upregulation of ZBP1 and Z-DNA within cardiac grafts, coinciding with activation of PANoptotic pathways. Importantly, donor heart–specific ZBP1 deficiency suppresses PANoptosis, reduces acute and chronic graft injury, attenuates anti-donor immune responses, and significantly prolongs graft survival.

Clinical Implication: These findings identify ZBP1-dependent PANoptosis as a previously unrecognized, therapeutically actionable mechanism of cardiac allograft rejection. Targeting ZBP1 offers a non-immunosuppressive strategy to simultaneously limit multiple programmed cell death pathways, preserve endothelial function, and improve long-term heart transplant outcomes.

Keywords: PANoptosis, Heart Transplantation, ADAR1-ZBP1, ZBP1-RIPK3

Session Abstract: 3

Presenter's Name: Li, Yueyang

Additional Author(s): Walsh, JC.

Abstract Title: Trends in Colorectal Cancer Diagnosed at London Health Sciences Centre (LHSC) from 2004 to 2023.

Abstract:
Background: Colorectal cancer (CRC) is the third most frequently diagnosed cancer in Canada and is the second-leading cause of cancer-related mortality. Although its overall incidence and mortality rate has decreased over the past several decades, cases among individuals under 50 years of age (early-onset CRC) have been increasing. Despite growing national and international data, there is limited information on how these trends manifest at the local level. Here, we present a review of all CRC cases diagnosed on resection specimens at LHSC between 2004 and 2023, examining temporal trends in patient age, tumour site, and pathological T-stage.

Methods: A total of 5,436 CRC resections diagnosed between 2004 and 2023 were identified. Pathology reports were reviewed, and patient age, primary tumour site, and pT-stage were recorded. Cases of recurrent disease or non-colorectal primaries (e.g., small bowel) were excluded. For specimens with multiple tumours, the lesion with the highest pT-stage was selected; if the pT-stages were equal, the larger tumour was selected. pT4a and pT4b categories were reclassified according to the most recent CAP protocol as needed. Data visualization and statistical analyses were conducted using RStudio.

Results: A total of 394 cases of early-onset CRC were identified, showing an overall increase across the study period. The rectum was the most common primary tumour site, and pT3 was the most frequently observed pathological stage. Variations in both tumour site and pT-stage distribution were noted over time. Preliminary comparisons between early-onset and non–early-onset CRC showed no major differences in pT-stage distribution but suggested a predominance of distal tumours among early-onset CRC cases.

Discussion: This study contributes to the growing Canadian literature on early-onset CRC, which collectively may have important public health implications in the future. At the local level, it highlights the need for increased awareness of early-onset CRC. These findings may encourage collaboration among pathologists, gastroenterologists, surgeons, and primary care providers to improve early detection and management.

Keywords: Colorectal cancer, Epidemiology, Early onset colorectal cancer, London

POSTER SESSION 2

Session Abstract: 4

Presenter's Name: Mihele, Maria

Additional Author(s): Greasley A, Chahal S, Nagpal D, Zheng X

Abstract Title: Mechanistic Investigation of Sodium Thiosulfate in Cardiac Transplant-Associated Ischemia Reperfusion Injury

Abstract:
Introduction: Heart failure affects more than 64 million people worldwide, and for patients with end-stage disease, heart transplantation remains the best treatment option. Despite advances in organ preservation, ischemia reperfusion injury (IRI) remains a major contributor to graft dysfunction and ineligibility. Sodium thiosulfate (STS) is a clinically safe, FDA-approved compound with anti-apoptotic, anti-inflammatory, and antioxidant properties. Acting as a hydrogen sulfide donor, STS promotes protein S-sulfhydration, a post-translational modification that can modulate protein function, signaling, and oxidative stress. Although STS has shown protective effects in several ischemic models, its role in heart-transplant-associated IRI has not been studied. We hypothesize that STS protects cardiac grafts from IRI by reducing oxidative stress and apoptosis through protein S-sulfhydration.

Methods: To test STS's protective effects in vitro, human cardiomyocytes (AC16 cells) were subjected to simulated IRI: 24 hours of cold hypoxia (4°C, 0.5% O2) followed by 24 hours of reperfusion (37°C, 21% O2). STS safety and dosing (50-1500 μM) were first evaluated under normoxia. Concentrations of 150 and 300 μM were selected for IRI experiments, with treatments administered 24 hours before hypoxia, during hypoxia, and at reperfusion. Different preservation solutions and reperfusion methods (media addition or replacement with media) were tested to model distinct regulated cell death pathways. Cell death was tracked dynamically during reperfusion using Cytation 5 imaging and quantified at endpoints with viability assays.

Results: STS was non-toxic under normoxic conditions and modestly improved viability at select doses. Among preservation models tested, University of Wisconsin (UW) solution with media addition during reperfusion produced the most consistent IRI response. In this model, 150 μM STS showed a trend toward reduced cell death compared with untreated controls.

Discussion: Ongoing work aims to assess apoptotic and stress-related gene expression (Caspase-3, IL-6, TNF-α) and validate protein-level changes by Western blot. Subsequent experiments will evaluate STS's effects in a heterotopic mouse heart transplant model and identify S-sulfhydrated protein targets underlying its protection. Together, these studies will clarify STS's mechanistic role in cardiac IRI and inform strategies to improve myocardial preservation in heart transplantation.

Keywords: Heart transplantation, Ischemia reperfusion injury, Sodium thiosulfate, S-sulfhydration, Oxidative stress, Organ preservation

Session Abstract: 5

Presenter's Name: Chen, Sharon

Additional Author(s): Dr. Ismail, O.

Abstract Title: Evaluating the Performance of the Alegria 2® Assays for Connective Tissue Disease Autoantibody Testing

Abstract:
Introduction: Autoimmune connective tissue diseases (CTDs) involve tissue-damaging autoantibodies. CTD screening relies on anti-nuclear antibody (ANA) testing with reflex testing for specific autoantibodies. Currently, ANA screening employs indirect immunofluorescence (IIF) on Hep-2 cells, with positive samples reflexed to enzyme-linked immunosorbent assay (ELISA) and/or immunoblot (IB) autoantibody-specific assays. The Alegria 2 (Sebia) is a fully automated, multiplexed ELISA-based instrument for ANA screening and CTD-specific autoantibody detection. This study aims to compare the performance of the Alegria 2 with the currently used ANA testing methods.

Methods: 179 routine remnant patient serum samples previously tested for ANA using IIF (Euroimmun) were de-identified and run on the Alegria 2 ANA screen assay (Sebia). IIF ANA positive samples with a titer of > 1:160 were reflexed for detection of specific antibodies using ELISA and/or IB (Euroimmun). Similarly, positive and borderline samples by Alegria 2 were reflexed to a CTD autoantibody panel (Sebia). Results were analyzed using the EP Evaluator.

Results: Overall, IIF and Alegria ANA screen agreement was 79.3%, improving to 88% if 1:80 titer IIF samples were excluded (n=18). Discrepant samples included 9 with a homogeneous pattern with titers of 1:80 (6), 1:160 (2), and 1:320 (1), and 13 with a speckled pattern with titers of 1:80 (11) and 1:320 (2). Most were negative for CTD autoantibodies upon reflex testing by both methods. One homogenous sample at 1:160 titer was weak positive for anti-histone on IB (negative on Alegria 2), and one speckled sample at 1:320 titer was weak positive for anti-RNP/Sm on IB (negative on Alegria 2). Both samples were negative for any CTD. Reflex test agreement with Alegria 2 was 100% for anti-centromere B (n=7), anti-Jo-1 (n=14), anti-Scl-70 (n=19), anti-Sm (n=14), anti-SS-A (n=14), and anti-SS-A 60 (n=14). Agreement was 96.9% for anti-dsDNA (n=32) and 92.9% for anti-Ro52 (n=14). Anti-histone (n=7), anti-RNP/Sm (n=14), and anti-SS-B (n=14) showed 85.7% agreement. Anti-nucleosome showed 42.9% agreement (n=7).

Discussion: The Alegria 2 ANA screen correlates well with IIF at a 1:160 cut-off. Most reflex autoantibody assays perform comparably across methods, except for anti-histone, anti-RNP/Sm, anti-SS-B, and anti-nucleosome assays. These variances likely stem from differences in assay antigens, emphasizing the need for clinical context in ANA interpretation.

Keywords: Antinuclear antibody (ANA), Indirect immunofluorescence (IIF), ELISA, Immunoblot, Alegria 2, Connective tissue disease (CTD)

POSTER SESSION 2

Session Abstract: 6

Presenter's Name: Wu, Eric

Additional Author(s): Naghavi NH, Nazari MHD, Zhang R, Shooshtari P, Pin C

Abstract Title: Integrative Genomic and Epigenomic Analyses to Uncover Gene Regulatory Mechanisms in Pancreatitis and Pancreatic Cancer

Abstract:
Background: Pancreatitis (acute or chronic) is a common inflammatory pancreatic disorder linked to higher risk of pancreatic cancer, including pancreatic ductal adenocarcinoma (PDAC), a highly lethal cancer often diagnosed at late stages. Although current GWAS have identified tens of risk loci for pancreatitis and pancreatic cancer, most risk variants (SNPs) lie in non-coding regulatory regions, complicating links to target genes and cell-type–specific regulatory mechanisms. This project will define the transcriptional and epigenetic mechanisms driving pancreatitis and pancreatic cancer risk and determine how inherited variants modulate them.

Methods: To address this, we have used RegSCOUT (Regulatory Single-Cell Omics for Unraveling Trait-loci), a data integration pipeline developed in Shooshtari Lab to identify cell-type and context-specific regulatory mechanisms in complex disease. First, we have fine-mapped GWAS loci to 95% credible sets while accounting for linkage disequilibrium, then overlapped candidate variants with pancreatic scATAC-seq peaks from ~47,000 cells spanning major cell types (islet, acinar, and ductal) to nominate cell-type–specific risk regulatory elements. Next, we ran TF motif analyses to prioritize "effect" variants predicted to alter TF binding and to identify transcription factors likely impacted. To link regulatory elements to target genes, we integrate peak co-accessibility (Cicero), 3D chromatin contacts (Hi-C), and eQTL evidence, prioritizing genes supported by at least two lines of evidence. Finally, we validate candidates using independent scRNA-seq expression across relevant cell states and interpret results using curated pathway resources (e.g., KEGG/Reactome) and protein–protein interaction networks.

Results: We have obtained one GWAS dataset for pancreatitis and pancreatic cancer, and one scATAC-seq data. The pancreatitis and pancreatic cancer GWAS contain 9,842,983 and 9,982,208 SNPs, respectively. RegSCOUT as been ran up until gene prioritization. The remaining work is to complete gene prioritization, then perform validation and pathway/network interpretation. Limitations include reliance on public datasets, European-ancestry–biased GWAS, and no sex-stratified analyses.

Conclusion: Overall, this work narrows the variant-to-function gap by identifying putative cell-type-specific regulatory mechanisms and candidate targets relevant to pancreatitis and pancreatic cancer.

Keywords: Pancreatitis, Pancreatic Cancer, GWAS, scATAC-seq, Gene Regulation, RegSCOUT

Session Abstract: 7

Presenter's Name: Li, Grace

Additional Author(s): Vinokurtseva A, Herspiegel W, Juncal V, Monali M, Hutnik CML

Abstract Title: Development of a Preference-Based Epiretinal Membrane-Specific Health-Related Quality of Life Instrument

Abstract:
Introduction: Patient-reported outcome measures (PROMs) are standardized, validated questionnaires used to guide patient care by evaluating the health-related quality of life (HRQOL) of various patient populations. Epiretinal membranes are among the leading causes of visual impairment worldwide. Unlike other ophthalmic procedures, ERM surgeries do not directly correlate with improvements in best-corrected visual acuity, complicating treatment decisions. Understanding the HRQOL impacts from ERM patients' perspectives can support the integration of patient values into clinical decision-making, with potential to improve patient outcomes and access to care. We hypothesize that by using a mixed-methods and multi-disciplinary team approach, we can generate and introduce an ERM-specific PROMs tool that accurately captures patients' pre- and post-operative HRQOL.

Methods: A scoping review of items relating to vitreoretinal disease patients' HRQOL informed the development of a thematic interview guide. Semi-structured interviews were then conducted with ERM patients at the Ivey Eye Institute to understand which HRQOL themes are most important to patients. Overarching HRQOL domains were determined using the Framework Method of thematic analysis to provide the foundation for the development of three different versions of the HRQOL instrument. Lastly, a pilot group study to inform optimization of the final version of the questionnaire will be conducted. Concurrently, a systematic literature review on ERM patients' HRQOL has been conducted to compare the interview findings and choice of domains with that of previous studies.

Results: The thematic interviews (n=19) identified 252 unique items across nine HRQOL domains: driving limitations [45/252, 17.9%], reading limitations [38/252, 15.1%], fine visual difficulties [38/252, 15.1%], mobility limitations [17/252, 6.7%], symptoms [44/252, 17.4%], social impacts [9/252, 3.6%], dependence on others [14/252, 5.6%], worries [33/252, 13.1%], and feelings towards eye disease [14/252, 5.6%].

Discussion: Implementing an ERM-specific HRQOL PROMs tool is vital to improving patient care in Ontario, where there is an increasing unmet demand for ophthalmic surgeries. This instrument will allow the prioritization of limited resources to those most likely to benefit from these procedures while tailoring alternative treatment routes for those less likely to do so, strengthening patient experiences throughout the course of care.

Keywords: Epiretinal membrane, Health-related quality of life, Patient reported outcome measures, Ophthalmology

POSTER SESSION 2

Session Abstract: 8

Presenter's Name: Zhurba, Juliya

Additional Author(s): Kum J, Cecchini M

Abstract Title: A novel approach using locally hosted large language models to support program-level evaluations in medical education.

Abstract:
Introduction: Ensuring the competence of future physicians depends on the quality of medical programs. Maintaining high program standards involve conducting rigorous evaluations despite having limited time, personnel, and administrative capacity. Large Language Models (LLMs) have recently gained attention for supporting educational tasks such as rubric-based assessments and feedback generation. However, their application to program-level evaluation remains insufficiently examined. This study examines how locally hosted LLMs can be integrated into program evaluation workflows in a secure and structured manner.

Methods: We developed five preliminary rubrics using multiple LLMs, based on key institutional reference documents aligned with national health education standards. Two faculty members independently assessed each rubric for validity, feasibility, and usefulness using a 5-point Likert scale, with Z-score normalization applied to standardize responses. Descriptive and comparative analyses assessed relative model performance. The rubric with the highest combined ratings and faculty consensus was selected for iterative refinement into a final version suitable for structured program evaluation.

Results: Evaluation of the five AI-generated rubrics showed variability in faculty ratings across models. After reviewing all assessments, the rubric generated by Claude Sonnet 4.5 received the highest overall ratings and unanimous faculty preference. This rubric was then refined through iterative discussion to ensure clarity, alignment with institutional standards, and suitability for structured program evaluation.

Discussion: The Claude Sonnet 4.5-generated rubric, after refinement, will be implemented in a locally hosted application that parses relevant medical program documentation into a structured intermediary summary aligned with rubric criteria. This approach focuses on the criteria listed in the final rubric in the evaluation, reducing noise and hallucinations from LLM outputs when used to evaluate the medical content. By demonstrating a secure, scalable approach to integrating locally hosted LLMs into program evaluation, this study addresses the limitations of evaluation capacity. Ultimately, it supports the preparations of competent physicians capable of delivering safe, effective patient care.

Keywords: Artificial Intelligence, Course Evaluations, Education, Large Language Models, Quality Improvement

Session Abstract: 9

Presenter's Name: Lee, Nathan

Additional Author(s): Zhang, Z. X.

Abstract Title: Investigating the Roles of CypD and Drp1 in TLR3-Mediated Necroptosis.

Abstract:
Introduction: Toll-like receptor 3 (TLR3) is expressed on the surface of endothelial cells, where it responds to double-stranded RNA. TLR3 has been implicated in regulation of mitochondrial dynamics and necroptotic cell death, however the mechanism remains unclear. Cyclophilin D (CypD), a regulator of mitochondrial permeability transition pore opening, and Dynamin-related protein 1 (Drp1), a key mediator of mitochondrial fission, are critical modulators of mitochondrial-dependent cell death. We hypothesize TLR3 signalling activates one or both proteins to drive mitochondrial fragmentation, resulting in necroptosis.

Methods: To test our hypothesis, B6 mouse microvascular endothelial cells were stimulated with a TLR3 agonist cocktail (PSI) in the presence or absence of the CypD inhibitor cyclosporin A, Drp1 inhibitor Mdivi-1 or general necroptosis inhibitor Necrostatin-1. Cell death was quantified using Sytox Green death assay. Protein levels of CypD and Drp1 were assessed with Western blot.

Results: Western blot analysis showed that compared to untreated and PS controls, CypD protein levels were elevated in the PSI group, which was attenuated by Necrostatin-1. Likewise, death assay showed PSI induced the highest levels of cell death, which was reduced by Necrostatin-1. Drp1 protein quantification and inhibitor experiments are still ongoing.

Discussion: These results suggest surface TLR3 activation upregulates expression of CypD which promotes necroptotic cell death, showing a potential molecular mechanism underlying TLR3-induced necroptosis.

Keywords: TLR3, endothelial cells, necroptosis, CypD, Drp1, mitochondrial fragmentation

POSTER SESSION 2

Session Abstract: 10

Presenter's Name: Carley, Barrett

Additional Author(s): Cecchini M

Abstract Title: Automated Peripheral Nerve Detection in Head and Neck Squamous Cell Carcinoma Using a Foundation Pathology Model

Abstract:
Introduction: Head and neck squamous cell carcinoma (HNSCC) is a globally prevalent malignancy associated with significant morbidity and mortality. Perineural invasion (PNI) is a critical histopathologic risk factor that frequently mandates post-operative radiotherapy in cases of HNSCC. The purpose of this work is to combine a pathology foundation model with an attention-based neural network to build a peripheral nerve detection algorithm to enhance the efficiency and accuracy of identifying PNI in HNSCC whole-slide images.

Methods: Whole-slide images were curated from The Cancer Genome Atlas Head and Neck Squamous Cell Carcinoma (TCGA-HNSC) dataset and manually annotated for peripheral nerves to generate pixel-level true positive nerve data. Whole-slide images were processed using the Virchow pathology foundation model serving as inputs to an attention-based neural network trained for spatial peripheral nerve segmentation. Tile predictions will be aggregated into whole-slide nerve probability heatmaps and matched to ground-truth nerve annotations. Performance will be evaluated using five-fold slide-level cross-validation and reported as free-response receiver operating characteristic (FROC) and sensitivity at fixed false positives per slide.

Results: If the hypothesis is supported, the model is expected to demonstrate accurate nerve detection with high sensitivity at clinically practical false-positive burdens. Performance will be demonstrated using free-response receiver operating characteristic (FROC) analysis, with anticipated sensitivities >80% at 2–5 false positives per slide.

Discussion: This study aims to develop a high-performance AI-assisted visual overlay tool for peripheral nerve detection in HNSCC. By improving detection sensitivity while maintaining a low false-positive burden, this approach has the potential to enhance diagnostic efficiency and accuracy of PNI detection in HNSCC cases. This work advances the use of foundation models and may establish a template architecture for automated detection of other rare histopathologic structures in digital pathology.

Keywords: Digital Pathology, Artificial Inteligence, Perineural Invasion, Head and Neck Squamous Cell Carcinoma, Foundation Model

Session Abstract: 11

Presenter's Name: Houpt, Jacob A.

Additional Author(s): Li Y, Yaghmoor W, Megyesi J, Howlett C, Ang LC

Abstract Title: Erdheim-Chester Disease Presenting as a Chronic Subdural Hematoma

Abstract: Erdheim-Chester disease (ECD) is a rare neoplastic histiocytosis that often involves multiple organs including the long bones of the extremities, kidneys, lungs, skin, and central nervous system. An initial presentation of neurological symptoms occurs in only around a fifth of ECD cases, while a minority of ECD cases demonstrate dural involvement, increasing the risk of atraumatic subdural hematomas (SDH). An initial presentation of ECD without bony involvement as an atraumatic SDH represents a significant diagnostic pitfall.

We report on a case of a 77-year-old woman who presented with headache, left-sided weakness, and issues with balance over the previous two weeks. She was found to have a large right hemispheric SDH by CT scan, for which she underwent evacuation and middle meningeal artery embolization. She was discharged and remained clinically and radiologically stable for several months, until her headaches worsened and the hematoma's size and mass effect increased. This necessitated re-evacuation and the specimen was submitted to neuropathology.

The specimen consisted of a hematoma with both acute and organizing components, replete with prominent reactive fibroblasts, histiocytes, and xanthomatous cells. The exuberant xanthomatous change and the presence of numerous Touton giant cells prompted further immunohistochemical investigations, revealing an abundance of cytoplasmic CD68, fascin, and factor 13A immunoexpression. S100 and CD1A were immunonegative throughout. Although initially called into question due to hemosiderin deposition, there was BRAFV600E immunopositivity throughout, leading to this mutation being confirmed by next-generation sequencing and to the diagnosis of ECD. The patient subsequently underwent an FDG PET/CT scan, revealing FDG-avid foci of long bone and possible perinephric involvement, a finding typical of this condition.

ECD, like all histiocytic neoplasms, is exceptionally rare. While its multisystemic involvement is characteristic, presentation with isolated CNS involvement, in particular as a recurrent subdural hematoma, is an admittedly unintuitive clinical scenario. As chronic hematomas can inspire extensive inflammatory reactions (including xanthomatous changes) this neoplasm can easily be missed. This case illustrates the importance of ancillary testing given sufficiently suspicious histological, immunohistochemical, and clinical findings in this rare initial presentation of a rare histiocytic neoplasm.

Keywords: Erdheim-Chester disease, Chronic subdural hematoma, Histiocytosis, Surgical neuropathology

POSTER SESSION 2

Session Abstract: 12

Presenter's Name: Quan, Trinity

Additional Author(s): Kwan K

Abstract Title: A Decade in the Making: Progressive Fibrous Dysplasia of the Rib

Abstract:
Introduction: Fibrous dysplasia is a rare, chronic benign bone disorder in which normal bone is replaced by abnormal fibrous tissue, resulting in structurally weakened bones and an increased risk of deformities and fractures. It is caused by a gene mutation on chromosome 20, affecting the region of Gs-α subunit, and leading to an overproduction of cyclic adenosine monophosphate (cAMP). This molecular alteration disrupts osteoblastic differentiation resulting in disorganized fibro-osseous tissue formation. Radiologically and histologically, fibrous dysplasia may mimic other benign and malignant bone lesions, including ossifying fibroma, osteoblastoma, and low-grade malignancies such as osteosarcoma and chondrosarcoma. Distinguishing fibrous dysplasia from these entities is critical, as early malignant lesions may lack overtly aggressive features. Careful evaluation for malignant osteoid or cartilage production, increased cellularity, cytologic atypia, and infiltrative growth is essential to ensure accurate diagnosis and appropriate clinical management.

Case: In 2013, the patient was found to have a posterior left eighth rib lesion that was biopsied and initially interpreted as bone dysplasia, with imaging demonstrating stability dating back to 2008 and thus managed with consistent observation. Over the subsequent decade, they developed progressive rib discomfort with marked interval enlargement of the lesion involving the entire left eighth rib, associated with expansile bone destruction, rib displacement, and suspected pathologic fracture, prompting repeat comprehensive evaluation and consideration of surgical resection despite biopsy findings consistent with fibrous dysplasia.

Discussion: Microscopic examination demonstrated a moderately cellular spindle cell lesion with bland cytology, inconspicuous mitotic activity, and no necrosis, with focal immature osteoid formation lacking mineralization or lamellar bone, and admixed osteoclast-type giant cells. These features are consistent with a benign fibro-osseous process characterized by disordered bone formation rather than malignant osteoid production. Although low-grade intramedullary osteosarcoma was considered, the non-aggressive histologic features and benign radiologic appearance make such diagnosis unlikely.

Keywords: Fibrous dysplasia, bone, osteoblasts, fibro-osseous lesion

Session Abstract: 13

Presenter's Name: Burr, Melanie

Additional Author(s): Kwan, K

Abstract Title: Case Study: Transverse Sectioning of a Total Laryngectomy Specimen with a Chondrosarcoma

Abstract:
Introduction: Chondrosarcomas of the larynx are rare and behave differently than chondrosarcomas that appear in the skeletal system. Chondrosarcomas of the larynx arise from the cricoid vs thyroid cartilage in a ratio of 3:1. Metastasis of chondrosarcomas of the larynx is rare. Despite this, total laryngectomy can be performed due to frequency of recurrence in cases of incomplete excision. Upon gross examination, chondrosarcomas of the larynx may be sectioned transversely rather than the standard parasagittal sectioning in order to better evaluate extension from laryngeal cartilages and assess margin status.

Case: The patient was a 73 year old male presenting with a 7 month history of stridor and shortness of breath. The patient presented to the ER and received a tracheostomy, panendoscopy and biopsy. CT showed a large cricoid mass obstructing the airway. Biopsy showed a laryngeal cartilaginous neoplasm with differentials of either chondroma or low grade chondrosarcoma. Intraoperative frozen section revealed cartilaginous-type tissue negative for malignancy at the distal tracheal margin. Upon gross examination of the total laryngectomy specimen, transverse sectioning revealed a mass 4.0 cm in greatest dimension arising from and obliterating the cricoid cartilage below the glottis. Microscopically, the mass was found to be a chondrosarcoma, predominantly grade 1 with focal areas bordering on grade 2 with invasion of laryngeal submucosa, perilaryngeal soft tissue and bone and marrow space and was 0.5 mm from the perilaryngeal soft tissue resection margin.

Discussion: Transverse sectioning of neoplasms of the larynx that are suspected to arise from cartilage is helpful in evaluating tumor involvement and invasion of adjacent structures. In this case, transverse sectioning allowed for precise assessment of the thyroid cartilage as well as the anterior and posterior soft tissue resection margins. It is important to properly assess margin status in a total laryngectomy specimen in order to ensure complete excision of the neoplasm. Complete excision prevents recurrence and subsequent patient burden imposed by further treatment.

Keywords: Larynx, chondrosarcoma, cricoid cartilage, gross examination, transverse sectioning, margin status

POSTER SESSION 2

Session Abstract: 14

Presenter's Name: Ahmadian, Shadi

Additional Author(s): McCord C

Abstract Title: Inflammatory Features and Microbial Burden of Chronic Osteomyelitis of the Jaws

Abstract: Chronic osteomyelitis of the jaws (COMJ) is an inflammatory condition affecting the bone, bone marrow, and periosteum of the facial skeleton, most frequently the mandible. The disease often arises from odontogenic infections, with Fusobacterium nucleatum previously identified as a bacterium of interest. Currently, routine treatment involves antibiotics and surgical resection of necrosed bone. Patients who respond well to standard treatment are classified as having non-refractory osteomyelitis, while patients who do not respond well and experience disease persistence are classified as having refractory osteomyelitis. The biological differences underlying the refractory versus non-refractory disease remain poorly understood. This retrospective cohort study aims to identify whether localized inflammation and/or burden of Fusobacterium nucleatum in patients is associated with progression to the refractory course of COMJ. Using the open-source digital pathology software QuPath, neutrophil density in inflammatory hotspots of COMJ patients will be quantified. Analysis will be conducted on refractory and non-refractory COMJ tissue samples stained with myeloperoxidase (MPO). Finalized cell classifiers have demonstrated 92% sensitivity and 97% precision for neutrophil detection. Broader inflammatory metrics, such as percentage of inflamed tissue between patients, will also be analyzed on H&E tissue. Histopathological metrics between refractory and non-refractory groups will be tested for normality and undergo MANOVA analysis using R statistical software. In parallel, RT-qPCR will be used to quantify Fusobacterium nucleatum RNA, as well as host immune transcripts indicative of neutrophils, cytotoxic T-cells, and regulatory T-cells. Expression levels will be compared across the two groups using statistical testing conducted using R. We hypothesize refractory COMJ cases to demonstrate higher neutrophil counts, more intense localized inflammation, and increased Fusobacterium nucleatum RNA levels, reflecting a greater bacterial burden and increased inflammation. Together, these findings may clarify biological factors contributing to disease persistence, inform more targeted treatment strategies, and provide insight into potential biomarkers for predicting clinical outcomes in COMJ. Additionally, this study represents one of the first attempts at digital histopathologic analysis of decalcified tissue, supporting future analysis of archival specimens from rare diseases.

Keywords: Chronic Osteomyelitis, Fusobacterium nucleatum, Oral Pathology, Digital Pathology, RNA Quantification, QuPath

Session Abstract: 15

Presenter's Name: Ryeed, Raffin

Additional Author(s): Ryeed R, Al Agbar S, Gunaratnam L, Sidahmed A

Abstract Title: The Inflammatory Response of Glomerular Endothelial Cells to Anti-AT1R Antibodies

Abstract:
Introduction: Antibody-mediated rejection (AMR) remains a significant barrier to long-term kidney transplant success. While donor-specific antibodies against human leukocyte antigen (HLA-DSAs) are well characterized, non-HLA antibodies, particularly anti–angiotensin II type 1 receptor (AT1R) antibodies, are increasingly recognized as important contributors to rejection. Anti-AT1R antibodies are associated with AMR and poor graft outcomes, both independently and in combination with HLA-DSAs. Unlike HLA-DSAs, anti-AT1R antibodies are proposed to act through receptor signaling pathways in endothelial cells and lead to an inflammatory response. We hypothesize that anti-AT1R antibodies promote proinflammatory cytokine and chemokine secretion by glomerular endothelial cells in a receptor-dependent manner, and that genetic deletion of AT1R and HLA molecules will attenuate this response.

Methods: Aim 1 is to generate and validate CRISPR/Cas9-mediated knockouts of HLA class I, HLA class II, and AT1R in human glomerular endothelial cells. Knockout efficiency is assessed at the genomic, transcript, and protein levels. Aim 2 is to treat wild-type and engineered endothelial cells with kidney transplant patient serum stratified by the presence or absence of anti-AT1R antibodies. Endothelial injury and inflammation are quantified by measuring cytokine and chemokine secretion profiles in the cell culture media using a multiplex Luminex assay.

Results: The CRISPR/Cas9 workflow has been successfully optimized and validated. Stable HLA class I and HLA class II knockout endothelial cell lines have been generated and confirmed, demonstrating selective loss of target expression while maintaining cellular integrity. Generation and validation of AT1R knockout cells are ongoing. These engineered models provide a platform to dissect the independent and combined effects of HLA and non-HLA antibodies on endothelial activation.

Discussion: This study will define the functional impact of anti-AT1R antibodies on glomerular endothelial cells and clarify the mechanisms by which non-HLA antibodies contribute to AMR. Elucidating receptor-dependent endothelial signaling pathways will inform improved risk stratification and targeted therapeutic strategies tackling AMR in kidney transplantation.

Keywords: Antibody-mediated rejection, Anti-AT1R antibodies, Human leukocyte antigen, Glomerular endothelial cells, CRISPR/Cas9, Inflammatory cytokines and chemokines

POSTER SESSION 2

Session Abstract: 16

Presenter's Name: Jose, Pious

Additional Author(s): Xiufen Zheng4,5,6,7

Abstract Title: Preventing Alloimmune Rejection in Transplantation using circMAP2K2 and circFSCN1 Silenced Tolerogenic Dendritic Cells

Abstract:
Introduction: Alloimmune rejection is an immune-mediated attack on transplanted tissue, requiring lifelong immunosuppressive therapy, which can increase infection and cancer risks. Dendritic cells (DCs) regulate immune tolerance by modulating T cell responses. Circular RNAs (circRNAs), particularly circMAP2K2 and circFSCN1, have been implicated in DC immunomodulation. Silencing these circRNAs promotes tolerogenic DC phenotypes in mice, suggesting a potential therapeutic strategy for transplantation. Such an approach may complement established protocols for generating tolerogenic DCs, including those utilizing Vitamin D3 and Interleukin-10 (IL-10). The present study investigates the synergistic and additive effects of siRNA-mediated circRNA silencing in mitigating alloimmune rejection.

Methods: Murine bone marrow-derived DCs (BMDCs) were transfected with siRNA targeting circMAP2K2 and circFSCN1 with and without Vitamin D3 and IL-10 treatment. After 48 hours, cells were stained for CD11c and MHC Class II, as well as the co-stimulatory molecules CD40, CD80, and CD86 to assess changes in DC phenotype via flow cytometry. To assess their resistance to maturation stimuli, the cells were challenged with Lipopolysaccharide (LPS).

Results: Preliminary data reveal a marked reduction in CD40+CD80+ and CD86+CD80+ cell populations in DCs subjected to single circRNA silencing relative to controls, while no statistically significant difference was observed between dual and single silencing conditions. Notably, silencing of circMAP2K2 in BMDCs treated with Vitamin D3 and IL-10 led to a significant decrease in both CD40+CD80+ and CD86+CD80+ cells, suggesting that circMAP2K2 may contribute additively or synergistically to the induction of a tolerogenic phenotype in dendritic cells. CircMAP2K2-silenced and Vitamin D3+IL-10-treated BMDCs also show promising trends of resistance to LPS maturation stimuli.

Conclusion: The findings demonstrate that circRNA silencing modulates the expression of key co-stimulatory molecules on dendritic cells, with single silencing of circMAP2K2 enhancing the tolerogenic phenotype induced by Vitamin D and IL-10 treatment. These results point to circMAP2K2 as a promising molecular target for promoting immune tolerance.

Keywords: Dendritic Cells (DCs), Alloimmune Rejection, Circular RNA (circRNA), siRNA silencing, Immunomodulation

Session Abstract: 17

Presenter's Name: Vij, Rahul

Additional Author(s): Tran H, Quiñones-Mateu ME, Cabrera A

Abstract Title: Building the Foundation of an NGS-based CMV Antiviral Resistance Assay: Primer Design, PCR Optimization, and Workflow Refinement

Abstract:
Introduction: Cytomegalovirus (CMV) antiviral resistance is mediated by mutations in the viral kinase (UL97) and DNA polymerase (UL54), conferring resistance to ganciclovir, foscarnet, and cidofovir. Although next-generation sequencing (NGS) offers improved sensitivity over Sanger sequencing for resistance detection, clinical implementation requires robust amplification for downstream library preparation. We aimed to develop and refine a targeted Nanopore-based sequencing workflow for CMV resistance-associated loci and extend analysis to the terminase complex (UL56 and UL89) to capture recently identified mutations linked to letermovir resistance.

Methods: Eight amplicons spanning resistance-associated regions of UL97 (2), UL54 (4), UL56, and UL89 were amplified using the wild-type WHO international standard (NIBSC code 09/162) as template. Hot Start Taq DNA Polymerase (NEB) was used for preliminary assessment of primer binding and specificity. Amplicon yield and specificity were assessed by agarose gel electrophoresis. An exploratory MinION (Oxford Nanopore Technologies) sequencing run confirmed end-to-end workflow feasibility. Regions of interest were designed based on the Human CMV Merlin strain reference genome, synthesized, and cloned into pUC57 (GenScript) to assess limit of detection.

Results: All eight targets were successfully amplified, confirming correct primer design. One primer pair (UL54-4) showed diminished amplification, suggesting primer-template mismatch. Our initial sequencing demonstrated excellent sequencing depth, ranging from ~7,250 to 130,000-fold, confirming DNA input is sufficient to recognize low-frequency variants. UL54 demonstrated the lowest coverage among targets.

Discussion: Development of this targeted CMV Nanopore workflow identified key technical determinants of assay performance, including polymerase-dependent amplification efficacy and locus-specific variability within UL54. Proof-of-principle sequencing demonstrated strong sequencing depth and the ability to detect minority variants across all resistance-associated loci. Although further analytical validation is required to define limits of detection and sequencing error profiles, these findings establish a foundation for minority variant detection and future clinical validation of this assay. The workflow is being refined using a high-fidelity polymerase to enhance accuracy, longer amplicons to streamline the workflow, and optimized sequencing parameters.

Keywords: Cytomegalovirus (CMV), Antiviral resistance, Next-generation sequencing (NGS), Nanopore sequencing

POSTER SESSION 2

Session Abstract: 18

Presenter's Name: Wei, Rilla

Additional Author(s): Howlett C, Wehrli B, Baranova K.

Abstract Title: A Case Study of Chondrosarcoma in a Left-chest mass resection

Abstract:
Introduction: Conventional chondrosarcoma accounts for ~80–85% of chondrosarcomas, commonly arising from the pelvis and long bones, with rib/chest wall involvement occurring in rarer cases. Histologic grade—driven by increasing cellularity, cytologic atypia, and mitotic activity—and margin status are key prognosticators. With no known causes, genetic components are thought to involve, namely IDH1/2 mutations reported in ~50–70% of conventional tumors. Chondrosarcoma has also been reported as late, secondary malignancy after radiotherapy.

Method: A woman >50 years presented with progressive enlargement of a left chest wall lesion. Past history included left breast cancer treated in 2014 by partial mastectomy followed by postoperative radiation. The patient underwent en bloc resection of the left chest wall including anterior ribs 3–5 (superior margin marked by suture). The specimen was inked (soft tissue and pleural surfaces), serially sectioned, and extensively sampled; rib margins were assessed using decalcified en face sections.

Results: The chest wall resection measured 11.3 × 10.0 × 6.4 cm and contained a well-circumscribed ovoid mass (7.7 × 7.4 × 6.3 cm) with a variegated cut surface: lobulated pale-grey firm areas, diffuse pale-tan rubbery solid regions, and central mucinous/necrotic change with friable soft tissue and bone fragments. The tumor obliterated the 4th rib, abutted the 5th rib, and possibly extended into the 3rd rib, protruding to the parietal pleura without gross involvement; the pleural surface was smooth with minimal fibrous adhesions. Microscopy demonstrated a malignant soft tissue neoplasm with cartilaginous differentiation; no additional sarcomatous elements were identified. All submitted soft tissue and bony margins were negative for malignancy. Final diagnosis was conventional chondrosarcoma, grade 2/3.

Discussion: This case illustrates a rib-destructive, pleura-abutting conventional chondrosarcoma whose gross heterogeneity should prompt a complete mapping of the largest cross section of tumor with all interfaces and margins to support grading and to exclude dedifferentiation. The >10-year interval following breast cancer radiotherapy raises clinical consideration of a post-radiation sarcoma and highlights the importance of multidisciplinary correlation. Proper surgical treatment with negative bony and soft tissue margins remains the mainstay for patient's prognosis.

Keywords: Chondrosarcoma, surgical pathology, gross examination, anatomical pathology

Session Abstract: 19

Presenter's Name: Sritharan, Sara

Additional Author(s): A.R.O Ferreira, S. Roh, M. Caverson, E.A. Day

Abstract Title: Investigating the role of LONP1 in macrophages

Abstract:
Introduction: Chronic inflammation, evident in atherosclerosis, is driven by dysregulated macrophages. Changes in mitochondrial metabolism can signal macrophages into a pro-inflammatory state. Under stress, mitochondria activate a protective stress-response pathway including the Integrated Stress Response Pathway (ISR), regulated by ATF4; the mitochondrial unfolded protein response (mtUPR), regulated by ATF5; and an antioxidant stress pathway regulated by NRF2. However, regulation of these pathways is incompletely understood. LONP1 is a mitochondrial protease that regulates stress responses through protein degradation. This study investigates the role of LONP1 in macrophage stress and inflammatory signalling using pharmacological inhibition.

Methods: Raw264.7 macrophage-like cells were treated with a dose response of two LONP1 inhibitors, CDDO-Me and LONP1 IN-2. Activation of stress-responsive pathways was measured by Western blotting for ATF4, ATF5, Nrf2, HO-1, and β-actin. Wild-type and ATF4 knockout Raw 264.7 cells were used to determine the role of ATF4 in stress signalling pathways. Gene expression was measured using qPCR. To test whether ACO2 is a marker of LONP1 activity, siRNA-mediated knockdown of LONP1 was performed, followed by CDDO-Me treatment and Western blotting for ACO2 and β-actin.

Results: LONP1 inhibition activated stress-response transcription factors ATF4 and ATF5 and increased Nrf2 activity, a transcription factor that helps limit inflammation, and antioxidant enzyme HO-1. While ATF4 knockout cells reduced basal ATF5 levels, ATF5 was still induced after LONP1 inhibition, indicating ATF4-independent regulation. Furthermore, Nrf2 activation and HO-1 induction occurred in both wild-type and ATF4 knockout cells, indicating that Nrf2 activation can occur independently of ATF4. Investigation of ACO2 as a marker of LONP1 activity showed no change in protein level following LONP1 siRNA-mediated knockdown or inhibition, indicating that ACO2 is not a reliable marker.

Discussion: LONP1 inhibition activates stress pathways involved in ATF4, which induces ATF5 and Nrf2, promoting antioxidant and anti-inflammatory defence in macrophages. Reduction in the expression of IL-1β demonstrates an anti-inflammatory effect of this pathway. Further studies should investigate LONP1's potential as a target for treating inflammatory diseases by determining if it consistently produces anti-inflammatory effects across various conditions.

Keywords: Macrophages, Inflammation, Atherosclerosis, Mitochondrial stress, LONP1, ATF4

POSTER SESSION 2

Session Abstract: 20

Presenter's Name: Barboza, Rachel

Additional Author(s): Barboza R [(1)], Win P [(1)], Chen SQ [(1)], Espin-Garcia O [(2,3,4)], Castellani CA [(1,2,5,6)]

Abstract Title: Investigating the mediating role of metabolites in mtDNA-CN and nuclear epigenome driven cardiovascular disease risk using a large-scale longitudinal cohort

Abstract:
Introduction: Variation in mitochondrial DNA Copy Number (mtDNA-CN), a proxy for mitochondrial function, is associated with complex diseases like cardiovascular disease (CVD) and neurodegenerative disorders. mtDNA communicates with the nucleus via epigenetic mechanisms that regulate nuclear gene expression, however, the role the metabolome plays in mediating these relationships remains unknown. Traditional mtDNA-CN estimates are derived from nuclear DNA (nDNA) using ratio-based computational methods, which provide a relative metric, but are often not readily available in cohort studies and fail to integrate multi-omic signatures associated with mtDNA-CN. This demonstrates the need for novel computational methods that can improve mtDNA-CN estimation.

Methods: The Canadian Longitudinal Study of Aging (CLSA) is a human cohort with matched genomic, metabolomic, and epigenomic data (N = 26,622; 9,992; and 1,479, respectively). MtDNA-CN estimates were derived at baseline, and 1,022 metabolites were tested for associations to mtDNA-CN. Associated metabolites were then mapped to biological pathways to assess their mediator role between mtDNA-CN and nDNA methylation. In addition, data from two follow-up visits were used to determine if metabolites mediate CVD risk using the R package mediate. Further, a heterogenous transfer learning (HTL) model was applied to all available multi-omic data to improve mtDNA-CN prediction.

Results: Ninety-three metabolites were associated with mtDNA-CN, including the epigenome-modifying metabolites S-adenosylhomocysteine (SAH) and alpha-ketoglutarate (N = 9,375, FDR = 4.25×10E-3, 2.93×10E-3). KEGG pathway analysis identified enrichment in amino acid biosynthesis pathways (FDR = 1.21×10E-8). mtDNA-CN associated metabolites, including cholesterol and sphingomyelins, were associated with myocardial infarction (57 metabolites, FDR < 0.05). The HTL model, which used disparate omic datasets, demonstrated the power to predict mtDNA-CN (R^2 = 0.504, Pearson's = 0.224).

Conclusions: Our findings identify associations between mtDNA-CN and the nuclear epigenome, mediated by epigenome-modifying metabolites in the methionine cycle. The methionine cycle facilitates the transfer of methyl groups from S-adenosylmethionine to nDNA, resulting in nDNA methylation and producing SAH (a methylation inhibitor). mtDNA variation therefore remodels the nDNA epigenome via metabolites which is associated with increased CVD risk.

Keywords: mtDNA-CN, metabolomics, disease risk, machine-learning, crosstalk

Session Abstract: 21

Presenter's Name: Abdelraheem, Omar

Additional Author(s): Dembski S, Forouzandeh N, Cameron L

Abstract Title: Elucidating the development and pathogenicity of dual-positive Th2-Th17 cells

Abstract:
Introduction: Asthma is a chronic inflammatory disease characterized by airway remodelling and hyperresponsiveness. It often manifests due to secretion of inflammatory cytokines (IL-4, IL-5, IL-13) by T-helper 2 (Th2) cells through activation of their surface receptor CRTh2. Asthma severity is associated with a predominance of Th2-Th17 cells: Th2 cells expressing the Th17 cytokine IL-17A. However, the mechanisms by which Th2-Th17 cells develop and mediate asthma severity are unknown. Two signalling pathways are known to induce pathogenic Th17 cells. The first is activation of the receptors EP2 and EP4 by prostaglandin E2 (PGE2), which promotes Th17 inflammation and downregulates anti-inflammatory genes like IL-10. The second is transforming growth factor beta (TGF-β)2/3 signalling, involved in airway remodelling. Since Th2 cells express CRTh2, EP2, and EP4, we hypothesized that Th2 cells can acquire pathogenic Th17 features upon PGE2 exposure, transitioning them into Th2-Th17 cells.

Methods: Th2 cells were treated with PGE2 to assess whether they promote Th17 features and induce TGF-β2/3 expression. PGE2 was administered over a 24-hour period to determine the effects of acute treatment. Th2 cells were then cultured with or without a cocktail of Th17-polarizing cytokines (TGF-β1 and IL-21) and treated over two weeks with PGE2 to assess the long-term modulation of Th17 features in pro-Th17 conditions. The expression of Th2 and Th17 cytokines/markers was assessed with qRT-PCR, ELISA, and flow cytometry.

Results: Th2 cells treated with PGE2 for 24 hours show a reduction in IL-10 mRNA and protein levels and an increase in TGF-β3 mRNA. These treated cells maintained expression of key Th2 cytokine markers like IL-13. By contrast, Th2 cells treated with PGE2 for two weeks showed a decrease in IL-13 mRNA and protein expression. IL-17A expression was not affected by acute PGE2 treatment; however, the effects of long-term PGE2 treatment on IL-17A are still being elucidated.

Discussion: Independent of Th17 effects, PGE2 signalling induces phenotypic changes in Th2 cells which may be pro-inflammatory (via decreased IL-10) and/or pro-remodelling (via increased TGF-β3). However, long-term exposure to PGE2 decreased expression of Th2 markers like IL-13. Better understanding PGE2 signalling dynamics in Th2 cells will help identify mechanisms that mediate asthma severity and novel avenues for therapy.

Keywords: Asthma, prostaglandin, TGF-β, Th2-Th17 cells, inflammation, remodelling

POSTER SESSION 2

Session Abstract: 22

Presenter's Name: Shah, Tisa

Additional Author(s): Chidiac, P

Abstract Title: Exploring the Effects of Psilocin on Serotonin 2A/Dopamine D2 Receptor Heterodimer Signaling

Abstract:
Introduction: Psilocybin is a perception-altering psychedelic found in over 200 species of mushrooms. It is metabolized into psilocin, which has greater affinity for the serotonin 2A receptor (5-HT2AR), a G-coupled receptor (GPCR). Originally used by the Mazatec People for spiritual healing, psilocin is playing a promising role in treating depression, anxiety, and addiction. Previous studies measuring the head-twitch response in 5-HT2AR knock-out and wild-type mice displayed biased agonism of the receptor through activation of a distinct hallucinogenic pathway with psilocin. 5-HT2AR is also known to form a functional heterodimer with dopamine receptor D2 (DRD2), and previous studies indicate the influence of psychedelics on 5-HT2AR-DRD2 cross-talk. The main goal of this research project therefore was to analyze signaling patterns of 5-HT2AR and 5-HT2AR-DRD2 complex in the presence of psilocin relative to non-hallucinogenic agonists. It was hypothesized that a difference will be observed in the signaling patterns.

Methods: Protein fragment complementation assay (PCA) was used to measure protein-protein interactions (PPI) in live HEK-293H cells. Each constituent protein is engineered to include one of three nanoluciferase (NanoLuc) fragments, which reconstitute to form a functional luminescent luciferase and form a signaling complex. Luminescence plotted as concentration-response curves and analyzed with an F-test in GraphPad Prism to evaluate significant differences in logEC50 values.

Results: This research project is currently being performed with results under investigation. Gαq, Gαi, and Gαs recruitment by serotonin and/or dopamine to the 5-HT2AR homomer and 5-HT2AR-DRD2 heterodimer are being analyzed and compared with recruitment by psilocin. Final results will be presented on poster day.

Discussion: These findings will provide insights into upstream 5-HT2AR/5-HT2AR-DRD2 hallucinogen-specific signaling and contribute to the development of future antipsychotic therapies. Beyond human health, psilocybin mushrooms are increasingly encountered in natural and urban environments, where animals may be exposed to their psychoactive compounds. This project therefore takes a One Health approach by connecting hallucinogen signaling research with ecological and public health considerations, clarifying how psilocin's presence in the environment may affect humans and other species, and highlights the value of community education on its risks and benefits.

Keywords: Psilocin, Serotonin 2A receptor, Protein fragment complementation assay, Biased agonism, Dopamine D2 receptor, One Health

Session Abstract: 23

Presenter's Name: Cheung, Tiffany

Additional Author(s): Gholami H, Figueredo R, Hong MMY, Davidson C, Maleki Vareki S

Abstract Title: Examining the effects of antibiotic-induced gut dysbiosis on antitumour immune responses in DNA mismatch repair-deficient colorectal cancers

Abstract:

Introduction: Immune checkpoint inhibitors (ICIs) treat solid cancers by enhancing the patient's existing antitumour T-cell responses. Colorectal cancer (CRC) is becoming increasingly diagnosed in people under the age of 45, with a 5-year survival rate of 65% and an overall poor response to ICIs. Antitumour immune responses are influenced by the gut microbiome, as certain commensal species and their metabolites have been found to modulate immune responses to dictate ICI outcomes. Antibiotic use been linked to worse outcomes in ICI patients with CRC. However, it is unknown how antibiotics influence T-cell antitumour responses. We hypothesize that antibiotics hinder antitumour immunity by disrupting the gut microbiome.

Methods: Mice were administered an antibiotic cocktail (vancomycin, neomycin, ampicillin, metronidazole) or vehicle control for 10 days, then injected with MC38 CRC cells. Stool was collected at baseline, 4 days post-antibiotic, and 1 month post-antibiotics for bacterial 16S gene-based taxonomic profiling to identify changes in gut microbiome composition. Tumours, tumour-draining lymph nodes, and spleens were analyzed using flow cytometry to characterize T-cell responses.

Results: Antibiotics accelerated CRC growth in mice and induced a global depletion of commensal bacteria, reducing microbiome diversity and shifting overall composition up to 1-month following withdrawal. This was accompanied by altered systemic expression of markers for T-cell activation, exhaustion, and dysfunction. Antibiotic treatment was associated with reduced production of pro-inflammatory cytokines necessary for coordinating effective antitumour responses. Interestingly, T-cells in antibiotic-treated mice showed increased cytotoxic potential and an increase in systemic central memory population.

Discussion: These findings reveal the devastating impact of antibiotics on beneficial commensal populations in the gut and its downstream systemic effects on hindering antitumour immune responses. Antibiotics modulate T-cell activation, polyfunctionality, and T-cell memory responses to weaken the host's ability to restrain cancer growth. These results highlight the need for judicious use of antibiotics in cancer patients.

Keywords: Cancer, antibiotics, gut microbiome, colorectal cancer, DNA mismatch repair

POSTER SESSION 2

Session Abstract: 24

Presenter's Name: Kaczmarek, Shania

Additional Author(s): Halari, Moheem M., Charyk Stewart, Tanya, McClafferty, Kevin J., Pellar, Allison. C., Shkrum, Michael J.,

Abstract Title: Correlation of Pedestrian Lower Extremity Injuries from Fatal Motor Vehicle Collisions to Motor Vehicle Front Geometry

Abstract:

Introduction: In 2021, 1.19 million people died worldwide due to road traffic injuries. Pedestrians accounted for 21% of deaths. In Canada, one in twelve pedestrian deaths involves a hit-and-run motor vehicle pedestrian collision (MVPC). By measuring lower extremity (LE) fractures during autopsies, pathologists may assist police in identifying a motor vehicle (MV) with a matching bumper height. Current Canadian bumper regulations and the frontal geometry of various modern MV types, may be factors in correlating LE injury heights with bumper heights. We hypothesize that in fatal frontal MVPCs, pedestrian LE injury heights and severity correlate to the front MV geometry heights.

Methods: Retrospective MVPC data from Ontario between 2013 and 2019 were collected from the Office of the Chief Coroner for Ontario and Transport Canada. A review of the literature identified several front MV geometry parameters and potential confounders (e.g., speed), that can influence pedestrian LE injury. A protocol based on the European New Car Assessment Programme's Vulnerable Road User Testing Protocol was developed to measure MV geometry height in SketchUp Pro software. MV images of the same year, make, and model as the MVs in the MVPCs were scaled to manufacturer's height in SketchUp Pro. The hood edge height (HEH), upper bumper height (UBH), lower bumper height (LBH), most protruding point (MPP), upper MPP (UMPP), and lower MPP (LMPP) were measured. Injury severity was ranked using the maximum abbreviated injury score (MAIS). MV geometry heights were correlated to single and upper (in cases of two injuries) LE injuries.

Results: 79 cases were analyzed using Spearman's rank correlation coefficient (rho). LE injury height was positively correlated to UMPP (0.242, $p=0.048$) and almost significantly correlated to HEH (0.203, $p=0.073$) and MPP/UMPP (0.220, $p=0.051$). LE injury height was positively but insignificantly correlated to UBH, LBH, LMPP, and LMPP/MPP. LE injury severity was positively correlated to MV speed (0.384, $p<0.001$), negatively correlated to UBH (-0.283, $p=0.011$), and negatively and insignificantly correlated to HEH, LBH, UMPP, LMPP, MPP/UMPP, and MPP/LMPP.

Discussion: Pedestrian LE injuries have a weak positive correlation to UMPPs. Injury severity is weakly and negatively correlated to UBH. MV speed is positively correlated to injury severity. Regression analysis should be done to account for confounding variables (e.g., impact speed, braking, etc.).

Keywords: Motor vehicle pedestrian collision, lower extremity injuries, motor vehicle bumpers, forensic pathology

Session Abstract: 25

Presenter's Name: Lovering, Liv

Additional Author(s): Chandiramohan A, Iannetta V, Herspiel W, Armstrong JJ, Hutnik CLM, Sharon T

Abstract Title: Advancing Glaucoma Care Through Virtual Reality: Comparative Performance of Virtual Reality-Visual Field Testing and Humphrey Perimetry

Abstract:
Introduction: Glaucoma is currently the leading cause of irreversible blindness across the world, and effective management of this disease relies on efficient and reliable visual field (VF) assessment. Despite its importance as the gold standard in perimetry testing, the Humphrey Visual Field (HVF) analyzer is limited by accessibility, cost, need for skilled manpower, and patient discomfort. The emergence of virtual reality-based perimetry offers an alternative that is portable, and addresses patient-specific inaccessibility factors. This study examines the reliability, accuracy, feasibility, and overall patient experience of the RetinaLogik VR Visual Field (VR-VF) device compared to the HVF analyzer in patients with different stages of glaucoma.

Methods: This study was conducted at the Ivey Eye Institute at St. Joseph's Health Care in London, Ontario. Both the 24-2C SitaFaster HVF and 24-2C SitaFast RVF200 (RetinaLogik Inc, Canada) were performed by participants ranging from healthy controls to those with advanced glaucoma. Primary outcomes of this study were Mean Deviation (MD), Pattern Standard Deviation (PSD), Visual Field Index (VFI), and numerical sensitivity plots. Statistical analyses included Pearson correlations, paired comparisons, and Bland–Altman plots. Secondary outcomes including test duration, patient satisfaction and operational metrics were recorded.

Results: Thirty-nine participants with various stages of glaucoma (mean age 68 years; 21 female) contributed 68 eyes (35 OD, 33 OS). Mean deviation (MD) values were comparable between devices (VR-VF: –4.89 dB; HVF: –3.8 dB). The RVF200 showed strong correlation with HVF for MD (r=0.96), PSD (r=0.93), and mean sensitivity (r=0.96). Bland–Altman analysis for mean sensitivity showed a bias of 1.35 dB with 95% limits of agreement of –1.96 to +1.96 dB. Average test durations were also similar (VR-VF 3.35 min vs HVF 3.32 min).

Discussion: Preliminary results show excellent concordance between VR-VF and HVF, offering comparable test durations alongside strong patient satisfaction. VR-based perimetry demonstrates great potential as an accessible and reliable alternative to the HVF in glaucoma diagnosis and monitoring, supporting its incorporation into both clinical and remote care settings.

Keywords: Glaucoma, Humphrey visual field (HVF) analyzer, RVF200, Virtual Reality, Accessibility, Patient Satisfaction

POSTER SESSION 2

Session Abstract: 26

Presenter's Name: Le, Nhi

Additional Author(s): Harrison Pan, Amir Karimi, MohdWessam Al Jawhri, Shengjie Ying, Senyang Wei, John W Barrett, Krista Joris, Halema Khan, Joe Mymryk, Matthew Cecchini, Anthony Nichols

Abstract Title: Investigating Combination Immunotherapy in a Head and Neck Cancer Model

Abstract: Head and Neck Squamous Cell Carcinoma (HNSCC) is an aggressive, solid tumour arising from the mucosal epithelium of the mouth, pharynx, and larynx. Despite advances in traditional therapies, the five-year survival rate is still as low as 25%, with over half of patients experiencing tumour recurrence and metastasis within three years. Immune checkpoint inhibitors (ICIs) have been an important step forward in care, but the overall response rate is still as low as 15%. This study evaluates anti-tumour efficacy of single and combination checkpoint inhibitors in an HNSCC HPV+ mouse model. C57BL/6 female mice were injected with the MEERL cell line (1 x 106 cells/100uL DMEM) in the flank. Mice were randomized to eight groups: control, monotherapy (anti-PD1, anti-TIM3, anti-LAG3, or anti-CTLA4), and combination therapy (anti-PD1 plus anti-TIM3, anti-LAG3, or anti-CTLA4). Treatment was initiated once mean tumor volume reached 50 mm3. Treatments were administered by IP injection three times weekly for four months. Tumour measurements were taken twice weekly using callipers. Mice that achieved complete responses were randomized to stop treatment for one month, followed by tumour re-challenged to investigate acquired anti-tumour immunity. Tumours were processed into viable single cell suspensions for single-cell analysis.

Monotherapy anti-TIM3, anti-LAG3, and anti-CTLA treated mice had a poor anti-tumour response compared with other groups. Anti-PD1 alone or in combination with the checkpoint targets induced complete response in ~75% of mice per arm. After treatment cessation and tumour re-challenge, 10 of 12 mice exhibited tumour rejection.

Findings suggests that PD1 blockade is the primary driver of response in this model. Adding TIM3, LAG3, or CTLA4 inhibition does not further improve efficacy. Long-term anti-PD1 therapy generates a robust anti-tumour immunity. Additional mouse models are needed to see if findings can be replicated and be translated into more effective therapies in the clinic.

Keywords: Head and Neck Cancer, Immunotherapy, Tumor microenvironment, Mouse model

Session Abstract: 27

Presenter's Name: Hosseini Naghavi, Nader

Additional Author(s): Shooshtari P.

Abstract Title: Integrating GWAS and Single-Cell Chromatin Accessibility Data to Study Gene Regulation in Multiple Sclerosis

Abstract: Multiple sclerosis (MS) is an immune-related disease impacting the central nervous system characterized by demyelination and axonal damage. Although the precise mechanisms of MS are not fully understood, comprehensive genome-wide association studies (GWAS) have identified thousands of single nucleotide polymorphisms (SNPs) associated with disease susceptibility. Notably, most of these risk-associated SNPs are located within open chromatin regions of immune cells. Integrating MS GWAS data with single-cell assay for transposase-accessible chromatin sequencing (scATAC-seq) profiles of immune cells offers a powerful framework to link MS-associated SNPs to regulatory programs in immune cells, and identification of immune-related gene regulatory mechanisms of MS.

In this project, we integrated the largest publicly available MS GWAS data, which identified 26,395 MS-associated SNPs, with a large-scale scATAC-seq data comprising 96,002 open chromatin regions across 17 immune cell types. We used RegSCOUT, a computational pipeline developed in Shooshtari Lab, that maps disease-associated SNPs onto open chromatin sites of cell types to identify disease-affected regulatory regions. RegSCOUT further identifies the candidate transcription factors likely to be affected by disease-associated SNPs on these regions. Finally, RegSCOUT links candidate risk-mediating regulatory regions to their target genes based on multiple lines of evidence including genomic proximity, long-range chromatin interactions and expression quantitative trait loci (eQTLs) in immune cell types.

RegSCOUT identified 414 MS-affected open chromatin regions, 374 transcription factors with affected binding patterns, and 145 target genes across immune cell types. Some affected regulatory regions, transcription factors, and genes were affected across most immune populations, while others were affected in specific cell types. BACH2 gene was affected across multiple immune cell types. BACH2 is known to be related to MS and immune regulation. CXCR5 gene was specifically affected in B cells, which is compatible with its role in B-cell-mediated central nervous system infiltration in MS. These genes are involved in immune pathways such as Toll Like Receptor 3 (TLR3) Cascade.

In conclusion, this study integrates MS GWAS data with single-cell ATAC-seq profiles of immune cells to uncover cell-type specific gene regulatory mechanisms by which MS-associated genetic variants drive gene dysregulation in immune cells.

Keywords: Multiple Sclerosis, Gene Regulation, GWAS, scATAC-seq, Data Integration

POSTER SESSION 2

Session Abstract: 28

Presenter's Name: Wang, Ryan

Additional Author(s): Abdo R, Megyesi J, Zhang Q

Abstract Title: Clinical and Molecular Features of Biomarker Shifting in Breast Cancer Brain Metastases

Abstract:
Introduction: Breast cancer brain metastases (BCBMs) are associated with poor prognosis and remain challenging to treat. BCBMs are known to differ molecularly compared to the primary breast tumour and biomarker shifting can commonly occur. However, the underlying mechanisms driving this shift are not known. This study aims to investigate the molecular underpinnings of BCBM biomarker shifting.

Methods: Patients with matched primary tumour and BCBM biomarker data were identified and clinical information was collected. Matched tumour tissue blocks were selected and a tissue microarray (TMA) was constructed. 10X Genomics Xenium spatial transcriptomic analysis using the Prime 5K gene panel was done. Downstream analyses will be conducted using Seurat.

Results: Fifty-one patients with matched biomarker data were identified. Ten (19.6%) patients exhibited a subtype switch with hormone receptor (HR) loss (6/10, 60.0%) being the most common change. Subtype switching did not impact OS (p=0.41), however it was associated with developing BCBMs later (p=0.012). For our Xenium experiment, tumour samples from seven patients with HR+, HER2+ or HR+, HER2- disease - four with subtype switching and three without switching - were arranged over two TMA blocks. The runs yielded 410206 cells in block 1 and 318755 cells in block 2. Downstream analyses will be conducted to examine cell population, tumour microenvironment, and gene expression differences related to subtype shifting.

Conclusions: BCBM biomarker shifting is common and may have important clinical implications. Spatial transcriptomic analyses of matched tumour samples may yield tumour microenvironment and molecular differences associated with subtype shifting.

Keywords: Brain metastases, breast cancer, spatial transcriptomics, biomarkers

Session Abstract: 29

Presenter's Name: Black, Morgan

Additional Author(s): Jeong WD, Lin S, Brown A, Cecchini M and Wasserman J

Abstract Title: Bridging the Pathology Communication Gap: Early Experience with Osler, a Patient-Facing AI Chatbot

Abstract: Patients increasingly access pathology reports directly through electronic portals, yet these reports are written for clinical audiences and are frequently misunderstood. Artificial intelligence–driven chatbots offer a potential mechanism to sup-port patient understanding, but concerns regarding accuracy, scope control, and safety remain significant barriers to clinical implementation. This study describes the development of Osler, a pathology-specific patient chatbot, and evaluates early real-world usage patterns following its deployment on MyPatholo-gyReport.com, an educational pathology website. Osler was developed using cu-rated, pathology-focused educational content from MyPathologyReport.com with embedded guardrails to limit scope, encourage uncertainty acknowledgment, and redirect users to their healthcare team when appropriate. The chatbot was embedded on the website and made available to patients on a voluntary, user-initiated basis. A descriptive analysis of user interactions was conducted over a 2-month period following launch (December 10, 2025 – February 9, 2026), examining us-er volume, interaction frequency, response characteristics, and safety-related behaviours. During the study period, the chatbot was accessed by 2,408 unique users from 75 countries, generating 5,860 total interactions (median 1.00; mean 2.43 queries per user). Scope-limiting or safety-redirect responses occurred in only 0.34% of interactions. Median response readability corresponded to a Flesch–Kincaid grade level of 10.37, and no clinically actionable medical advice was identified. Early real-world use of Osler demonstrates the feasibility of deploying a pathology-specific patient chatbot with explicit safety and scope controls, supporting further prospective evaluation of patient-facing AI tools in pathology and oncology communication.

Keywords: Patient-centred AI, Pathology Communication, Patient Education, Digital Health

POSTER SESSION 2

Session Abstract: 30

Presenter's Name: Proulx, Ella

Additional Author(s): Joseph M, Galloway-Kay K, Sharma A

Abstract Title: Squamomelanocytic Tumor in Xeroderma Pigmentosum: Immunohistochemical and Molecular Characterization of a Novel Case

Abstract:
Background: Squamomelanocytic tumors (SMT) are exceedingly rare cutaneous neoplasms which present challenges in diagnosis and treatment. A subtype of SMT includes biphenotypic tumors where cells demonstrate both squamous and melanocytic differentiation. To our knowledge, this is the first case of a true biphasic tumor in a pediatric patient with xeroderma pigmentosum (XP), a condition characterized by ineffective DNA repair following exposure to ultraviolet (UV) light.

Case Description: We present a case of a 15-year-old male with XP (Group C) who presented with a facial lesion clinically concerning for basal cell carcinoma. Histological examination revealed a complex melanocytic lesion with intimately associated squamous cell differentiation. Dual chromogen analysis with SOX10/HMWCK and p40/HMB45 highlighted three distinct populations, including single cells co-expressing both melanocytic and squamous cell markers.

Molecular Findings: Next-generation sequencing performed on the tumor identified three significant mutations; biallelic mutations in NF1, and a TERT promoter mutation. Characteristic UV-signature mutations were identified, highlighting the volatile molecular environment that could lead to mixed-lineage differentiation.

Conclusion: To our knowledge, this is the first case of a true biphasic SMT in a patient with XP. It is hoped that this case will add valuable insight into the elusive nature of these tumors. Further, this case highlights the use of dual chromogen staining and electron microscopy to help classify complex and rare tumors.

Keywords: Dermatophathology, Xeroderma pigmentosum, Squamous cell carcinoma, melanoma, biphasic

Session Abstract: 31

Presenter's Name: Syed, Anna

Additional Author(s): Khan ZA, Howlett CJ

Abstract Title: Identifying age-related mitochondrial dysfunction in bone marrow endothelial cells and its impact on tissue resident stem cell niche

Abstract:
Introduction: Ageing is characterized by a progressive decline in tissue regenerative capacity, driven in part by dysfunction of tissue-resident reparative stem cells. Increasing evidence demonstrates that this decline is strongly influenced by alterations in the stem cell niche microenvironment. In the hematopoietic system, ageing impairs hematopoietic stem cell (HSC) self-renewal and differentiation, resulting in reduced regenerative potential. Previous work from our laboratory has identified significant deterioration of the ageing bone marrow niche, including structural decay and mitochondrial dysfunction in some but not all endothelial populations. Based on these findings, I hypothesize that age-associated mitochondrial dysfunction in specific bone marrow endothelial subtypes drives niche degradation that actively impair stem cell function.

Methods: To test my hypothesis, I will isolate arteriolar and sinusoidal endothelial cells from young and aged mice and subject the cells to multi-platform functional analyses to assess mitochondrial integrity. These analyses will quantify reactive oxygen species production, bioenergetic capacity, and markers of oxidative and genotoxic stress. In parallel, transcriptomic profiling using bulk and single-cell RNA sequencing in bone marrow will identify age-dependent alterations in mitochondrial pathways and stem niche factors that may destabilize niche architecture. Finally, structural and functional consequences of niche deterioration will be evaluated.

Results: Transcriptomic analyses are expected to reveal altered expression of genes regulating mitochondrial function and stress responses in aged endothelial cells, consistent with bioenergetic decline. Functional assays are anticipated to demonstrate increased reactive oxygen species and oxidative stress. These changes are expected to correspond with the emergence of niche-derived factors that disrupt stem cell retention and impair normal stem cell trafficking.

Discussion: If proven, my studies will support a model in which ageing is driven not solely by intrinsic stem cell failure, but by active suppression from a dysfunctional niche. Identifying altered niche factors responsible for its deterioration may reveal novel therapeutic targets aimed at restoring niche function, representing a new strategy to improve tissue regeneration in ageing.

Keywords: Ageing, Hematopoietic stem cells, Endothelial cells, Mitochondrial dysfunction, Bone marrow niche, Regenerative decline

POSTER SESSION 2

Session Abstract: 32

Presenter's Name: Shaker, Nader

Additional Author(s): Jackson-Boeters L, McDonald L. JJ, Darling M, Cicchini M

Abstract Title: S100A7 expression in oral potentially malignant disorders: verrucous hyperplasia and verrucous carcinoma

Abstract:
Introduction: Verrucous hyperplasia (VH) is an oral potentially malignant disorder that may progress to verrucous carcinoma (VC) or oral squamous cell carcinoma (OSCC). VC is a low-grade SCC variant that rarely metastasizes but can undergo malignant transformation. Reliable biomarkers predicting progression remain unclear. S100A7 is implicated in MAPK signaling and OSCC development, while DNA-licensing proteins (MCM2, Geminin) and proliferation marker Ki-67 reflect cell-cycle activity. This study evaluates biomarker expression patterns and the predictive potential of an image-analysis algorithm for malignant transformation.

Methods: A retrospective review of pathology archives (2006–2016) identified VH and VC cases. Formalin-fixed paraffin-embedded specimens underwent immunohistochemistry for S100A7, MCM2, Ki67 and Geminin. Quantitative S100A7 risk stratification was performed using an image-based algorithm. Cases were correlated with clinical progression to OSCC.

Results: Preliminary analysis demonstrates biologic differences between transforming and non-transforming lesions. Lesions progressing to OSCC showed increased proliferative licensing (MCM2) and coordinated cell-cycle progression (Ki-67 and Geminin). Non-transforming lesions demonstrated proliferative entry without completion of replication cycles. These findings suggest early dysregulation of cell-cycle control in lesions destined for malignant transformation. Quantitative S100A7 analysis is ongoing.

Discussion: Malignant progression in VH and VC appears associated with coordinated cell-cycle activation rather than simple hyperproliferation. Proliferation biomarkers may complement S100A7-based risk assessment to improve identification of high-risk lesions. Improved risk stratification could guide earlier intervention and reduce morbidity and mortality associated with OSCC.

Keywords: Verrucous Hyperplasia, Verrucous Carcinoma, Oral Squamous Cell Carcinoma, Mcm-2, S100A7, Geminin

Session Abstract: 33

Presenter's Name: Davidson, Chloe

Additional Author(s): Davidson C, Hong MMY, Figueredo R, Cheung T, Maleki S

Abstract Title: cDC1-Driven Cross-Priming Shapes Anti-PD-1 Response in Mismatch Repair-Deficient Colorectal Cancer

Abstract:

Introduction: The DNA mismatch repair pathway (MMR) corrects errors in DNA base pairing, and a deficiency (dMMR) in this pathway leads to increased tumour immunogenicity and likeliness to respond to immune checkpoint inhibitors (ICIs) like anti-programmed cell death protein 1 (PD1) therapy. Despite this, just 45% of dMMR colorectal cancer (CRC) patients respond to anti-PD1 therapy. This signifies an importance to identify factors beyond tumour mutational burden that influence ICI response, such as the role of dendritic cell (DC) subsets, specifically type 1 conventional DCs (cDC1s), and their ability to activate and recruit tumour-specific T-cells within dMMR CRC tumours, which remains unexplored. We hypothesize that anti-PD1-resistant dMMR tumours lack maturation and recruitment of cDC1s, which ultimately impacts T-cell activation and responsiveness to anti-PD1 therapy.

Methods: To test this hypothesis, we used induced dMMR CT26 cell lines to investigate immune profiles within the tumours along with their ability to respond to anti-PD1 therapy when supplemented with other treatments including Flt3L to promote cDC1 differentiation and/or anti-CD40 to promote maturation. We injected dMMR CT26 cells into BALB/c mice and administered Flt3L daily for nine days post tumour injection. Anti-CD40 was given every five days for three injections and anti-PD1 was administered when tumours became palpable every three days for three injections. Tumours were then harvested, stained for maturation and activation, then analyzed using flow cytometry.

Results: Our results show that dMMR CT26 tumours are resistant to anti-PD1 therapy alone, however when given with Flt3L or anti-CD40, we saw slightly hindered tumour growth but still resistance to these treatments. We noted a low frequency of cDC1s within the tumours and also a lack of CD40 expression, a co-stimulatory molecule present on mature cDC1s. However, when all three treatments were given in combination, there was increased maturation, frequency, and infiltration of cDC1s, resulting in enhanced cross-priming abilities with T-cells. This increased the tumour's sensitivity to treatment by significantly hindering tumour growth and ultimately improved response to anti-PD1 therapy.

Discussion: These findings show that cDC1 proliferation, differentiation, and maturation are crucial to cross-prime cytotoxic T-cells needed to drive tumour destruction and ultimately the response to anti-PD1 therapy.

Keywords: Mismatch repair deficiency, Colorectal cancer, Immunotherapy, Dendritic cells, Immune checkpoint inhibitor, Tumour mutational burden

POSTER SESSION 2

Session Abstract: 34

Presenter's Name: Dutrizac, Victor

Additional Author(s): Dutrizac V, Manorathan S, Wang J, Gunaratnam L

Abstract Title: Role of KIM-1 Shedding in Regulating Metastasis in Renal Cell Carcinoma

Abstract:

Introduction: Renal cell carcinoma (RCC) is the deadliest form of kidney cancer. There were approximately 8600 Canadians diagnosed with kidney cancer in 2023, of which 85% were RCC. RCC is a cancer that arises from renal proximal tubule epithelial cells (PTECs). Due to its aggressive nature, it is expected that greater than 30% of patients develop metastases which migrate to the lungs. Current treatments such as radiation, hormone, and chemotherapy are ineffective due to patients showing resistance, leading to a 2-year survival. Kidney injury molecule-1 (KIM-1/HAVCR1) is a type 1 transmembrane glycoprotein highly expressed in RCC and is cleaved near the membrane by ADAM metalloproteases (notably ADAM10 and ADAM17), generating soluble (shed) KIM-1 detectable in the urine and plasma. We hypothesize that membrane-bound KIM-1 suppresses RCC metastasis, and that preventing ADAM-mediated shedding via a Δ278–283 mutant will reduce migration, invasion, and lung colonization compared with wild-type (WT) KIM-1.

Methods: A male RCC cell line, 786-O cells, knocked out for KIM-1, will be used to generate stably expressing cell lines containing wild-type KIM-1, a shedding-defective KIM-1 mutant (Δ278–283), and an empty vector control. Expression of our constructs will be verified using Western blot analysis and immunofluorescence. Verification of shedding loss in our cell line will be assessed by collecting conditioned media and performing western blot analysis to quantify soluble KIM-1. Migration and invasion will be assessed using wound-healing and Boyden chamber assays. In vivo metastatic outcomes will be assessed by injecting our respective stable cell lines intravenously into Rag-/- BALB/c mice, observing over 17 days, and negatively staining for lung nodules (India black ink) for quantification.

Results (Expected): We expect KIM-1 Δ278–283 cells to retain surface KIM-1 with reduced soluble KIM-1, show decreased migration, invasion, and form fewer lung metastases than KIM-1 WT cells.

Discussion: This project would support the idea that membrane-bound KIM-1 has an anti-metastatic effect and could point towards soluble/circulating KIM-1 being pro-metastatic, supporting the spread of RCC. This would show that the KIM-1 Δ278–283 mutant would keep KIM-1 attached to the tumour membrane and reduce migration, invasion and lung colonization. This research can identify KIM-1 as a potential novel therapeutic target to treat RCC.

Keywords: Renal Cell Carcinoma (RCC), KIM-1, Cancer, Metastasis, Ectodomain shedding, 786-O

Session Abstract: 35

Presenter's Name: Ying, Shengjie

Additional Author(s): Zeng P, Barrett JW, Khan H, Joris K, Karimi A, Jawhri W, Le N, Wei S, Cecchini MJ, Fung K, Mymryk J, Dumeaux V, Lin RJ, Nichols AC

Abstract Title: Single-cell landscape of sex- and etiology-shaped fibrotic programs in upper airway stenosis

Abstract:
Background: Subglottic stenosis (SGS) is a severe recurrent upper airway disorder that can cause life-threatening shortness of breath. Among adults, SGS can result from prolonged intubation/trauma (tSGS) or be of unknown cause (i.e., idiopathic SGS/iSGS). Notably, iSGS is a rare disorder where >98% of patients are female, whereas tSGS has no known sex-bias. To uncover the molecular basis of SGS along with its etiological and sex differences, we constructed large-scale single cell atlas from biopsied stenotic and healthy upper airway tissue.

Methods: We performed single-nuclei RNA sequencing of 48 biopsied subglottis or paired epiglottis samples, totalling 229,296 nuclei, from participants with iSGS, tSGS, or healthy airway (control) (n=2–9 per sex-stratified group). Standard quality control, normalization, clustering, and cell type annotation was performed using Scanpy. Sccomp was used to perform differential cell type abundance analysis and cell modules were derived from non-negative matrix factorization of cell type proportions.

Results: Comprehensive fine-grained annotation of our single-nuclei atlas revealed 50 cell subtypes across 5 major cell classes (fibroblast, endothelial, epithelial, myeloid, and lymphocyte). Overall, transcriptional changes in disease vs control comparisons occurred predominantly in the subglottis rather than the epiglottis. Within subglottic tissue, the most profound cell composition changes occurred among stromal cells where RUNX2+ myofibroblasts and COL4A1+ angiogenic endothelial cells were nearly exclusively found in iSGS (both sexes) and female tSGS tissue. Male tSGS samples were instead enriched for RGS5+ pericytes (all comparisons FDR<0.05). Subsequently, a holistic analysis of cell subtype co-occurrence revealed 3 distinct cell type composition patterns, termed cell modules (CMs). Nearly all iSGS samples (n=10 of 11) exhibited a fibrotic CM. In contrast, tSGS samples either belonged to the same fibrotic CM as iSGS samples (n=3 of 9) or possessed a distinct highly vascularized CM (n=6 of 9).

Conclusion: Our systematic dissection of the upper airway cellular landscape uncovered a targetable population of RUNX2+ myofibroblasts that dominates iSGS, along with substantial heterogeneity within tSGS, including sex differences and distinct biological subtypes.

Keywords: Subglottic stenosis, fibrosis, single cell RNA sequencing, sex differences, respiratory disease, myofibroblast

POSTER SESSION 2

Session Abstract: 36

Presenter's Name: Tahir, Rizwan

Additional Author(s): Dick F.

Abstract Title: Investigation of Wnt Signaling in Dormant Ovarian Cancer

Abstract:
Introduction: Cancer dormancy is a state in which cancer cells exit active proliferation. As current cancer therapeutics target rapidly proliferating cells, these dormant cells are difficult to treat and can later reawaken, resulting in cancer recurrence. This contributes to the high recurrence rates observed in ovarian cancer, which commonly forms dormant spheroids in the peritoneum. Previously, knocking out Wnt8B and Wnt9B in dormant ovarian spheroids decreased expression of stemness genes including ALDH1A1 and CD44, resulting in decreased spheroid viability. Based on previous knockout experiments, the signalling does not appear to occur through the canonical β-catenin pathway, but instead through either the planar cell polarity (PCP) or Ca2+ pathways. This study aims to investigate the pathway used by Wnt to regulate stemness genes in ovarian spheroids.

Methods: We use CRISPR-Cas9 to knock out target genes in the PCP and Ca2+ pathways in an epithelial ovarian cancer cell line, OVCAR8. Cells are then plated on ultra-low adherence plates to form spheroids. RNA is harvested and RT-qPCR is used to both confirm target gene disruption and measure expression levels of stemness genes in the knockouts, with comparison to a β-galactosidase-targeted negative control and a positive control consisting of a Wnt8B/9B double knock-out.

Results: We expect that knockout of pathway components mediating Wnt8B/9B signalling will mimic the Wnt8B/9B double knock-out in reducing stemness gene expression, identifying the active non-canonical branch.

Discussion: Identifying the specific non-canonical Wnt pathway responsible for maintaining ovarian spheroid viability will provide novel therapeutic targets that can be used to eliminate dormant ovarian cancer cells and reduce recurrence rates in ovarian cancer.

Keywords: Cancer dormancy, Ovarian cancer, Non-canonical Wnt pathways, Dormant spheroids

Session Abstract: 37

Presenter's Name: Hill, Malcolm

Additional Author(s): Searle T, Dick F.

Abstract Title: Investigation of HGSC spheroid dependency on netrin signaling via UNC5 antibody-mediated inhibition

Abstract:
Introduction: High-Grade Serous Carcinoma (HGSC) represents the most common ovarian cancer and the 8th leading cause of cancer mortality in women. While currently available treatments such as platinum-based chemotherapeutics may show an initially promising response, full recovery is complicated by the tendency of the disease to remain at residual levels as dormant, chemotherapy-resistant spheroids. These dormant cells may persist undetected allowing for disease recurrence. Thus, development of adjuvants to improve current treatments is necessary.

Methods: Studies have identified netrin signaling as a pro-survival pathway in HGSC. To investigate netrin signaling dependence of dormant HGSC spheroids, humanized recombinant bivalent antibodies and short chain variable fragments (scFvs) designed to bind UNC5 family receptors were obtained from NRC. Flow cytometry was used to validate the binding of the antibodies to OVCAR8 UNC5 receptors. OVCAR8 cells were next cultured in ultra-low attachment plates to allow for spheroid formation in the presence of carboplatin or trametinib, and selected antibodies or scFvs. Upon re-adherence, crystal violet staining was used to determine OVCAR8 spheroid viability relative to isotype antibody, and drug-only controls. Western blot and ELISA for detection of phospho-ERK downregulation will be used to confirm inhibition of netrin-UNC5 signaling by antibody treatment. Competitive binding assays will also be used to confirm steric inhibition of netrin-UNC5 binding by antibody treatment. Upon validation of UNC5 signaling inhibition and reduced spheroid viability in cell culture by antibody and drug treatment, murine xenograft experiments will be used to establish efficacy of this treatment in vivo.

Results: Flow cytometry has confirmed binding and specificity of antibodies and scFvs to endogenous OVCAR8 UNC5. Furthermore, preliminary antibody-drug assays shows significantly decreased spheroid viability under selected antibody treatment paired with trametinib relative to isotype-only, and drug-only negative controls.

Discussion: Confirmation of HGSC spheroid survival dependency on netrin signaling by antibody-mediated UNC5 inhibition will provide a novel therapeutic target for the treatment of HGSC. Considering the substantial mortality of HGSC and relatively modest efficacy of current treatments targeting dormant spheroids, further study is warranted to develop anti-UNC5 signaling therapeutic antibody treatments.

Keywords: High-Grade Serous Carcinoma, Ovarian Cancer, Antibody inhibitor, Antibody Therapeutic, Chemotherapeutics

POSTER SESSION 2

Session Abstract: 38

Presenter's Name: Zhao, Hanjia

Additional Author(s): Wang C, Passos D, Dick F, Peng T

Abstract Title: A 10-Amino Acid Deletion at N-terminus of DNA Damage Inducible Transcript 3 Confers Protection Against Doxorubicin-Induced Cardiotoxicity

Abstract:
Introduction: Doxorubicin is a potent antitumor drug whose clinical use is limited by dose-dependent cardiotoxicity, a phenomenon known as doxorubicin-induced cardiotoxicity (DIC). Although reactive oxygen species generation and topoisomerase II poisoning have been demonstrated as the main mechanisms of DIC, targeting these upstream pathways has shown limited success. Emerging evidence suggests that multiple regulated cell death pathways contribute to the pathogenesis of DIC, highlighting novel interventional targets for its prevention. DNA damage-inducible transcript 3 (DDIT3) is a stress-responsive transcription factor induced by doxorubicin and is best known for promoting apoptosis. Our previous work identified a novel 10-amino-acid N-terminal domain (Glu19-Val28) of DDIT3 that is required for necroptosis and demonstrated that Ddit3-/- mice were protected from DIC, suggesting that DDIT3 functions as a multifactorial regulator of cell death in this context. However, the relative contribution of DDIT3-mediated apoptosis versus necroptosis remains unknown. We therefore investigated whether deletion of the necroptosis-mediating N-terminal domain confers protection against DIC.

Methods: Primary cardiac cells were isolated from C57BL/6J and Ddit3Δ10aa/Δ10aa mice and exposed to doxorubicin as an in vitro model. C57BL/6J and Ddit3Δ10aa/Δ10aa mice were treated with doxorubicin as in vivo models. Echocardiography was used to assess cardiac function. Serum cardiac troponin I levels were measured to evaluate cardiac injury. Cell death was assessed by LDH assay. The expression of DDIT3, as well as apoptosis and necroptosis markers, was evaluated by western blot.

Results: Doxorubicin increased the levels of DDIT3 protein and induced LDH release in cardiac cells. LDH release and necroptosis markers were much lower in Ddit3Δ10aa/Δ10aa cells compared with wild-type cardiac cells in response to doxorubicin. Under normal conditions, Ddit3Δ10aa/Δ10aa mice were not phenotypically different from wild-type C57BL/6J mice. After doxorubicin injection, however, Ddit3Δ10aa/Δ10aamice showed significantly higher myocardial function and lower serum cardiac troponin I levels compared to wild-type mice.

Significance: This study illuminates the relative importance of necroptosis in the mechanism of DIC, which may provide new targets for therapeutic intervention, with the final goal of improving the quality of life for patients receiving doxorubicin-containing chemotherapy.

Keywords: Doxorubicin, Doxorubicin-induced Cardiotoxicity, DDIT3, Necroptosis, Apoptosis

Session Abstract: 39

Presenter's Name: Chander, Shagun

Additional Author(s): Kalisa, E

Abstract Title: The Effects of Heat and Air Pollution on Academic Performance in Schoolchildren From Sub-Saharan Africa

Abstract:
Introduction: African schoolchildren experience disproportionate exposure to extreme heat and air pollution, yet the combined effects of these environmental stressors on learning remain unclear. Despite contributing minimally to global greenhouse gas emissions, Sub-Saharan African countries face severe climate impacts that threaten students' cognitive and academic outcomes. Most existing studies examine heat or air pollution independently, leaving a critical gap in understanding co-exposure pathways. This review hypothesizes that concurrent exposure to high heat and air pollution has a greater negative impact on academic and cognitive outcomes than either exposure alone.

Methods: This scoping review follows the PRISMA-ScR framework. Studies are identified through four electronic databases and grey literature using predefined inclusion criteria. Records are screened and managed using Covidence software. Extracted data include study type and geographic distribution, definitions and measurements of heat and air pollution exposures, definitions and measurements of academic outcomes, and reported associations between exposures and outcomes. Findings are synthesized descriptively to map existing evidence and identify research gaps.

Results: The study is still being conducted and results remain under investigation. Preliminary synthesis focuses on mapping the geographic distribution of studies, characterizing exposure and outcome measurement approaches, and identifying reported associations between environmental stressors and academic performance. Final results will be presented on poster day.

Discussion: Grounded in a One Health framework, this review recognizes the interdependence of environmental and human health in shaping educational outcomes. By clarifying how environmental co-exposures influence learning, this work highlights environmental inequities in low-emitting regions and identifies priorities for interdisciplinary research and policy. The findings aim to inform context-specific, evidence-based strategies to improve school environments in a changing climate.

Keywords: Heat, air pollution, academic performance, schoolchildren, Sub-Saharan Africa, climate change

POSTER SESSION 2

Session Abstract: 40

Presenter's Name: McKeown, Isaac

Additional Author(s): Donovan J, AlMutawa F, Quiñones-Mateu ME

Abstract Title: Investigating the Impacts of Airborne Microplastics on Viral Respiratory Infections

Abstract:
Introduction: Microplastic (MP) pollution poses a global risk to human, animal, and environmental health. These small plastic particles (<0.5 mm in diameter) can penetrate cells and disrupt physiological processes upon ingestion or inhalation. Recent research identifies airborne MPs as a potential contributor to viral respiratory disease, suggesting they may facilitate viral spread by carrying viruses into the nasal tract, providing novel attachment sites, and/or weakening immune responses. This research project aims to examine the impact of airborne MP exposure on viral respiratory infection and severity.

Methods: We identified different plastics with potential respiratory implications, including microfibers (shed from synthetic clothing), polypropylene (used in food packaging), and tire rubbers (generated by road friction). These materials were used to establish an MP detection system by grinding them to generate a solution of MPs in 1× PBS, which was then quantified using optical stereoscopic microscopy. Ongoing research involves obtaining nasopharyngeal swabs from healthy individuals and spiking the universal transport medium with different concentrations of these MPs to validate the current MP detection protocol. Finally, using a retrospective case-control study (n=200), clinical nasopharyngeal aspirate samples will be obtained from individuals previously tested for respiratory viruses. We are currently evaluating these samples to quantify MPs and associate their accumulation with respiratory disease prevalence and severity.

Results: Preliminary results indicate MPs of various sizes, both experimentally derived and environmentally occurring, are detectable and quantifiable via optical stereoscopic microscopy. A greater MP burden in the respiratory tract is expected to be associated with an increased likelihood of viral respiratory infection and greater clinical severity.

Discussion: This study addresses a critical knowledge gap in MP research by providing direct human evidence linking MP exposure in the respiratory tract with viral respiratory disease occurrence and clinical severity. Findings may identify MPs as an environmental risk factor for viral infection, expanding on current knowledge of their imposed risks on humans. This could prompt further research investigating the mechanisms behind MPs' contributions to viral disease, as well as inform current public health intervention strategies aimed at reducing airborne MP exposure.

Keywords: Microplastics, air pollution, viral respiratory infection, respiratory system, immune system, inhalation

Session Abstract: 41

Presenter's Name: Noori, Asiba

Additional Author(s): Khan ZA

Abstract Title: Identifying postnatal hematovascular progenitor signatures and their age-related decay

Abstract:
Introduction: Hemangioblasts are bipotent progenitors of hematopoietic and endothelial cell lineages. While defined in embryos, their postnatal existence remains debated. This conflict centers on two models: the hemangioblast theory, proposing a shared mesodermal ancestor, versus the hemogenic endothelium theory, where blood cells emerge from specialized vascular lining via endothelial-to-hematopoietic transition (EHT). My study investigates whether a hemangioblast-like program exists in the mouse tibia and how ageing, characterized by chronic inflammation and myeloid skewing, may remodel this program.

Methods: I analyzed single-cell RNA sequencing datasets from C57BL/6N mice across young (1 m), middle-aged (6 m), and old cohorts (20 m). Focusing on cells expressing Kdr/Vegfr2, Tal1, and CD31, hematopoietic competence and endothelial maturation states were determined. These studies are currently being supplemented by immunohistochemistry to localize these cells in mouse femur and tibia.

Results: A rare Kdr+Tal1+ population was identified that retains a hematovascular transcriptional imprint. These cells are enriched for Gata2 and Lmo2 compared to standard endothelium. However, the absence of active EHT markers (Runx1, Gfi1, Itga2b) and early mesodermal markers like Brachyury suggests a primed rather than primitive state. Cell frequency declined with age (from approximately 0.37% to 0.16%), while the surviving population in aged mice showed a transcriptional shift toward megakaryocytic and myeloid-skewed lineages, correlating with increased inflammatory markers such as S100a8/9.

Discussion: My findings support the postnatal persistence of hematovascular-primed cell states, though their molecular profile suggests a specialized hemangioblast-like signature rather than a primitive embryonic identity. The observed age-associated decline and lineage remodeling of these cells may contribute directly to the loss of vascular integrity and hematopoietic homeostasis characteristic of the ageing marrow. To further clarify these roles, my future research will utilize trajectory analysis to determine if these cells transition into functional hematopoietic stem cells under stress and employ spatial transcriptomics to map their proximity to specific marrow vessels, such as H-type or L-type. Additionally, in vitro functional assays are necessary to definitively test the bipotency of isolated Kdr+Tal1+ adult marrow cells.

Keywords: Hemangioblasts, Hematovascular priming, Bone marrow ageing, Single-cell RNA sequencing, Kdr/Flk1/Vegfr2, Tal1/Scl

POSTER SESSION 2

Session Abstract: 42

Presenter's Name: Kabak, Yuliya

Additional Author(s): Jia, J, Sarvananthan K, Saylor B, Mohesni Meybodi A, Lalonde E.

Abstract Title: Comparison of microarray and NGS for copy number variant detection in melanocytic neoplasms

Abstract:
Introduction: The current melanoma diagnostic pipeline at London Health Sciences Centre (LHSC) relies on histopathology as the gold standard for differentiating benign, intermediate, and malignant melanocytic skin lesions. In some cases, histology alone is insufficient as histological features of ambiguous intermediate lesions overlap melanoma, highlighting the need for ancillary testing to improve diagnostic accuracy. Different types of melanocytic skin lesions harbour distinct numbers of whole chromosome arm copy number variations (CNVs). The gold standard for CNV detection is microarray, however, it is not routinely used for skin lesions at LHSC. Comparatively, next generation sequencing (NGS) with the Oncomine Comprehensive Assay v3 (OCAv3) is currently being used at LHSC to report on DNA sequence variants of a subset of genes in diagnosed melanoma lesions. While NGS platforms are capable of CNV detection, there is limited evidence evaluating OCAv3's ability to identify CNVs. This study aims to determine whether OCAv3 can reliably detect whole arm CNVs and replace microarray as part of the melanoma diagnostic workflow.

Methods: Parameters for CNV identification with OCAv3 were defined through a validation analysis on a subset of samples using microarray and NGS, with microarray serving as the reference standard. 49 melanocytic samples, diagnosed by pathologists at LHSC, were analyzed using NGS and microarray techniques to identify clinically relevant CNVs.

Results: Preliminary data shows discrepancies between NGS and microarray in 1 of 25 melanoma samples, where differences in the number of detected CNVs would have altered the diagnostic classification. In addition, NGS most frequently failed to detect gains on 17q and losses on 9p, while overestimating gains on 4q and losses on 19p.

Discussion: Accurate detection of whole chromosome arm CNVs on OCAv3 would enable simultaneous reporting of CNVs and sequence variants from a single assay that is already in clinical practice. Based on preliminary data, the difference in the number of CNVs called by NGS and microarray can be sufficient to alter the diagnostic outcome. Additional optimization of the NGS CNV detection algorithm may reduce such discrepancies. Further comparisons of CNV burden across lesion types are required to determine if NGS-based CNV assessments could reliably support differentiation of ambiguous lesions from melanoma, thereby enhancing diagnostic confidence and improving patient care.

Keywords: Melanoma, copy number variants, next generation sequencing, OCAv3, microarray

Session Abstract: 43

Presenter's Name: Kim, Ashlyn

Additional Author(s): Keller B

Abstract Title: Colorectal Adenocarcinoma Arising in Juvenile Polyposis Syndrome: A Case Report

Abstract:
Introduction: Juvenile polyposis syndrome (JPS) is a rare hereditary condition characterized by multiple hamartomatous polyps throughout the gastrointestinal tract. Although these polyps are benign, patients with JPS have a 39-68% increased risk of developing colorectal cancer.

Case: A patient in their late forties had a history of bloating, vomiting, and black to red diarrhea. Genetic testing confirmed a diagnosis of JPS with a SMAD4 pathogenic variant. Endoscopic evaluation demonstrated extensive colonic polyposis, with approximately 50 polyps in the cecum and ascending colon and more than 50 polyps in the hepatic flexure, as well as markedly thickened gastric folds with large gastric polyps. Subsequent imaging revealed hyperdense material present within the cecum, and biopsy confirmed this as adenocarcinoma. The patient received a subtotal colectomy to remove the carcinoma and a large number of polyps, with future plans to do a gastrectomy. Upon gross examination, the colon revealed numerous pedunculated polyps ranging in size from 0.2 - 3.5 cm. Within the ascending colon, a distinct 5.7 cm polypoid mass was identified among the polyps, with gross involvement of the pericolic soft tissue. The gross examination involved thorough assessment of the mass, describing the depth of invasion and distance to resection margins. Sections of the largest polyps were taken, which demonstrated inflammatory polyps without dysplasia.

Discussion: This case illustrates a rare hereditary polyposis syndrome complicated by colorectal adenocarcinoma. In JPS, malignant transformation is thought to arise from adenomatous foci developing within juvenile polyps, emphasizing the importance of lifelong endoscopic surveillance for these patients. The gross examination is essential to accurately assess tumor extent, margin status, and the background polyposis, all of which impact staging and clinical management.

Keywords: Juvenile polyposis syndrome, SMAD4, Colorectal adenocarcinoma, Hamartomatous polyps, Gross examination

POSTER SESSION 2

Session Abstract: 44

Presenter's Name: Patel, Darshil

Abstract Title: Beyond the Thyroid: An Uncommon Case of Vascular Thrombosis

Abstract: Aggressive papillary thyroid carcinoma (PTC), like other aggressive forms of cancer, is characterized by extension beyond the organ and metastasis to lymph nodes through preferential lymphatic spread. Although uncommon, PTC may be associated with a more aggressive pattern of dissemination, namely hematogenous spread. The following case highlights this rare mode of dissemination and underscores the importance of meticulous gross examination, sectioning and histological evaluation to appropriately characterize the extent of disease. The patient presented with progressive compressive neck symptoms prompting referral to an ENT. Imaging identified a large left thyroid mass with extension to the isthmus, right thyroid lobe and a tumour thrombus involving portions of the internal jugular vein (IJV) and brachiocephalic vein. Fine-needle aspiration biopsies and a surgical biopsy of the neck was completed leading to a working diagnosis of follicular carcinoma. The mass was removed by total thyroidectomy including multi-level neck dissections and segments of the innominate, subclavian and internal jugular veins. Gross and histological examination both confirmed features of PTC along with involvement of soft tissue and venous structures. Patient prognosis, risk of distant metastasis, and likelihood of recurrence have been shown to correlate with the presence and extent of vascular invasion. Pathologists' Assistants (PAs) play a critical role in the meticulous gross examination of such specimens and the deliberate submission of high-yield, representative sections to ensure accurate pathologic staging and diagnosis.

Keywords: Gross examination, Thyroid Cancer, Histopathology, Pathologists' Assistant

Session Abstract: 45

Presenter's Name: Khanal, Luna

Abstract Title: The Cardioprotective Role of DLC1

Abstract:
Introduction: The heart is a muscular pump composed of three layers, with the cardiomyocyte-rich myocardium being particularly vulnerable during heart transplantation. During cold storage, the donor heart undergoes ischemia, and restoration of blood flow in the recipient causes ischemia–reperfusion injury (IRI), which exacerbates tissue damage through oxidative stress, inflammation, calcium overload, and cell death. Deleted in Liver Cancer 1 (DLC1) is a RhoGTPase-activating protein involved in cytoskeletal regulation. The cardiac-enriched isoform DLC1β is essential for heart development, and its loss is linked to congenital heart defects. By modulating pathways like the Rho-ROCK signaling pathway, which affects cytoskeletal stability, cell death, and inflammation, DLC1β is a promising target for cardioprotection and may offer strategies to reduce IRI and improve transplant outcomes. I hypothesize that upregulating DLC1β has cardioprotective effects through the suppression of inflammatory and immune pathways.

Methods: To fulfil this hypothesis, H9C2 and HL-1 cells are cultured under hypoxia and normoxia conditions. Cell death, immune infiltration and mechanistic pathways will be identified using markers including Propidium Iodide (PI), Annexin V and CD3 and RNA-sequencing data. Findings will be further validated in-vitro by using a mouse heart transplant model.

Results: Upregulating DLC1β is expected to reduce cardiomyocyte death following IRI through the suppression of inflammatory pathways and immune activation, including reduced expression of pro-inflammatory cytokines and decreased immune cell infiltration. These effects are anticipated to improve cardiac graft integrity for better transplant outcomes.

Discussion: If increasing DLC1β lowers cardiomyocyte death, it would indicate that DLC1β regulates pathways controlling cytoskeletal stability and immune responses. This is important for heart transplant, where IRI often lead to cell death, graft damage and rejection. Understanding the pathways regulated by DLC1β could reveal new mechanisms of its cardioprotection, thus guiding the development of new therapeutic strategies to reduce the effects of IRI. Further animal studies will be necessary to validate the protective effects and determine clinical potential.

Keywords: Ischemia-Reperfusion Injury, DLC1β, Heart Transplant, Cardioprotection, Immune Rejection, Regulatory Pathways

POSTER SESSION 2

Session Abstract: 46

Presenter's Name: Kelawan, Chad

Abstract Title: Investigating the Crosstalk of Netrin and WNT signaling in High-Grade Serous Carcinoma

Abstract: Despite an initially positive response to treatment, a common occurrence among patients diagnosed with high-grade serous carcinoma (HGSC) is the development of chemoresistance and subsequent disease relapse. This recurrence is attributed to cellular aggregates, termed spheroids, which exhibit characteristics of dormancy. These non-proliferative cells evade eradication and disseminate, thereby supporting the persistence of minimal residual disease. While previous research has identified crucial mechanisms in the Netrin and Wnt signaling pathways that support spheroid survival, the complex regulatory interactions among their signaling networks remain to be elucidated. Further investigation to uncover potential crosstalk among these pathways will enable us to gain insight into the signals that coordinate to regulate dormancy and uncover potential genetic dependencies that can be targeted for therapeutic intervention. To accomplish this, the current study will probe knockout HGSC cells for crosstalk between these signaling pathways and assess gene candidates that exhibit increased expression in dormancy conditions, suggesting a potential dependency for spheroid viability, to determine the key intracellular messengers underlying their putative interaction. In addition, as HGSC spheroids are resistant to the conventional platinum-based chemotherapeutics used for this disease, such as carboplatin, deletions of the identified intracellular messengers will be investigated to determine if inhibiting crosstalk increases the sensitivity of HGSC cells in suspension to treatment. Moreover, to substantiate the therapeutic potential of targeting prospective intracellular messengers mediating pathway crosstalk, mouse models for minimal residual disease and metastatic spread will be used to determine if terminating crosstalk compromises dormancy, impedes dissemination, and increases sensitivity to platinum-based chemotherapeutics, thereby decreasing spheroid viability in the abdomen, leading to longer survival and reduced tumor burden. Overall, this project is anticipated to provide insight into a potential genetic dependency in HGSC pathogenesis, which can be exploited as a novel therapeutic target to overcome dormancy, sensitize to chemotherapy, and eradicate residual disease, mitigating the substantial risk of relapse.

Keywords: High-Grade Serous Carcinoma, Ovarian Cancer, WNT Signaling, Netrin Signaling, Signaling Crosstalk, Cancer Dormancy

Session Abstract: 47

Presenter's Name: Donovan, Justin

Additional Author(s): Kaur N, Kim M, Santoro D, Arts EJ, Quiñones-Mateu ME

Abstract Title: Linking sewer chemistry to viral RNA recovery in wastewater surveillance using a sewer physical twin model

Abstract:
Introduction: Wastewater-based epidemiology (WBE) is an essential tool for tracking community-level pathogen circulation; however, interpretation of viral signals remains limited by an incomplete understanding of in-sewer physicochemical processes. Municipal collection systems frequently employ nitrate and iron salts for odor and corrosion control, yet these treatments may alter biofilm stability and suspended solids that can affect viral transport. As viruses such as SARS-CoV-2 are predominantly solids-associated, shifts in particulate matter may significantly influence viral RNA recovery. Here, we investigated how chemical dosing affect solids shedding and viral detectability using a controlled Sewer Physical Twin (SPT) model.

Methods: Three parallel 5-loop SPT systems were operated under control, nitrate-dosed, and iron-dosed conditions, supplied with municipal wastewater (London,ON). Suspended solid measurements were quantified during biofilm shedding assays under control and continuous chemical addition conditions. Viral RNA recovery was also measured using RT-qPCR for a panel of viruses, including SARS-CoV-2 and known enteric viruses, collected from circulating wastewater in the intermediate loops and effluent.

Results: Chemical dosing produced distinct solids and viral profiles. The iron-treated line exhibited the highest suspended solids due to flocculation, precipitation, and biofilm destabilization. Control and nitrate-treated lines showed the lower solids, consistent with enhanced biofilm stability. Viral measurements mirrored these patterns where the iron-dosed system showed the highest viral RNA recovery, while the control and nitrate-treated systems showed lower recovery corresponding to reduced solids shedding.

Discussion: These findings show that iron dosing enhances viral RNA recovery in wastewater by substantially increasing suspended solids through flocculation, biofilm disruption, and precipitation. By contrast, nitrate suppresses solids release, thereby reducing viral adsorption surfaces and lowering detectable viral RNA. This suggests that chemical dosing practices can significantly bias WBE signals, with iron-treated systems potentially inflating viral concentrations and nitrate-treated systems potentially underrepresenting true viral burdens. Accounting for chemical treatment systems and solids dynamics is therefore essential for accurate interpretation of wastewater surveillance data across heterogeneous municipal networks.

Keywords: Wastewater-based epidemiology (WBE), SARS-CoV-2, viral RNA, sewer physical twin, chemical treatment, biofilm

POSTER SESSION 2

Session Abstract: 48

Presenter's Name: Wang, Xiaopu

Abstract Title: Primary Burkitt Lymphoma of the Terminal Ileum in an Older Adult: A Case Report

Abstract:
Introduction: Burkitt lymphoma (BL) is a highly aggressive but potentially curable non-Hodgkin's lymphoma (NHL) with three subtypes: endemic, sporadic and immunodeficiency related. The sporadic type mainly affects the gastrointestinal (GI) tract and is rarely seen in older adults.

Case: A 62-year-old male patient presented with unexplained weight loss, extreme fatigue, tiredness, and arthralgias and was otherwise healthy. Imaging revealed a near-circumferential mass with lymphadenopathy in the terminal ileum. Subsequent colonoscopy, however, could not locate the mass, and the biopsy results were insignificant, showing no dysplasia or malignancy. Therefore, a right hemicolectomy was performed to remove the mass. Upon gross examination, a well-circumscribed, pink-tan and fleshy submucosal mass was identified in the terminal ileum with possible involvement of the ileocecal valve and cecum. Histologically, the proliferating malignant cells were medium sized with high rates of mitosis and apoptosis. Numerous tingible-body macrophages were diffusely identified, creating a "starry sky appearance". Special stains were positive for BL, with the Ki67 proliferation index approaching 100%. Cytogenetic testing showed positive cMYC gene rearrangement, confirming the diagnosis of BL. In this case, the mass was a primary GI BL, confined to a single extralymphatic organ with no lymph node involvement, making it Stage I according to the Ann Arbour system.

Discussion: The nonspecific symptoms and unfruitful colonoscopy presented challenges in patient care. In cases like this, it is important for PAs to recognize the gross features and review the CAP protocol to develop a grossing plan. There is no standardized grossing protocol for BL; therefore, this specimen was grossed as if it was an adenocarcinoma in the bowel, which was beneficial for assessing involvement of extranodal sites and local lymph nodes for staging. Due to BL's specific diagnostic criteria, thorough gross examination, histological features, special stains and cytogenetic testing are necessary to rule out differential diagnoses.

Keywords: Burkitt lymphoma, cytogenetics, Non-Hodgkin's lymphoma, special stains

Session Abstract: 49

Presenter's Name: Wei, Senyang

Abstract Title: Testing Combined Immunotherapy for the Management of Anaplastic Thyroid Cancer

Abstract:
Introduction: Anaplastic thyroid cancer (ATC) is an aggressive malignancy with historical overall survival <6 months. For the 40-60% of ATC harboring BRAF V600E, dabrafenib plus trametinib (DT) can produce rapid regression and improve median overall survival to ~9-14 months, yet resistance inevitably emerges within months, and effective post-resistance options remain limited.

Immunotherapy, such as anti-PD1 agents, offers a mechanistically distinct approach that may overcome such resistance. Clinical data suggest ATC may be more responsive to anti PD-1 than other thyroid cancers. However, anti PD-1 monotherapy remains modest overall, suggesting the present of additional immunosuppressive forces. Therefore, we hypothesize that PD-1-based combination immunotherapy will improve tumor control in ATC management.

Aims: We will (i) establish and validate DT resistance using DT-resistant TBP-3743 tumor suspensions derived from heavy DT-treated B6129SF1 mice, with in vivo confirmation showing significantly reduced DT responsiveness versus DT-naïve parental controls ($p<0.0001$); (ii) test anti-PD-1 combinations (± anti CTLA-4, LAG-3 and TIM-3) in DT-resistant tumors; and (iii) define treatment-associated tumor microenvironment remodeling via IHC, flow cytometry, and scRNA-seq.

Methods: TBP-3743 tumors will be treated with DT in B6129SF1 mice until resistance emerges, then processed into DT-resistant tumor suspensions. These suspensions will be re-implanted without intermediate in vitro expansion to preserve in vivo heterogeneity and resistance-associated adaptations. Resistance are be confirmed by implanting DT-resistant suspensions alongside DT-naïve controls and treating with DT.

Mice bearing established DT-resistant tumors will then be randomized at 200 mm^3 to control, single immunotherapy agents or combinations of anti-PD-1 with each partner antibody.

To map treatment-induced remodeling and resistance programs, tumors will be analyzed by immunohistochemistry for spatial immune infiltration, scRNA-seq with DESeq2 differential expression and pathway inference, and orthogonal flow cytometry to quantify major immunocell subsets and functional states.

Significance: By treating DT resistance as the starting point, and using uncultured resistant tumor suspensions, this work better mirrors real-world treatment than studies in therapy-naïve models and can identify actionable combination strategies and biomarkers for post-DT ATC.

Keywords: Anaplastic Thyroid Cancer, Immunotherapy, Target Therapy, Drug Resistance, Animal Trial

POSTER SESSION 2

Session Abstract: 50

Presenter's Name: Ugulini, Samuel

Additional Author(s): Hardy DB, Dhanvantari S

Abstract Title: CBD Exposure Impairs Mechanisms of Glucagon Trafficking and Secretion in Pancreatic Alpha Cells

Abstract:
Introduction: Pancreatic α-cell glucagon plays a central role in maintaining glucose homeostasis. Although glucagon secretion is controlled by nutrient, paracrine, and neural inputs, emerging evidence indicates that the islet endocannabinoid system (ECS) and its receptors may additionally regulate α-cell function. While phytocannabinoids such as CBD are known to interact with the ECS, whether it alters α-cell function in ways that disrupt glucagon secretion has not been proven. Recent data from our group indicates that gestational exposure to CBD impairs glucose tolerance in adult male offspring. Complementary to this, in an α-cell model, we found that high doses of CBD disrupt glucagon trafficking through lysosomal pathways, suggesting a link between ECS signalling and secretory function. However, CBD exposure did not alter transcript expression of ECS receptors, creating a disconnect between transcriptomic and functional outcomes. To address this, we used RNAseq to discover novel pathways affected by CBD exposure, and a more physiologically relevant dose of CBD and its inactive metabolite to determine whether altered glucagon trafficking reflects CBD-specific signaling rather than nonspecific cannabinoid effects.

Methods: For RNA-seq, α-TC1-6 cells were exposed to vehicle or 3μM CBD for 24 hrs (n=5); DESeq2 and GO/KEGG databases were used for differential expression and enrichment analysis to identify important pathways affected by CBD-exposure. For confocal microscopy, cells were exposed to vehicle, 3 μM CBD or 7-COOH-CBD for 24 hrs (n=6) to elucidate functional changes in glucagon trafficking.

Results: RNA-seq revealed that 3 μM CBD downregulated pathways implicated in glucagon trafficking and secretion, and reduced expression of genes such as: synaptotagmin V (SytV), which is important for granule secretion; and glucagon (FDR<.05). Via confocal microscopy, we found 3 μM CBD increased glucagon in Lamp1+ lysosomes ($p<.05$) and increased the colocalization of Lamp1 with SytV ($p<.05$), with 7-COOH-CBD having no effect on glucagon trafficking. This data suggests that secretory granules containing glucagon and SytV are being rerouted into lysosomes through CBD-dependant pathways, disrupting glucagon trafficking and secretion.

Discussion: CBD modulates glucagon trafficking and secretion through the reprogramming of lysosomal and secretory machinery in α cells. Collectively, this may mediate the glucose intolerance observed in CBD-exposed offspring.

Keywords: Alpha cell, Pancreas, Lysosomes, Glucagon trafficking and secretion, Cannabis

Session Abstract: 51

Presenter's Name: Lauzon-Young, Carolyn

Additional Author(s): Sadegheh Hagshenas, Ananilia Silva, Jennifer Kerkhof, Jessica Rzasa, Michael Levy, Bekim Sadikovic

Abstract Title: Development of a Hierarchical Support Vector Machine (H-SVM) Framework for the Epigenetic Classification of Myeloid Malignancies

Abstract:
Background: Myeloid malignancies comprise a heterogeneous group of hematologic neoplasms that pose significant diagnostic challenges. Despite advancements in next-generation sequencing (NGS), many patients lack a definitive diagnosis due to the prevalence of genetic variants of uncertain significance (VUS). This ambiguity complicates diagnostic interpretation of NGS and delays optimal therapeutic intervention. We propose a novel classification strategy that leverages DNA methylation episignatures, utilizing a hierarchical Support Vector Machine (H-SVM) framework. This model integrates the structured decision-making of a branching tiered system like a random forest network, with the robust categorization power of SVMs. Objective: To develop and validate an analytical H-SVM framework capable of accurately classifying myeloid malignancies into clinical subtypes based on distinct DNA methylation profiles.

Methods: DNA is obtained from peripheral blood samples of patients with clinically diagnosed myeloid malignancies including acute myeloid leukemia (AML), myelodysplastic neoplasms (MDS), and myeloproliferative neoplasms (MPN); and samples from non-cancerous myeloid conditions (NCMC) including anemias, cytopenias, and cytoses of myeloid cell lines. DNA methylation is profiled using Illumina Infinium EPIC arrays. Following Euclidean clustering and multidimensional scaling (MDS) to visualize cohort separation, an H-SVM classifier is developed. Each level of the hierarchy is trained to evaluate likely sample class with optimized sensitivity and specificity, with samples progressing through sequential SVMs based on prior classification.

Results: Preliminary evidence revealed distinct DNA methylation patterns capable of separating myeloid malignancies from unaffected controls and NCMC. The H-SVM approach to malignancy classification proved effective with over 95% sensitivity and specificity in stratifying patients with malignancies and NCMC relative to healthy controls. Preliminary results for subsequent tier analyses based on clinical subtypes in ongoing.

Conclusions: These findings demonstrate that H-SVM-based episignature analysis can effectively stratify myeloid malignancies from NCMCs and healthy controls with high precision. This provides a scalable framework for resolving diagnostic ambiguity. Future work will focus on refining the subsequent tiers of the H-SVM to improve the granular subtyping, ultimately facilitating more personalized clinical management.

Keywords: Myeloid malignancy, Machine learning, Biomarker, Episignature, DNA methylation, Hematology

POSTER SESSION 2

Session Abstract: 52

Presenter's Name: Menard, Melissa

Additional Author(s): McDonald LJ, Cecchini MJ

Abstract Title: Digital Cytometric Analysis for the Evaluation of Mismatch Repair Protein Immunohistochemistry in Colorectal Specimens

Abstract:
Introduction: Immunohistochemical assessment of mismatch repair (MMR) proteins is routinely performed and contributes substantially to pathologist workload. While focal or clonal abnormalities in MMR expression may carry clinical relevance, they can be difficult to detect on routine review. Digital pathology allows for automated image analysis of immunohistochemistry, offering potential improvements in efficiency and consistency when evaluating biomarkers such as MMR.

Methods: Thirty colorectal adenocarcinoma cases were digitized using a Grundium Occus 40 and Aperio slide scanners. A semi-automated analysis workflow was developed in QuPath using a two-class object classifier, with optical density values exported for downstream analysis in RStudio. Digital cytometric analysis (DCA) was generated for tumour and stromal compartments based on MMR IHC optical density. Results were compared with conventional glass slide review.

Results: Across 120 slides, DCA demonstrated a sensitivity of 76.9% and specificity of 99%, compared with 94.12% sensitivity and 100% specificity on glass slide assessment. In 3.3% of cases, interpretation based on DCA was deferred to glass review. Reduced sensitivity was attributable to small clonal areas of MMR loss that were not initially detected digitally; subsequent glass slide review confirmed these findings. Mean review time was significantly shorter with DCA than with glass slides (4.3 seconds vs 19.57 seconds; $p < 0.001$).

Conclusions: Digital cytometric analysis represents a rapid approach for assessing mismatch repair status. However, further refinement is required to improve detection of subclonal MMR loss. Although conventional microscopy remains essential, this method shows promise for enhancing biomarker assessment and improving diagnostic workflow efficiency.

Keywords: Digital pathology, Biomarkers, Colorectal Carcinoma, Digital cytometric analysis

Session Abstract: 53

Presenter's Name: Behjati, Fatemeh

Additional Author(s): Behjati B, Pons EJ, Yan B, Sey M, Campbell J, Hussain N, Leslie K, Klassen Z, Pin C, Shooshtari P

Abstract Title: Interpretable variational autoencoder for integrating epigenetic and transcriptomic profiles in Pancreatic Cancer

Abstract: Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal cancers, characterized by profound heterogeneity and resistance to current therapies. A critical knowledge gap lies in understanding how epigenetic regulation shapes tumor behavior and the tumor microenvironment (TME). Among key modulators are cancer-associated fibroblasts (CAFs), particularly the inflammatory (iCAF) and myofibroblastic (myCAF) subtypes, whose epigenetic influence on tumor cells is poorly defined.
To address these gaps, we generated multi-modal data from patient-derived organoids (PDOs) treated with conditioned media from iCAF or myCAF and performed RNA-seq and ATAC-seq to assess the effects of CAF signaling. Integration with clinical metadata enabled correlation of molecular features with patient outcomes.

Leveraging this comprehensive dataset, we sought to uncover molecular signatures and regulatory mechanisms underlying PDAC heterogeneity. We developed a dual-channel attention-based variational autoencoder (VAE) to identify and prioritize regulatory regions from ATAC-seq data binned around transcription start sites. Recognizing CAF heterogeneity, iCAF and myCAF ATAC-seq profiles were modeled as distinct channels within the VAE, enabling integration into a shared latent space that reflects the complexity of the TME in organoids. Additionally, we incorporated an attention mechanism together with a regression head into our model to provide interpretable weights that highlight chromatin regions most predictive of transcriptional output for each CAF subtype.

Our VAE model demonstrated strong predictive performance, enabling the identification of CAF-associated transcription factors that govern gene networks our framework classified as epigenetically active yet transcriptionally silent. Analysis of attention-derived regulatory regions revealed distinct chromatin accessibility signatures linked to these transcription factors. By assessing the expression levels of these transcription factors and their binding affinity to the predicted regulatory regions, we highlight potential therapeutic targets for epigenetic remodeling in PDOs in response to the TME.

In summary, this interpretable deep learning framework advances our understanding of PDAC biology, particularly its epigenetic landscape, and offers a foundation for precision oncology by linking molecular s

Keywords: Deep learning / variational autoencoder, attention mechanism, pancreatic cancer, transcriptomics, epigenomics

POSTER SESSION 2

Session Abstract: 54

Presenter's Name: Sampy, Stefan

Additional Author(s): Peng, T.

Abstract Title: Nicotinamide mononucleotide promotes autophagy and bacterial clearance in endotoxin-stressed neutrophils

Abstract:
Background: Sepsis is a time-critical syndrome in which dysregulated innate immunity and microvascular injury drive organ failure and death. Neutrophil antimicrobial failure is therefore a clinically actionable bottleneck. Autophagic flux, a lysosome-dependent quality-control pathway, is increasingly recognized as a determinant of phagocyte fitness, yet flux execution is energetically demanding and may be selectively vulnerable during endotoxin stress. Nicotinamide mononucleotide (NMN), an immediate precursor in NAD+ salvage, may restore immunometabolic capacity and re-enable degradative flux.

Objective: Define the impact of LPS endotoxin on neutrophil autophagy and test whether NMN restores autophagic status with concordant improvement in bacterial clearance.

Methods: Murine bone-marrow–derived neutrophils (BMDNs) and human peripheral blood neutrophils (PBNs) were exposed to LPS (100 ng/mL, 24 h) ± NMN (500 μM). Autophagic status was assessed by immunoblot quantification of autophagy-related protein, LC3-II. Antibacterial function in BMDNs was quantified by CFU assays using live E.coli, measuring early uptake (5 min) and intracellular survival (95–115 min).

Results: LPS triggered a robust accumulation of LC3-II in BMDNs and PBNs ($p<0.001$ and $p<0.01$ respectively) suggesting an abnormality in autophagy. Remarkably, NMN reversed this stress signature, reducing LC3-II in BMDNs ($p<0.01$) and PBNs ($p<0.01$), consistent with autophagic rescue. From a functional standpoint, NMN significantly increased early E. coli uptake (5 min, $p<0.01$) and intracellular killing, reducing bacterial burden at 95 min ($p<0.01$) and 115 min ($p<0.05$).

Significance: Sepsis outcomes hinge on neutrophil bacterial clearance; failure permits pathogen persistence, sustaining inflammation, driving organ injury, and increasing secondary infection risk. Here, intracellular pathway readouts (autophagy signatures) are linked to the functional performance (phagocytosis and bacterial killing), enabling mechanistic findings to be judged by host-defense performance. Furthermore, replication in mouse and human neutrophils supports biological conservation and a clear translational trajectory for this work. In parallel, a newly designed colony-forming unit, time-course killing workflow captures neutrophil antimicrobial kinetics across multiple time-points while being reproducible across experimental variables, enabling robust bench-marking and treatment sensitivity testing

Keywords: Sepsis, Neutrophils, Nicotinamide mononucleotide, Endotoxin, Autophagy, Bacterial Killing

Session Abstract: 55

Presenter's Name: Keating, Alexandra

Additional Author(s): Clarke JP, Strong MJ

Abstract Title: The role of extracellular vesicle-mediated SARS-CoV2 nucleocapsid protein and TAR DNA-binding protein 43 aggregate transmission in amyotrophic lateral sclerosis

Abstract:
Introduction: Amyotrophic lateral sclerosis is a fatal neurodegenerative disease in which alterations in the metabolism of the RNA binding protein TDP-43 characterized by intraneuronal cytoplasmic aggregates and a nucleocytosolic redistribution are observed in 97% of cases. Our laboratory has shown that the SARS-CoV-2 nucleocapsid protein (NCP) interacts with TDP-43 in forming biomolecular condensates in silico. We hypothesize that NCP forms condensates with TDP-43 in spinal motor neurons in ALS and that extracellular vesicles (EVs) mediate the intercellular transfer of these condensates resulting in disease propagation.

Objectives: 1) determine whether TDP-43/NCP biomolecular condensates form in spinal motor neurons; 2) determine whether there is evidence to support the EV-mediated intercellular transport of TDP-43/NCP condensates between spinal motor neurons.

Methods: We examined post-mortem spinal cord from a representative sample of ALS cases. Antibody-mediated immunohistochemistry (IHC) and immunofluorescence (IF) were utilized to detect TDP-43, NCP, and EV markers (CD63 and CD81). Visualization was completed using brightfield and confocal microscopy. To assay for co-aggregation, co-immunoprecipitation assays were performed.
Preliminary Results: Using IHC, we first confirmed the specificity of anti-NCP antibodies using SARS-CoV-2 infected human lung tissue. We then confirmed the presence of TDP-43 cytoplasmic inclusions in spinal motor neurons from neuropathologically-confirmed cases of ALS. Using confocal microscopy, we observed both TDP-43 neuronal cytoplasmic inclusions typical of ALS and punctate cytosolic NCP expression with colocalization observed in some, but not all cases. This latter finding was further supported by the co-immunoprecipitation of NCP and TDP-43 from ALS spinal cord protein lysates. We also observed extraneuronal deposits of TDP-43/NCP protein condensates, suggested to be transported in EVs. This was further examined by confocal microscopy, where the presence of EV biomarkers, CD63 and CD81, were confirmed.

Discussion: These preliminary data will be greatly expanded upon, but support a model where viral protein-host RNA binding protein interactions stabilize TDP-43 condensates and exploit EV pathways to spread pathology. This study is significant as it may provide insight into the mechanisms by which viral infection can affect the pathogenesis of neurodegenerative disease.

Keywords: Amyotrophic lateral sclerosis, Extracellular vesicles, SARS-CoV-2, Biomolecular condensates, TAR DNA-binding protein 43, Nucleocapsid protein

POSTER SESSION 2

Session Abstract: 56

Presenter's Name: Setayeshi, Niloofar

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

Abstract Title: Microbiome-Driven Restoration of MAdCAM-1 to Boost ICI Efficacy in metastatic renal cell carcinoma

Abstract:
Introduction: Metastatic renal cell carcinoma (mRCC) is still one of the most challenging cancers to treat. Immune checkpoint inhibitor (ICI) therapy reactivates the patient's immune system to eliminate cancer cells, but is often limited by toxicity, and most patients with mRCC show primary resistance to ICIs. Gut dysbiosis plays a vital role in tumor resistance to ICI therapy by reducing intestinal expression of Mucosal Vascular Addressin Cell Adhesion Molecule-1 (MAdCAM-1), an adhesion molecule that regulates immune-trafficking of T-cells in mucosal sites. Circulating levels of soluble MAdCAM-1 (sMAdCAM-1) in plasma reflect its intestinal expression. Our lab previously showed that fecal microbiota transplantation (FMT) from healthy donors could improve response to ICIs and mitigate toxicity in patients with mRCC. However, it is still unknown if actively boosting MAdCAM-1 in patients would improve their cancer outcomes. We now hypothesize that FMT can restore sMAdCAM-1 levels, leading to improved clinical outcomes in mRCC.

Method: We will first measure sMAdCAM-1 levels with ELISA in bio-banked blood samples from our mRCC trial and correlate the levels with the clinical outcomes of patients in the trial. Moreover, we will use the syngeneic mouse RCC RENCA model to assess whether modulating the microbiome with FMT can enhance ICI efficacy. Animals will receive a broad-spectrum antibiotic cocktail to induce gut dysbiosis, and then be randomized to receive either FMT from a human stool donor or from healthy naïve mice. Mice will then be injected with RENCA cells and treated with anti-CTLA-4 and anti-PD-1. The experimental endpoints will include quantification of sMAdCAM-1 in plasma and MAdCAM-1 expression in the ileum.

Expected Results: We anticipate that patients exhibiting higher sMAdCAM-1 levels following FMT will demonstrate greater donor microbiome engraftment, a lower incidence of toxicity, and an improved clinical response to ICI therapy. We expect that FMT will restore ileal MAdCAM-1 expression and circulating sMAdCAM-1 levels, thereby re-establishing the intestinal endothelial barrier's capacity to regulate immune trafficking of regulatory T-cells within the tumor microenvironment.

Discussion: This research will establish the causal role of MAdCAM-1 in driving immunotherapy outcomes. We aim to identify whether modulation of the gut–immune axis through FMT can restore MAdCAM-1 signaling and enhance ICI efficacy in both murine models and patients.

Keywords: Metastatic renal cell carcinoma, immunotherapy, fecal microbiota transplantation, immune checkpoint inhibitors, gut microbiota, MAdCAM-1

Session Abstract: 57

Presenter's Name: Duffy, Laura

Additional Author(s): Kord D, Gillentine MA, Hamdan F, Michaud JL, Campeau PM, Maftei C, Scott P, Srour M, Wang T, Eichler EE, Sadikovic B, Siu VM

Abstract Title: Recurrent CHD6 Variant Associated with a Neurodevelopmental Syndrome and Episignature

Abstract: The Chromodomain Helicase DNA-Binding (CHD) gene family consists of nine chromatin remodeling enzymes (CHD1–9). CHD6 and 9 are the only genes not yet associated with a genetic syndrome. Pathogenic variants in CHD2, 4, 7, and 8 are associated with neurodevelopmental syndromes and distinct episignatures. This study sought to identify a syndrome and episignature associated with CHD6.
Patients with CHD6 variants of uncertain significance (VUS) were identified via GeneMatcher and internal cohorts. Genome-wide DNA methylation analysis using Infinium EPIC array identified differentially methylated CpG sites to build support vector machine classifiers distinguishing CHD6 cases from controls.

Nineteen CHD6 variants (seven truncating, 12 missense) were identified in 24 patients; 19 heterozygous, including seven with a de novo recurrent missense variant (c.2957G>A; p.Arg986Gln) and one heterozygous for an adjacent variant (c.2960C>T; p.Thr987Met). Fifteen samples underwent DNA methylation analysis (five p.Arg986Gln, one p.Thr987Met, one compound heterozygous, three heterozygous missense, five truncating).

Analysis revealed a distinct, specific episignature for p.Arg986Gln and p.Thr987Met and a more sensitive, broader episignature including c.2113A>G; p.Asn705Asp, but not other missense or truncating variants. Truncating variants suggested a possible separate episignature but failed cross-validation. All p.Arg986Gln and p.Thr987Met cases had developmental delay and/or intellectual disability with variable ADHD, seizures, precocious puberty, digital anomalies, and nonspecific dysmorphisms. Minimal data was available for p.Asn705Asp. Among truncating variants, most were inherited from parents lacking neurodevelopmental impairment and one arose de novo.

A distinct episignature was identified for adjacent missense CHD6 variants (p.Arg986Gln/p.Thr987Met), associated with neurodevelopmental impairment, seizures, and precocious puberty. Findings support a dominant-negative or gain-of-function mechanism; lack of a reproducible episignature in truncating variants and unaffected carrier parents argues against dominant loss-of-function, though recessive inheritance remains possible. Functional studies are needed to distinguish VUS from pathogenic variants and assess effects on protein function. A larger cohort is needed to validate the episignature, assess additional missense variants, and clarify if CHD6 loss-of-function defines a separate episignature and syndrome.

Keywords: Epigenetics, DNA Methylation, EpiSign, CHD6, Episignature, Neurodevelopmental Disorder

POSTER SESSION 2

Session Abstract: 58

Presenter's Name: Al Jawhri, Wessam

Additional Author(s): Joris K, Khan H, Ying S, Zeng PYF, Karimi A, Le N, Wei S, Rotenberg B, You P, Husein M, Strychowsky J, Mymryk J, Barrett JW, Nichols AC

Abstract Title: Decoding Tonsillar Hypertrophy in Obstructive Sleep Apnea

Abstract:
Introduction: Tonsillar hypertrophy is the leading cause of pediatric obstructive sleep apnea (OSA), affecting 1-5% of children and necessitating adenotonsillectomy as first-line therapy. Despite its prevalence, the immunological, genetic, and microbial mechanisms driving tonsillar enlargement remain poorly understood, limiting non-surgical interventions. This study leverages single-cell RNA sequencing and microbiome analysis to identify hypertrophy-specific pathways distinguishing OSA from recurrent tonsillitis (RT).

Methods: Publicly available single-cell RNA sequencing data from human tonsils were re-analyzed to compare OSA (n=4) and RT (n=5) samples. Differential cell-type abundance analysis, gene expression profiling, and cell-cell communication network analysis were performed. Microbial profiling assessed bacterial diversity and compartmentalization across immune populations.

Results: OSA tonsils exhibited higher proportions of naïve and memory B cells, while RT tonsils were enriched for germinal center B cells (GCBCs). RT GCBCs upregulated XBP1, consistent with GC-to-plasma-cell differentiation, alongside genes linked to early B-cell programs (VPREB1) and mitochondrial stress/apoptosis (ENDOG). OSA GCBCs displayed a survival-adapted phenotype, with upregulation of mitochondrial cytoprotective genes (MTRNR2L8, SLC25A27, SMAD9) and enhanced BAFF/APRIL–TACI pro-survival and BTLA–HVEM checkpoint signaling. OSA tonsils harbored higher bacterial diversity (Shannon p=0.02; PERMANOVA R^2=0.09, p=0.005) with polymicrobial colonization across myeloid, B, and T cells (Prevotella, Mycoplasma, Fusobacterium), while RT showed restricted Haemophilus enrichment.

Discussion and Conclusion: OSA hypertrophy was associated with B-cell survival programs and polymicrobial colonization, while RT displayed inflammatory responses to pathogenic bacteria. Survival signaling and microbe-immune interactions represent potential therapeutic targets to reduce surgical burden in pediatric OSA. Expanded cohorts with Periodic Fever, Aphthous Stomatitis, Pharyngitis, and Adenitis (PFAPA) and healthy controls will further define hypertrophy-specific mechanisms.

Keywords: Obstructive Sleep Apnea, Tonsillar Hypertrophy, Recurrent Tonsillitis, Tonsil immunology, B Cells, Single-cell RNA Sequencing

POSTER SESSION 2

Session Abstract: 59

Presenter's Name: Lu, Rainy

Additional Author(s): Forbes A, Delport J, Bagga R

Abstract Title: From Latex to Lateral Flow : Advancing Cryptococcal antigen diagnostics

Abstract:
Introduction: Rapid and accurate detection of cryptococcal antigen (CrAg) in serum and cerebrospinal fluid (CSF) is essential for the timely diagnosis and management of cryptococcal meningitis. The current diagnostic gold standard, the cryptococcal antigen latex agglutination system (CALAS®, Meridian Bioscience), is associated with biosafety concerns, longer turnaround times, and reduced sensitivity at high antigen titers. This study compares the performance of the FungiXpert™ Cryptococcal capsular polysaccharide detection K-set (Genobio Pharmaceutical, China) and IMMY CrAg® (Immuno-Mycologics, USA) lateral flow assays with CALAS®.

Methods: Thirty clinical samples, including 20 CrAg-positive and 10 CrAg-negative specimens, were evaluated. Positive samples of Cryptococcus neoformans spanning low (1:2–1:32) to high (1:256–1:1024) titers were included, along with samples spiked with Cryptococcus gattii. Four non-cryptococcal fungal or bacterial isolates were tested to assess cross-reactivity. Assays were compared for sensitivity, specificity, positive and negative percent agreement, titer correlation, reproducibility, ease of use, testing time, and biosafety.

Results: FungiXpert™ demonstrated 100% qualitative concordance with both IMMY and CALAS®. Endpoint titers closely aligned with IMMY, whereas CALAS® showed diminished sensitivity at higher titers. Both lateral flow assays detected titers exceeding 1:80,000 without evidence of antigen excess or prozone effects and reliably identified C. gattii. Cross-reactivity was observed only with Trichosporon asahii, consistent with known antigenic overlap, with no reactivity to Rothia, Candida species, or Capnocytophaga. FungiXpert™ exhibited superior analytical sensitivity and reproducibility, eliminated the need for boiling and centrifugation, and reduced assay time to approximately five minutes compared with approximately twenty minutes for CALAS®.

Discussion: FungiXpert™ addresses critical limitations of latex agglutination by providing rapid, highly sensitive, and biosafe CrAg detection in a closed, single-step format. Its robust performance, including reliable detection of emerging pathogens such as C. gattii, positions FungiXpert™ as a next-generation diagnostic tool capable of improving laboratory efficiency and accelerating clinical decision-making in cryptococcal meningitis.

Keywords: Fungal diagnostics, Biosafety, Cryptococcal meningitis, Operational efficiency, Quality assurance