Research Day Abstracts

2025

4th Year Honours Specialization Students

Presenter's Name: Ali, Anorin
Additional Authors: Jabbarizadeh B, Maleki S
Abstract Title: Integrating Fecal Microbiota Transplantation Data on an R Shiny App

Abstract:
Introduction: Resistance to immune checkpoint inhibitors (ICIs) presents a significant challenge in treating cancers. Recent clinical trials indicate that fecal microbiota transplantation (FMT) can modify gut microbiome composition to improve ICI efficacy. However, discrepancies in data processing and analysis across trials hinder a comprehensive understanding of FMT's role in reshaping the microbiome to overcome resistance and complicate cross-study comparisons. This project aims to standardize and integrate metagenomic sequencing data from multiple FMT trials into a unified, interactive R Shiny application to facilitate comprehensive data processing, analysis and visualization.

Methods: Raw sequencing data from three clinical trials were retrieved from NCBI's Sequence Read Archive (SRA). A metagenomics pipeline was employed to preprocess the data, including quality control, taxonomic profiling using MetaPhlAn, functional analysis with HUMAnN, and strain-level analysis using StrainPhlAn. Statistical analyses were conducted to assess alpha and beta diversity, microbial composition, and functional pathway alterations in response to FMT. Results were combined across studies to facilitate cross-data analyses. An R Shiny application was developed to provide an interactive platform for reactive data visualizations and statistical analyses.

Results: The R Shiny app provides real-time data exploration, customizable visualizations, and statistical analyses, enabling researchers to dynamically query microbiome shifts and their associations with treatment responses.

Discussion: This project establishes a standardized framework for processing, analyzing, and visualizing FMT clinical trial data. The platform enhances accessibility and reproducibility in microbiome research.

Presenter's Name: Chen, Steven
Additional Authors: Barboza R, Win PW, Espin-Garcia O, Castellani CA
Abstract Title: Predicting Mitochondrial DNA Copy Number using Heterogeneous Transfer Learning and Multiomic Data

Abstract:
Introduction: Mitochondria are essential energy-producing organelles with their own circular DNA (mtDNA). Recent literature has shown that variation in the number of copies of mtDNA (mtDNA-CN) is associated with various chronic diseases. Further, mtDNA-CN can affect disease onset through interactions with nuclear genomics, epigenomics, and metabolomics. However, mtDNA-CN estimates are seldom readily available in large cohort datasets that contain nuclear omic data. An emerging method for making predictions in missing data settings is heterogeneous transfer learning (HTL). HTL leverages large datasets with partial data to improve the predictive performance of a model. We aim to develop a novel HTL model to accurately predict mtDNA-CN using multiomic data.

Methods: The heterogeneous transfer learning R package HTL-GMM was used to create a predictive model for mtDNA-CN. The model leveraged data from the Canadian Longitudinal Study on Aging, including age and sex (N = 24,113), genomic (N = 24,113), metabolomic (N = 10,204), and epigenomic (N = 1,440) signatures. Individuals with matched measurements for all 3 omics signatures were used as the main dataset (N = 1,380), individuals with a partial subset of these measures were used as auxiliary datasets (N = 8,169 [metabolomic + genomic], N = 14,564 [genomic only]). The model was trained on complete data from the main study and leveraged partial information from the auxiliary datasets to improve the model's predictive performance. HTL-GMM performance was evaluated by comparing to other models such as glmnet and testing of the model will be done on independent cohort datasets, such as ARIC.

Results: Our results show that leveraging auxiliary datasets using HTL-GMM improves model performance. The HTL-GMM model performed better (Spearman's rho = 0.172, mean-squared error = 0.869) compared to a glmnet-only trained model on the main dataset (Spearman's rho = 0.044, mean-squared error = 0.914). To further refine the model, we are incorporating epigenetic age clock measures and single-nucleotide polymorphism data as predictors for epigenomic and nuclear genomic signals, respectively.

Discussion: These results show that leveraging partial omic information from larger datasets improves the predictive capability of mtDNA-CN, demonstrating the potential use of HTL methods to obtain accurate mtDNA-CN estimates. Such advances will help to further understand the underlying biological mechanisms behind complex disease onset.

MEDICAL BIOINFORMATICS

Presenter's Name: Ennema, Grace
Additional Authors: Wu E, Hosseini N, Derakhshan Nazari HM, Cameron L, Shooshtari P
Abstract Title: Integrative Genomic and Epigenomic Analyses to Identify Gene Regulatory Mechanisms in Asthma Across Diverse Ancestries

Abstract:
Background: Asthma affects 300 million people globally, causing significant health and economic burden. It arises from genetic and environmental factors, with ancestry influencing prevalence and severity. Immune cell-type-specific gene regulation plays a crucial role in asthma pathogenesis, yet how genetic variation influences these mechanisms remains poorly understood. Many asthma-associated genetic variants reside in non-coding regions, highlighting the need of determining their impact on gene regulation.

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

Methods: A computational pipeline developed in the Shooshtari Lab integrated multi-ancestry (European (EUR), East Asian (EAS), South Asian) genome-wide association study (GWAS) datasets from the Global Biobank Meta-Analysis Initiative (153,763 cases; 1,647,022 controls) with single-cell ATAC sequencing (scATAC-seq) data from 17 immune cell types to map asthma-associated SNPs to regulatory elements. We identified SNPs linked to altered transcription factor (TF) binding and gene regulatory regions in each immune cell type. Several methods were used to link regulatory elements to genes, including Cicero, Hi-C, and eQTL. Network analysis and gene set enrichment were used to explore involved biological pathways.

Results: Cross-ancestry analysis revealed shared TFs and genes influencing asthma risk. Meta-analysis identified 12 significant genes across all ancestries, including BACH2, IL2, IL6R, NDFIP1, TNFAIP8, and TNFRSF18. This suggests shared regulatory mechanisms across ancestries. Some associations were ancestry-specific, such as IL4R in EUR and STAT6 in EAS, highlighting population differences in asthma pathogenesis at some genomic loci. Pathway analysis in the largest populations (EUR and EAS) identified TNF-? signaling via NF-κB, a key mediator of inflammation, and IL2/STAT5 signaling, which promotes TH2 differentiation. These findings highlight key immune pathways as potential universal therapeutic targets for asthma.

Discussion: This novel multi-ancestry integration reveals how noncoding SNPs influence immune cell gene expression. Identifying shared and ancestry-specific regulatory elements enhances our understanding of the genetic architecture of asthma and immune interactions. These findings are expected to provide new targets for functional validation and lay the groundwork for ancestry-aware precision medicine in asthma treatment.

Presenter's Name: Phan, Tu Van
Additional Authors: Muñoz-Baena L, Poon AFY
Abstract Title: Detecting Overlapping Genes in Viral Genomes

Abstract:
Overlapping genes occur when the same nucleotide sequence encodes two or more proteins in different frames. Overlapping genes are common in viruses where they are hypothesized to reduce genomic length and play a role in the emergence of de novo genes. These genes often encode proteins that are involved in viral pathogenesis or transmission. Identifying overlapping genes can enhance genomic annotations and provide insights into viral pathogenicity. Conventional approaches for gene detection assume that genes do not overlap and are predominantly developed for prokaryotes and eukaryotes. In this study, we propose a new method to detect overlapping genes in viral genomes by analyzing the rates of non-synonymous and synonymous substitutions across all possible reading frames. A Python script was used to generate a hypothetical viral genome of 3000 nucleotides and 4 genes, 2 of which are overlapping. An empty phylogenetic tree with 100 tips was created, and HexSE, an evolution simulation model that accounts for overlapping genes in any reading frames, was used to generate evolved sequences for the hypothetical genome at the tree's tips. The aligned sequences were shifted across all six reading frames and selection pressures acting on each site were calculated using FUBAR from the HyPhy package. The selection pressure was analyzed using Principal Component Analysis and a sliding window analysis of average substitution rates. The findings will help us determine whether overlapping genes exhibit a distinct pattern. This pattern can then be used to detect overlapping genes in real-world genomic data, potentially guiding future studies.

MEDICAL BIOINFORMATICS

Presenter's Name: Randhawa, Bhavnit
Additional Authors: Randhawa B, Zhang H, Hallett M
Abstract Title: Deep Generative Approaches to Ablating Nuisance Parameters in Fungal Filamentation Imaging

Abstract:
Introduction: The morphological plasticity of Candida albicans plays a crucial role in its pathogenicity, as the ability to transition between yeast, pseudohyphal, and hyphal forms influences tissue invasion, immune evasion, and biofilm formation. Deep learning models, such as Variational Autoencoders (VAEs), have been employed to classify filamentation patterns and uncover correlations with clinically relevant metadata. However, biologically irrelevant imaging artifacts, such as intensity variations, confound the latent space, reducing the model's reliability in distinguishing meaningful morphological features. This study aims to disentangle nuisance technical factors from biologically relevant features in the latent space using a simplified dataset, with the intention of extrapolating these findings to a more complex dataset of C. albicans colony images. This will ultimately enable a more precise discovery of biologically significant morphological patterns that contribute to pathogenicity and clinical outcomes in Candida albicans infections.

Methods: A synthetic dataset was constructed using Python to control for variations in intensity, size, and morphology. A VAE was trained on this dataset with a custom loss function incorporating Structural Similarity Index Measure (SSIM) and Kullback-Leibler (KL) divergence. A discriminator penalizes the model for encoding intensity in the latent representation, while the original image's intensity is directly provided to the decoder. This approach ensures accurate image reconstruction while reducing the strain on the latent space to store intensity information.

Results: The expected results is that the VAE is able to successfully distinguish relevant features from nuisance variables resulting in more meaningful latent space representations. With the more complex dataset this will allow for clusters that are better aligned with clinically relevant metadata, such as strain origin and infection outcomes.

Discussion: This study presents a novel approach to improving the interpretability of deep learning models in biological imaging. By disentangling technical artifacts from morphological features, the optimized VAE enhances the reliability of automated classification in C. albicans research. This framework can be extended to other biological datasets where confounding technical noise limits the utility of computational models.

MEDICAL BIOINFORMATICS

Presenter's Name: Ray, Ankit
Additional Authors: Abeyesekera L, Lynn K, Black M, Grindrod N, Brackstone M, Lohmann A, Jerzak K, Dumeaux V
Abstract Title: Systemic B-cell Responses to Neoadjuvant Therapy in Breast Cancer Patients

Abstract:
Introduction: Pre-operative neoadjuvant therapy (NT) is routinely used for treating locally advanced breast cancer (BC), particularly HER2-positive BC defined by tumors with a high expression of the human epidermal growth factor receptor 2 (HER2). This population often receives Trastuzumab, an antibody that activates cell-mediated cytotoxicity and also inhibits the pro-oncogenic functions of the HER2 receptor. NT can lead to pathologic complete response, the complete resolution of the tumour, which has been associated with long-term survival in patients. However, the effectiveness of NT varies as up to 50% of patients have residual disease after NT, leading to an increased risk of cancer recurrence. This could be explained by variations in the systemic immune system, which has been implicated in prior literature in facilitating tumoural activity and treatment responses. Thus, we hypothesize biomarkers within immune cell populations can be used to predict responses to NT.

Methods: Blood samples were collected from eight BC patients at two time points, before and after NT. Patients were then classified as responders, partial responders and non-responders using tumour characteristics at the time of their surgery. B-cells were isolated and single-cell RNA and B-cell receptor sequencing was performed using the 10x v3 GEM-X Multiplex kit(~5K cells/sample; total = 80K cells). After data preprocessing and quality control, a variational autoencoder is trained to fit the expression data and identify B-cell subpopulations used to compare patient groups (responders vs non-responders) across time points.

Results: For each patient, single-cell RNA profile analysis of B-cells will provide a detailed characterization of B-cell subpopulations, cell differentiation trajectories, as well as clonality, diversity and affinity of B-cell immune repertoire. Those attributes will be analyzed at both time points (before and after NT) across treatment response groups (responders vs non-responders) providing a high-resolution look into the difference in the systemic B-cell profiles over time between responders and non-responders.

Discussion: The project will deliver knowledge that will transform our understanding of immunity associated with HER2+ BC and B-cell responses to NT. The goal is to find new ways to predict disease progression and treatment response, and identify new drug targets to enable the development of more targeted and effective combinations of therapies.

Presenter's Name: Southworth, Athena
Additional Authors: Randhawa G, Chereddy S, Hill KA
Abstract Title: Organism and technology-agnostic supervised machine learning achieves rapid and accurate classification of single-nucleotide polymorphism genotypes

Abstract:
Introduction: Modern genomic datasets contain massive amounts of data and increase in quantity daily. Classifying the identity of incoming samples with supervised machine learning (ML) methods allows researchers to identify organisms simultaneously with the high rate of data acquisition. Single nucleotide polymorphism (SNP) genotyping data that identifies major homozygous (AA), minor homozygous (BB), or heterozygous (AB) alleles for a large number of loci is a data format in need of rapid classification. I hypothesise that supervised ML applied to genotype data will produce accurate classification of organism strain and population.

Methods: A tool designed to apply Machine Learning with Digital Signal Processing (MLDSP) originally intended for use on nucleotide data but modified for use with genotyping data was used to conduct supervised classification tests. The first tests were conducted on 840 mice genotyped at 493290 SNP loci per mouse using the Mouse Diversity Genotyping Array to classify by taxonomy. Class labels included inbred, outbred, hybrid, recombinant, and wild mice. Intra-class diversity testing will be conducted with wild mice to distinguish between species including Mus musculus and Mus musculus castaneus. The second set of tests will be conducted on 299 thin-horn sheep (Ovis dalli) from the Yukon Wildlife Preserve sequenced at 9536 SNP loci per sheep with short-read SNP sequencing to classify by population. Class labels include the region from which the sheep were sequenced.

Results: Overall classification accuracy of mouse taxonomy was 95%. Mouse classification tests based only on heterozygosity, or homozygosity, produced accuracies between 80 and 90%. It is expected that classifying sheep based on geographic region will produce a smaller range of diversity between the samples, accentuating existing diversity for classification.

Discussion: MLDSP applied to genotyping data produces accurate classification regardless of the technology used to acquire the genotyping, and is applicable to any organism so long as the genotypes can be acquired. Accurate classification of mouse taxonomy validates the effectiveness of supervised ML techniques in classification. Classification by sheep geographic region can inform the number of populations and their genotypic variation. Future applications of this method to human genotypes can classify newly generated data for a case and assign it to a class based on its phenotype.

Presenter's Name: Wang, William
Additional Authors: Poon AFY
Abstract Title: Evaluating the Impact of Viral Recombination on Phylogenetic Methods of Estimating Basic Reproduction Number

Abstract:
Introduction: The basic reproduction number (R_o) is a measure of transmission, and it is defined as the expected number of secondary infections from an infected individual. R_o can be inferred through analyzing phylogenetic trees generated from sampled genetic data, as the internal nodes of the tree approximates transmission events. However, some viruses can undergo genetic recombination: the exchange of homologous genetic material. Current phylogenetic methods to estimate R_o assume no recombination. In the presence of recombination, a single tree cannot represent the evolutionary history of the virus. We hypothesize that recombination results in altered estimated values of R_o.

Methods: Using the REMASTER program's susceptible, infected, and recovered model for simulating an epidemic, we generated 5 replicates. For each replicate, we fixed their R_o to 1.90, and we sampled 100 infections of 9000 nucleotides in length across an average of 70 years. We stimulated recombination by modifying the true phylogenetic tree with up to 1000 breakpoints. Finally, we estimated R_o from the simulations using the Phylodynamics package in the BEAST2 program.

Results: R_o estimations for the true trees averaged to 1.97. All five replicates showed a diminishing increase in R_o proportional to the amount of recombinations. To address the non-linearity in the relationship between the number of breakpoints and R_o, a square root transformation was applied to the number of breakpoints prior to conducting a linear regression analysis. Regression results of all trials indicated that the number of breakpoints was significantly associated with R_o ($\beta = 0.025$, $p < 0.001$, $R2 = 0.51$).

Discussion: Our results indicate that it is necessary to account for recombination when using phylogenetic methods to estimate R_o. In public health, R_o has significance in determining the rate of spread of an epidemic, and overestimating R_o will result in an exaggeration of the potential scale of an outbreak. These actions may result in inappropriate or excessive public health interventions, diverting resources away from viruses that pose a more immediate and significant threat.

MEDICAL BIOINFORMATICS

Presenter's Name: Yang, Wenqi
Additional Authors: Andrews T, Ho J
Abstract Title: Single-Cell Multiomic Analysis of Leukemic Transformation in Myeloproliferative Neoplasms

Abstract:
Introduction: Myeloproliferative neoplasms (MPNs) are chronic blood cancers with a substantial risk of progression to acute myeloid leukemia (AML), leading to poor clinical outcomes. Previous studies using transcriptomic profiling of CD34+ blasts in patients with myelofibrosis, an MPN subtype, have identified altered transcriptional pathways during leukemic transformation. Because CD34+ blasts include both early and mature hematopoietic stem and progenitor cells, their heterogeneity makes it hard to pinpoint exactly which populations drive disease progression. Thus, this study employs a single-cell multiomic approach to overcome these limitations. We hypothesize that specific hematopoietic stem and progenitor cell populations undergo genetic and biological alterations that contribute to leukemic transformation in MPNs.

Methods: Sample cells were isolated from 12 MPN patients (6 transformed to AML and 6 untransformed) and used a single-cell multiomic approach to simultaneously capture gene expression and chromatin accessibility. Data integration and quality control were performed with Seurat, while the Milo framework was employed for differential abundance testing. The differential expression (DE) analysis on pseudo-bulked data was conducted using DESeq2, and FGSEA (Fast Gene Set Enrichment Analysis) was used to identify enriched biological pathways.

Results: Our analyses disclosed distinct cell subpopulations with significant shifts in abundance between transformed and untransformed patients. Differential expression analysis identified several key genes that are significantly up- or down-regulated in the transformed state. FGSEA further highlighted critical regulatory pathways and gene networks potentially driving the transformation process.

Discussion: These findings underscore the utility of single-cell approaches to resolve cellular heterogeneity and clarify the mechanisms of leukemic transformation in MPNs. The integration of differential expression and pathway analyses provides a comprehensive understanding that may guide the development of improved prognostic biomarkers and targeted therapeutic strategies.

Presenter's Name: Airhart, Emily
Additional Authors: Kalisa E
Abstract Title: Do car-free days reduce air pollution? Evidence from Rwanda

Abstract:
Introduction: Air pollution poses significant human, animal, and environmental health risks, particularly in urban areas where motor vehicle emissions are a major contributor. Car-free days are increasingly implemented as an intervention to reduce traffic-related air pollution (TRAP). In Kigali, Rwanda, biweekly car-free Sundays were introduced in 2018 to restrict vehicular movement and promote public health. This study examines the effectiveness of car-free days in reducing fine particulate matter (PM2.5) concentrations by analyzing ambient air quality data in Kigali.

Methods: Hourly PM2.5 concentration data were collected from two air quality monitoring stations in Kigali from 2022 to 2024. An independent t-test was used to compare average PM2.5 concentrations during the car-free hours (7:00 AM – 11:00 AM) between car-free Sundays and normal Sundays on which traffic was not restricted. An independent t-test also compared PM2.5 levels during car-free hours and the hours following traffic restrictions (11:00 AM – 9:00 PM) on car-free Sundays. Finally, an independent t-test compared daytime PM2.5 levels (6:00 AM – 6:00 PM) to nighttime levels (before 6:00 AM and after 6:00 PM) on car-free Sundays.

Results: Mean PM2.5 concentrations were significantly lower during car-free hours on car-free Sundays compared to the same period on normal Sundays. However, mean PM2.5 levels increased after the traffic restrictions ended at 11:00 AM, exceeding car-free hour concentrations. Additionally, mean PM2.5 levels were significantly lower during the daytime hours compared to nighttime hours on car-free Sundays.

Discussion: The observed PM2.5 concentrations during car-free hours confirm the short-term effectiveness of traffic restrictions in lowering air pollution. However, the subsequent rise in PM2.5 levels after restrictions are lifted suggests that vehicular emissions are not the sole contributors to air pollution in Kigali. Additional factors such as industrial and residential emissions and meteorological conditions can also play a role in urban air pollution. Further studies incorporating additional air quality monitoring locations and meteorological variables are needed to assess long-term trends and optimize urban air quality management strategies. This study highlights the importance of a One Health approach in urban air quality policies and identifies key stakeholders for sustainable environmental health initiatives.

Presenter's Name: Anphalagan, Swathi
Additional Authors: Sibbald SL
Abstract Title: Integrating Indigenous Perspectives in Health Systems Transformation through a One Health lens

Abstract:
Introduction: Indigenous peoples in Canada face health disparities, challenges in healthcare access, and poorer outcomes compared to non-Indigenous populations. In response, the Government of Canada and the Truth and Reconciliation Commission issued Calls to Action in 2015 to support Indigenous health through healthcare reform. While Indigenous-led partnerships have been found to improve health outcomes, gaps remain in understanding how to include Indigenous voices in Canadian healthcare contexts. The main goal of this research project was to identify effective interventions for including Indigenous peoples in health system reform. Specifically, it aimed to explore key Indigenous health perspectives essential for reform and evaluate existing inclusion efforts.

Methods: A rapid review was conducted using PubMed to screen primary and secondary studies published between January 2019 and November 2024. Eligible studies were screened based on inclusion criteria and critically appraised. After a full-text review, 30 articles were selected for analysis. The selected studies provided insights into Indigenous health perspectives, existing inclusion efforts, and barriers within the healthcare system. Given the deep connection between Indigenous health outcomes, the environment, and animals, this project used a One Health approach to assess key stakeholders.

Results: Five themes were identified in the literature around Indigenous inclusion in health system reform: 1) decolonization of health systems, 2) holistic models for care, 3) health system barriers, 4) Indigenous-led health system initiatives, and 5) building capacity in the health system.

Discussion: The findings underscored the importance of Indigenous involvement and the integration of traditional healing practices, such as healing circles, to promote culturally sensitive care. Key barriers, including limited culturally conscious dialogue and restricted access to appropriate services, were identified. To address these challenges, the literature recommends integrating holistic care models, implementing culturally sensitive practices, and strengthening capacity within Indigenous communities. These insights can help policymakers and healthcare leaders implement reforms that respect and incorporate Indigenous knowledge.

Presenter's Name: Anphalagan, Shurabi
Additional Authors: Malik S, Sibbald SL
Abstract Title: Exploring the Psychosocial Factors That Impact Pain Management in Advanced Cancer Patients: Perspectives from Care Providers

Abstract:
Introduction: Many patients with advanced cancer experience severe and untreated pain. There has been evidence of barriers to effective pain management that occur at patient, provider and health system levels. However, there is a lack of studies that provide a detailed understanding of these barriers in a Canadian context. This study aimed to develop a deeper understanding of the psychosocial factors (beliefs, trauma, social support, coping skills, family relationships) and barriers affecting pain management in advanced cancer patients. The specific objectives were to identify key psychosocial factors, challenges, and perceptions of intervention effectiveness across various disciplines, as well as to examine access barriers to pain management for both providers and advanced cancer patients.

Methods: This study employed a constructivist grounded theory approach, which recognizes that individuals' experiences are multifaceted. Semi-structured interviews were conducted with providers in Southwestern Ontario, which were coded for thematic analysis. Once themes were constructed, a stakeholder analysis was conducted to examine pain management as a one health issue.

Results: Eleven participants participated in this study, including oncologists (n=3); nurses (n=2); general practitioners (GP) (n=4); other specialist physicians (n=2). When exploring experiences with pain management, four main themes were identified: complexities in pain management, psychosocial dimensions of pain management, provider related challenges, and health related challenges.

Discussion: These themes highlight the multifaceted challenges in managing cancer pain, encompassing patient, provider, and systemic factors. This study contributes to an understanding of cancer pain management within the Canadian context of Southwestern Ontario, addressing a gap in literature by focusing on the experiences of healthcare providers, who play a vital role in pain management. This can help inform context-specific and targeted pain management interventions for advanced cancer patients in Southwestern Ontario, ultimately enhancing patient outcomes and holistic care approaches.

ONE HEALTH

Presenter's Name: Bursey, Victoria
Additional Authors: Kalisa, E
Abstract Title: Impacts of Electric School Bus Adoption on Schoolchildren's Pollutant Exposure: A Scoping Review

Abstract:
Introduction: In the United States (US) and Canada, hundreds of thousands of diesel school buses are used to transport millions of children. It is known that children riding diesel school buses are exposed to diesel pollutants, in which some components, such as fine particulate matter (PM2.5: particles with a diameter of less than 2.5 micrometers) that can penetrate deep into the lungs, have been shown to impact cognitive development and lung function in children and other sensitive populations. School bus electrification efforts are in early stages in the US and Canada, with various funding programs and initiatives targeting the adoption of electric buses. As these new buses hit the roads and begin to transport children, it is imperative that their effectiveness at reducing air pollution exposure and subsequent health outcomes be evaluated.

Methods: A scoping review was conducted to determine the air pollution, climate, and health benefits of converting diesel school buses to electric, as well as analyze the current state of the literature on this topic. Searches were conducted in online academic databases using keywords related to school bus electrification, and its impact on air pollution, climate, and health. Sources of evidence were identified following PRISMA guidelines. The results were presented in a figure of a flow chart for the included/excluded studies and a table of extracted information. A One Health approach was used to identify key stakeholders involved in the school bus electrification movement in North America, and to highlight areas for future collaboration.

Results: Thirteen sources of evidence were included and were primarily case studies or reports from early adopters of electric school buses, with twelve of them conducted in the US. Four main themes were identified from the selected case studies' findings, including economic savings, reductions in some types of greenhouse gases and traffic-related air pollutants, potential health benefits, and mechanical and logistical challenges.

Discussion: Significant knowledge gaps remain regarding children's health outcomes and exposure from in-cabin air pollutant levels after electrification, especially in colder climates requiring diesel heating systems. Case studies in countries other than the US are lacking and are crucial to inform policy and guide future funding efforts.

Presenter's Name: Gupta, Diya
Additional Authors: Fearon D
Abstract Title: Exploring the Differences between Western Medical Models and Indigenous Approaches in Care for Bipolar Disorder among Indigenous Canadians

Abstract:
Bipolar disorder is a chronic mental health condition characterized by mood fluctuations, including manic, hypomanic, and depressive episodes. While the disorder has been extensively studied within Western medical frameworks, the experiences of Indigenous Canadian populations remain largely unexplored. Indigenous communities face a disproportionate burden of mental health conditions due to historical trauma, systemic barriers, and cultural disconnect from Western medical practices. Hence, this research aims to explore the differences between Western medical models of care and Indigenous approaches to managing bipolar disorder, particularly within Indigenous Canadian communities. The primary objective of this project is to conduct a comprehensive scoping review of existing literature on both Indigenous and Western care practices. Specific sub-objectives include identifying contemporary literature, research gaps, and best practices for integrating Indigenous healing traditions with Western psychiatry in the future. To achieve this, a comprehensive search of peer-reviewed studies using the MEDLINE (Ovid) database was conducted. This involved using the systematic PRISMA framework, which includes a process of identification, screening, and applying inclusion criteria for retrieved studies. Currently, results are being compiled to identify emerging themes, trends, and critical gaps in the literature. Through this, we expect to identify key differences between Western and Indigenous models of care, particularly with Western models emphasizing evidence-based interventions and Indigenous approaches' integrating more holistic care practices. We also expect that the research will uncover disparities in cultural sensitivity and trust in healthcare systems, particularly due to the impact of historical trauma on healthcare relationships. These findings will contribute to a deeper understanding of how both Indigenous and Western healthcare systems manage bipolar disorder, with implications for improving healthcare accessibility. By applying the One Health framework—which recognizes the interconnectedness of human, animal, and environmental factors.—this research project seeks to explore bipolar disorder in a holistic context, bridging gaps to improve care outcomes for Indigenous Canadians.

ONE HEALTH

Presenter's Name: Lee, Irene
Additional Authors: Olea Popelka, FJ
Abstract Title: Examining the Use of Plant-Based and Traditional Indigenous Medicines for Intervention in Human and Bovine Tuberculosis

Abstract:
Introduction: Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis, while bovine TB (bTB), caused by M. bovis, affects livestock and can be transmitted to humans as zoonotic TB (zTB). Transmission occurs through unpasteurized dairy or close contact with infected animals, posing public health risks. Standard TB treatment includes isoniazid, rifampicin, pyrazinamide, and ethambutol, but rising multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) complicate treatment. The World Organisation for Animal Health (WOAH) has published TB control guidelines, acknowledging gaps in research on alternative treatments, particularly Indigenous and traditional medicinal methodologies.

Methods: A rapid review, guided by Cochrane methodologies, analyzed peer-reviewed and grey literature on Indigenous medicinal plants for TB treatment. The study aimed to (1) identify commonly used plants and (2) evaluate their antibacterial efficacy against M. tuberculosis and M. bovis. A One Health framework assessed TB transmission across human, animal, and environmental health sectors. Stakeholder analysis identified key actors across health, government, academia, private industry, and the public with vested interests in integrating traditional medicine into TB treatment.

Results: The review identified 60 medicinal plants used across Indigenous communities, with variations in plant selection and preparation. Among these, Lantana camara, Allium sativa, and Artemisia afra were frequently cited for antimicrobial properties against M. tuberculosis and M. bovis, including MDR-TB strains, with minimum inhibitory concentrations (MICs) comparable to first-line TB drugs. Variability in extraction methods and plant part usage influenced efficacy. Stakeholder analysis highlighted limited collaboration between Indigenous knowledge holders and biomedical researchers, emphasizing the need for stronger cross-sector partnerships.

Discussion: Medicinal plants show promise for TB drug development as antibiotic resistance rises. However, most studies assessed antibacterial activity in vitro, rather than in clinical settings, limiting their application. Limited accessibility of Indigenous medicinal knowledge further challenges its integration into biomedical frameworks. Strengthening collaboration between Indigenous and biomedical researchers, alongside clinical validation, is essential for advancing traditional medicinal approaches in TB management.

Presenter's Name: Saini, Anuveer
Additional Authors: Jessani, A
Abstract Title: Assessing and Mapping the Global Prevalence of Oral HPV in Key Populations

Abstract:
Introduction: Oral human papillomavirus (HPV), a sexually transmitted infection, disproportionately affects vulnerable key populations such as men who have sex with men (MSMs), transgender individuals, sex workers, prisoners, and people who inject drugs. Current research often generalizes HPV prevalence, failing to focus on oral HPV in these populations, creating a critical knowledge gap. This study addresses this gap by hypothesizing that oral HPV prevalence varies significantly among key populations, and it is necessary to address this. The primary goal of this project is to assess the global prevalence and burden of oral HPV in key populations. Specific objectives include identifying relevant studies on oral HPV in these groups and exploring global variations in prevalence linked to social influences.

Methods: A scoping review will be conducted using the PRISMA-Scr framework and Joanna Briggs Institute Manual. Databases such as EMBASE, Scopus, and MEDLINE will be searched using a structured strategy to capture all relevant papers. Papers will be screened based on defined inclusion and exclusion criteria, with collaborative evaluations facilitated by Covidence software.

Results: Currently, the results are being identified as we go through the screening process of this scoping review and all results will be compiled for presentation. However, this study is expected to compile a comprehensive summary of oral HPV prevalence in key populations in different countries, thus providing a global map. The findings will also illuminate the unique health challenges faced by these populations and offer insights into the social factors influencing disparities in healthcare access.

Discussion: By providing a standardized perspective on oral HPV prevalence, this research will inform targeted public health interventions, guide future research, and contribute to global health equity. The findings will also align with United Nations Sustainable Development Goals (SDGs) by promoting improved health outcomes and reducing inequalities for marginalized groups.

ONE HEALTH

Presenter's Name: Zajdlik, Madeleine
Additional Authors: Olea-Popelka, FJ
Abstract Title: Knowledge Dissemination: A Key Tool for Alternative Bovine Tuberculosis Management Strategy Education

Abstract:
Introduction: Caused by the bacterium Mycobacterium bovis, a member of the Mycobacterium tuberculosis complex, bovine tuberculosis (bTB) is primarily a lung-based disease that can spread between both cattle and humans (Anaelom et al., 2010). With approximately 3.27% (2.11-5.05%) of cattle and 18.09% (11.20-27.90%) herds infected globally (Bezerra et al., 2024), bTB is a pressing burden for both cattle and the humans that live amongst and rely upon them. Compounding this burden, the test and slaughter approach to bTB control–involving the identification and subsequent culling of infected cattle–is the present prevalent management strategy for the disease (World Organization for Animal Health, 2024). However, this practice has negative implications for the physical and socioeconomic health of populations reliant upon cattle and that of the animals themselves, across environments, classifying bTB as a One Health issue. As a result, the World Organization for Animal Health (WOAH) released a set of guidelines in October 2024 outlining alternative, comprehensively sustainable management strategies that can be implemented–and thus reduce bTB burdens–on a global scale (WOAH, 2024). Preceding such implementation, interventions increasing community awareness and thus adoption of such strategies on an international scale are required. Therefore, this thesis' main goal is to work towards dissemination and sharing the 2024 WOAH guidelines with key different global stakeholders.

Methods: To accomplish this, a knowledge dissemination (KD) project was conducted, focused on increasing awareness of and thus adoption of feasible and comprehensive bTB management strategies. More specifically, this project sought to establish relevant KD principles for effective global intervention development and implementation, a key initial step in the KD process, through primary stakeholder interviews.

Results: This project identified stakeholder-specific guidelines for effective and integral KD interventions in 6 global and regional stakeholders across relevant sectors of society.

Conclusion: Ultimately, this thesis' importance rests within its broader implications for both zoonotic tuberculosis eradication, and the development of an internationally relevant KD framework for global zoonoses, presented across stakeholder categories for ultimate global KD replication.

Presenter's Name: Avis, Peyton
Additional Authors: Ballesteros BR, Quinones-Mateu M
Abstract Title: A Bacteriophage-based Platform to Study the Evolution of Eukaryotic Viruses

Abstract:
Introduction: With over 776 million cases and over 7 million deaths to date, the COVID-19 pandemic demonstrated the devastating global impacts that a zoonotic disease can have. As human actions such as travel, hunting, and urbanization bring us closer to animals, it increases the risk of further zoonotic transmission. Thus, it is essential to begin preparing for the next viral outbreak before it arises. Here, we are developing an innovative T4 bacteriophage system to study the evolution of eukaryotic viruses. We plan to first use this novel platform to safely increase the diversity of coronaviruses (CoV) and generate novel recombinant spike proteins to identify ones with potential human tropism and assess them as potential vaccine candidates.

Methods: We are using a series of complex methodologies, including CRISPR-Cas9 genome editing, to create the virus recombination system in bacteriophages. We have established a system to clone CoV spike genes, starting with SARS-CoV-2 Omicron BA.5 and SARS-CoV, into the T4 bacteriophage Hoc gene. Following successful validation, we will introduce spike proteins from 15 different a- or b-CoVs known to infect humans into the system to direct evolution by safely selecting bacteriophages expressing recombinant (chimeric) CoV spike proteins.

Results: We have designed and constructed all the tools (i.e., plasmids, bacteriophages), including cloning cassettes flanked by a combination of four different reporter genes (Myc, His8, HA, and FLAG tags) to facilitate the identification and selection of chimeric CoV spike proteins. We will describe preliminary results showcasing the early steps of the platform, including the feasibility to safely direct CoV evolution in vitro.

Discussion: To our knowledge, this is the first study designed to use T4 bacteriophages to safely pre-empt coronavirus evolution (Note: invention disclosure in process). The novel platform has the potential to generate a large library of novel recombinant CoV spike proteins, critical to fully understanding the CoV features that could lead to human tropism, eventually driving zoonosis events.

ONE HEALTH

Presenter's Name: Battick, Briana
Additional Authors: Khan ZA
Abstract Title: Identification of adipocyte markers in mouse bone marrow

Abstract:
Introduction: Bone marrow adipose tissue is a unique fat depot located in the bone marrow cavity of various bones including the femur and tibia. Increased accumulation of bone marrow adipose is observed in ageing and in several clinical conditions such as diabetes, obesity, anorexia nervosa, and chemotherapy treatment. Previous studies suggest that accumulation of bone marrow adipocytes may suppress osteogenesis and negatively alter the bone marrow environment. A key knowledge gap that our study aims to fill is the identification of specific markers which could be used to mark adipocytes and advance our understanding of these cells in disease conditions.

Methods: Based on transcriptomic profile of bone marrow-derived adipocytes, we identified Pparg, Cebpb, and Foxo1 as potential markers of bone marrow adipocytes. We have optimized immunohistochemical staining protocols for PPARG, CEBPB and FOXO1 using decalcified mouse bone tibia and femur specimens. We will stain tibia and femur of C57BL/6 mice at different ages for PPARG, CEBPB, and FOXO1 and analyze the expression using QuPath.

Results: We expect to observe increased expression of PPARG, CEBPB and FOXO1 in bone tissues of older mice compared to younger mice. We also expect these markers to mark pre-adipocytes that are usually indistinguishable using routine hematoxylin and eosin staining.

Discussion: This study will contribute to our understanding of bone marrow adipocytes by identifying specific markers of pre-adipocytes and fully differentiated and lipid-laden adipocytes. Identifying these markers will facilitate further research on the roles of these cells in the bone marrow stem cell niche and their potential involvement in various diseases.

Presenter's Name: Berti, James
Additional Authors: Steriopoulos J, Zhang ZX
Abstract Title: Investigating the Role of CaMK1, CaMK2 and CaMK4 in RIPK3 Activation in TLR3-Initiated Cell Death in Mouse Microvascular Endothelial Cells

Abstract:
Introduction: Acute and chronic allograft rejection continues to be a significant challenge in heart transplantation. A critical mechanism contributing to heart allograft rejection is pro-inflammatory cell death in endothelial cells, particularly by necroptosis. Previous studies from our lab have demonstrated toll-like receptor 3 (TLR3) as a receptor capable of initiating necroptosis. Additionally, our lab has identified the potential role of the Ca2+/calmodulin-dependent protein kinase family (CaMK) in receptor-interacting protein kinase 3 (RIPK3) activation in endothelial cell death. The role of CaMKs in RIPK3 activation following TLR3 stimulation has yet to be characterized in mouse microvascular endothelial cells (MVECs). We hypothesize if CaMK1, CaMK2, and CaMK4 expression are abrogated, TLR3 activation and signalling will not lead to activation of RIPK3 via its phosphorylation, nor subsequent activation of other necroptotic molecules, under pro-necroptotic conditions in MVECs.

Methods: MVECs will be cultured and used in cell death assays under pro-necroptotic conditions following TLR3 stimulation. Following verification of these conditions, CaMK 1, CaMK 2 and CaMK 4 will be silenced, and cell death will be induced in the same manner. Alterations in cell death patterns and key necroptotic effector molecules will be quantified and compared against controls.

Results: These results will provide insight into the mechanism of TLR3-initiated necroptosis and the role of the CaMKs in endothelial cell necroptotic signalling. If the CaMKs have a role in activating RIPK3, we expect to see attenuated cell death in CaMK1/2/4 silenced samples. Further, we expect to see a decrease in phosphorylated RIPK3 and activation of other effector molecules compared to controls.

Discussion: Pro-inflammatory cell death of MVECs in heart allografts increases the risk of organ rejection in both the short and long term. Elucidating the role of the CaMKs in MVEC necroptotic cell death will reveal more about the mechanism of necroptosis in heart allografts. With a greater understanding of the mechanism, novel targets may be developed to attenuate rejection. Beyond transplantation, an increased understanding of the molecular players in necroptosis may be applied to other conditions such as cancers, neurodegenerative diseases, and autoimmune diseases.

PATHOLOGY

Presenter's Name: Bi, Lisa
Additional Authors: Cecchini M
Abstract Title: Detecting Errors in Simulated Pathology Reports Using Large Language Models

Abstract:
Introduction: Errors in pathology reports, including misinterpretations, transcription mistakes, and discordant findings, can significantly impact patient care, particularly in cancer diagnostics. Pathologists often struggle to detect subtle errors due to cognitive biases, workload, and case complexity. Advances in large language models (LLMs), especially reasoning-based models, offer potential solutions by assisting in error identification. This study evaluates the accuracy of various LLMs in detecting errors in simulated pathology reports, hypothesizing that reasoning-based models will be the most effective.

Methods: A total of 100 synthetic lung cancer pathology reports were generated using GPT-4o, with 13 intentional errors introduced. These reports were analyzed using multiple LLMs (GPT-4o, GPT-o1, DeepSeek, DeepSeek R1, LLaMA 405B, Gemini 1.5, and Gemini 2.0) alongside human experts. Sensitivity, specificity, and processing speed were measured.

Results: Among all models, GPT-o1, a reasoning-based LLM, demonstrated the highest accuracy, with 78.57% sensitivity and 100% specificity, outperforming human experts and other LLMs. Its sensitivity was 16% higher than DeepSeek R1 (the second-best model) and 200% higher than human experts, who exhibited high specificity but very low sensitivity. GPT-o1's sensitivity was statistically significantly higher than that of DeepSeek, Gemini 2.0, Gemini 1.5, and human experts, while its specificity was statistically significantly higher than that of Gemini 2.0, DeepSeek, and DeepSeek R1. Certain models, particularly DeepSeek, over-detected errors, reducing specificity. However, DeepSeek excelled at typographical error detection, while GPT-o1 and DeepSeek R1 were best at identifying staging discrepancies. LLaMA 405B had the fastest processing speed, followed by Gemini 1.5 and GPT-4o. While GPT-o1 was the slowest among LLMs, it was still 22% faster than human experts.

Discussion: These findings suggest that LLMs, particularly reasoning-based models, can enhance pathology error detection, improving sensitivity while maintaining specificity. While human experts remain more precise in avoiding false positives, AI-human collaboration may balance efficiency and accuracy. Future research should explore LLM integration into clinical workflows to enhance diagnostic reliability while reducing over-detection.

Presenter's Name: Chang, Rachel
Additional Authors: Pejhan S, Zhang Q
Abstract Title: The Disease Burden of Frontotemporal Lobar Degeneration: A Macro- and Microscopy Correlation Study

Abstract:
Introduction: Frontotemporal lobar degeneration (FTLD) is a neurodegenerative disorder primarily affecting behavior and language, often presenting with progressive atrophy in the frontal and temporal lobes. However, the relationship between clinical symptoms, neuroimaging findings, and underlying pathological changes remains poorly understood. While the presence of pTDP-43 and pTau protein deposits is well-documented in FTLD, the direct correlation between these histopathological hallmarks and structural brain changes, particularly in regions like the hippocampus, has not been fully explored. This study seeks to investigate whether hippocampal atrophy, measured from post-mortem brain slices, is associated with the distribution and presence of pTDP-43 and pTau pathology in FTLD cases.

Methods: 33 cases of clinically and pathologically confirmed FTLD cases were identified from the Dale E. Creighton Brain & BioBank. Hippocampal volume will be measured from gross brain slices using ImageJ. Histopathological analysis for pTDP-43 and pTau will be performed on tissue sections using immunohistochemistry and image analysis in QuPath. Statistical correlation tests will be applied to evaluate the relationships between gross atrophic changes, microscopic disease burden and clinical patterns.

Results: The study will determine whether significant hippocampal atrophy correlates with the presence of pTDP-43 and pTau deposits, indicating whether these protein accumulations contribute to neurodegeneration in FTLD. It will also explore the role of additional factors, such as neuroinflammation, and identify clinical patterns associated with these pathological changes.

Conclusion: These findings will enhance our understanding of FTLD pathophysiology and may contribute to refining diagnostic criteria and identifying new approaches for diagnosing, treating, and potentially preventing this devastating disease.

PATHOLOGY

Presenter's Name: Chen, Katherine
Additional Authors: Wang C, Ni R, Peng T
Abstract Title: Investigating Gene Therapy with the First 90 Amino Acids of Cytomegalovirus M45 for Doxorubicin-induced Mouse Cardiac Endothelial Cell Necroptosis

Abstract:
Introduction: Doxorubicin (DOX) is an effective chemotherapeutic drug but its use is limited by dose-dependent cardiotoxicity, leading to endothelial dysfunction and congestive heart failure. Necroptosis, a regulated form of necrosis mediated by RIPK1/RIPIK3/MLKL, is a crucial driver of DOX-induced cardiac cell death. Recent studies have shown that the first 90 amino acids (or N90) of the M45 protein from murine cytomegalovirus (MCMV) can inhibit necroptosis through interactions with RIPK1 and RIPK3's RHIM domain. Based on this, we hypothesize that the administration of N90 of M45 from MCMV can reduce doxorubicin-induced cardiac endothelial cell death by necroptosis and improve cell survival.

Methods: Mouse cardiac endothelial cells (MCECs) will be cultured and treated with DOX to induce necroptosis. Cell damage and viability will be quantified using lactate dehydrogenase (LDH) and CCK-8 assays respectively. Necroptosis will be confirmed through a western blot for phosphorylated RIPK3. MCECs will then be transfected with a plasmid expressing N90 and the effects will be evaluated through LDH and CCK-8 assay again at endpoint. A western blot and fluorescence microscopy for GFP signals will be performed to evaluate transfection efficiency.

Results: We expect DOX treatment to induce significant cell damage and death through necroptosis. We also expect that N90 expression will inhibit necroptosis, reduce cell damage and improve cell viability in DOX treated MCECs.

Discussion: Our findings will provide critical insight into the role of necroptosis in DOX-induced cardiotoxicity and highlight the potential of N90 as gene therapy to mitigate endothelial cell damage. This study lays the foundation for novel cardioprotective therapies to improve the safety and tolerability of DOX usage in the clinic.

Presenter's Name: Imlach, Camri
Additional Authors: Vytlingam K, Min W
Abstract Title: Piezo1 regulates DC-mediated immunomodulation during alloimmune rejection

Abstract:
Introduction: Heart transplantation is a life-saving procedure for patients facing end-stage heart failure. Recipients require a lifelong regimen of generalized immunosuppressive drugs to decrease rates of alloimmune rejection, leaving them vulnerable to infections and cancer. To lessen these risks, emerging therapies seek donor antigen-specific tolerance, such as by inducing tolerogenic dendritic cells (Tol-DCs). Recent evidence suggests an endogenous ion channel, Piezo1, modulates the immune response in DCs, thereby shaping T cell responses. This study aims to investigate if modulating Piezo1 function could induce Tol-DCs and to further explore the role of this channel on DC phenotype and immune function. We hypothesize that the Piezo1 channel is upregulated in immune reactive DCs and downregulated in Tol-DCs. Thus, Piezo1-specific activation in DCs will increase the differentiation of Type 1 Helper (Th1) T cells and suppress the generation of regulatory T cells (T regs) in an in vitro model of alloimmune rejection.

Methods: To test these hypotheses, we analyzed the mRNA expression of Piezo1 in LPS-stimulated immune reactive and vitamin D3-induced tolerogenic murine bone marrow-derived dendritic cells (BMDCs) via qRT-PCR. Then, we treated BMDCs with a Piezo1-specific agonist, Yoda1, before characterizing their immune phenotype (i.e., expression of MHC II and co-stimulatory markers) using flow cytometry. Finally, we will perform a mixed lymphocyte reaction (MLR), in which Yoda1-treated BMDCs are co-cultured alongside allogeneic T cells, to assess T cell proliferation and generation of cytokines and T regs.

Results: We found increased Piezo1 mRNA expression in LPS-stimulated immune reactive DCs and decreased Piezo1 expression in Tol-DCs when compared with naïve DCs. Our data from DC phenotyping showed that Piezo1-specific activation may push DCs to develop a more immune reactive phenotype. In the MLR, we expect to see increased T cell proliferation and Th1-associated cytokines, as well as reduced Treg generation in the reaction containing Yoda1-treated DCs.

Discussion: Our results will provide further insight into the role of the Piezo1 channel in DC immune function and explore an alternative method of inducing Tol-DCs for cell-based therapies. By probing candidates for more targeted, donor antigen-specific immunosuppressants, this project may contribute to increased quality of life and survival for patients receiving heart and other organ transplants.

PATHOLOGY

Presenter's Name: Joyce, Ryan
Additional Authors: Joyce R, Sidahmed A
Abstract Title: Quantitative analysis of Eplet Load in Liver Transplant Success: Evaluating the Significance of Mismatches across different Human Leukocyte Antigen Loci

Abstract:
Liver transplantation is a life-saving intervention for patients with end-stage liver disease, however, immune-mediated graft rejection remains a major barrier to long-term success. Current methods for assessing compatibility between recipients and donors rely on broad human leukocyte antigen (HLA) matching. However, this approach fails to capture the specific immunogenic differences between patients at the molecular level, known as eplet mismatches. The clinical significance of eplet mismatches across different HLA loci in liver transplantation remains poorly understood currently, representing a critical knowledge gap to fill. This study aims to evaluate the associations between eplet mismatch loads and transplant outcomes, identify loci and specific mismatches with the strongest impact on poorer outcomes, and determine the ability of transplant success to be predicted by HLA typing data. Our hypothesis is that higher eplet mismatch loads, particularly at specific HLA loci, correlate with increased graft rejection and poorer long-term outcomes. To test this hypothesis, we will analyze retrospective data from liver transplant recipients and their donors. Eplet mismatches will be quantified using the HLA Matchmaker software, and their association with key outcomes will be assessed. Statistical and machine learning approaches may also be used to rank the significance of mismatches, identify the most relevant eplets affecting outcomes, and develop predictive models for transplant success.

We anticipate that eplet mismatch loads will show a significant correlation with adverse transplant outcomes and that specific HLA loci, such as HLA-DR and HLA-DQ, will exhibit the strongest associations. Furthermore, we expect that the models will demonstrate high accuracy in forecasting transplant success and provide a valuable tool for clinical decision-making. The findings from this study will advance our understanding of the role of eplet mismatches in liver transplantation and highlight their potential as biomarkers for graft rejection risk. This study will contribute to the development of precision medicine approaches in transplantation, enhance transplant outcomes, and optimize long-term graft survival.

Presenter's Name: Klaassen, Madeline
Additional Authors: Cecchini M, Darling M
Abstract Title: Chronic Hyperplastic Candidiasis as a Potentially Cancerous Lesion

Abstract:
Introduction: Chronic Hyperplastic Candidiasis (CHC) is a potentially cancerous oral lesion primarily caused by the fungal pathogen Candida albicans. Although withdrawn from the classification in 2022, there is still debate as to whether CHC should be considered an Oral Potentially Malignant Disorder (OPMD), a group of lesions with an elevated risk of transforming into Oral Squamous Cell Carcinoma (OSCC). OSCC is the 6th most prevalent malignancy worldwide; however, there is currently no single or set of biomarkers that can reliably predict malignant transformation rates of OPMDs to OSCC. One potential biomarker is the S100A7 protein, which is overexpressed in various cancers and plays key roles in tumour growth, angiogenesis, and metastasis. S100A7 may serve as a valuable diagnostic and therapeutic target for OPMDs and OSCC, allowing for early detection of a malignant transformation risk. We hypothesize that S100A7 is increased in the epithelium of CHC which transforms into cancer.

Methods: To test this hypothesis, we determined S100A7 expression levels in CHC which had transformed to OSCC, non-transforming CHC, and normal tissue controls (NTC). This was done using a positive cell detection in QuPath and measuring the optical density sum to obtain H-Score values. Results were compared with an S100A7 immunohistochemistry-based algorithmic score in the form of the Straticyte™ test.

Results: Our results show that the expression levels of S100A7 protein in the epithelium of lesions that have transformed to cancer are not significantly increased over non-transforming CHC. However, S100A7 levels are significantly elevated in both non-transforming and transforming CHC compared to NTC. In the Straticyte™ test, the probability of transformation is significantly increased in CHC lesions that transformed to cancer compared to non-transforming CHC.

Discussion: These findings suggest that while S100A7 expression is not significantly higher in transforming compared to non-transforming CHC, its elevated levels in both CHC types, relative to NTC, indicate its potential as a biomarker for CHC lesions. Further investigation is warranted into S100A7's utility as a diagnostic or prognostic biomarker for the progression of OPMDs to OSCC. Discrepancies between the Straticyte™ test and QuPath highlight potential limitations in QuPath's quantification of S100A7, with the Straticyte™ test possibly offering a more comprehensive prediction of OSCC progression.

PATHOLOGY

Presenter's Name: Li, Stella
Additional Authors: Lave M, Renaud S
Abstract Title: The Effect of Lipopolysaccharide Exposure to Pregnant Rats on Inflammatory Cytokines and Immune Cell Distribution in the Placenta and Fetal Brain

Abstract:
Introduction: Successful pregnancy requires proper placental development for nutrient and oxygen supply. Inflammation during pregnancy is associated with poor placentation and adverse outcomes, including neurodevelopmental disorders in offspring. Lipopolysaccharide (LPS) is commonly used to model maternal immune activation, but whether LPS exposure triggers acute fetal brain inflammation remain unclear. Few studies have examined how maternal inflammation alters inflammatory cytokine profiles in placental cells and the spatial distribution of placental immune cells, particularly uterine natural killer (uNK) cells and placental macrophages. Using a rat model, our study aims to investigate whether maternal inflammation induces fetal neuroimmune responses and alters placental inflammatory cytokine production and immune cell distribution.

Methods: Pregnant Wistar Kyoto rats were injected intraperitoneally with a low dose of LPS (25 µg/kg) or saline on gestation day 15.5 and were euthanized 5 hours later. Maternal blood plasma, placentas and fetal brains were collected. Portions of the collected placentas were dissected into three regions: maternal-derived decidua, and fetal-derived labyrinth and junctional zones. Inflammatory cytokine levels in maternal plasma were evaluated by multiplex Luminex assays, while the levels of transcripts encoding inflammatory cytokines in placental tissues and fetal brain were assessed via qRT-PCR. Immunohistochemistry was performed on formalin-fixed paraffin-embedded whole placentas to localize perforin-expressing uNK cells and CD68-positive placental macrophages.

Results: Results are expected by March. We anticipate elevated proinflammatory cytokine levels in maternal plasma and increased expression of inflammatory cytokine genes in placental and fetal brain tissues of LPS-treated rats. The decidua region is expected to show the most pronounced increase in inflammatory cytokine production, whereas the fetal-derived placenta regions and fetal brain may have subtler effects. LPS-treated rats are also likely to have altered placental immune cell distribution and density.

Discussion: This study will provide insight into whether LPS-induced maternal inflammation induces acute neuroinflammation in the fetus and alters placental immune cell distribution. Findings will contribute to maternal-fetal immunology by clarifying fetal susceptibility to maternal inflammation and the role of placental immune cells in inflammatory conditions.

Presenter's Name: Lin, August
Additional Authors: Donovan J, Quiñones-Mateu M, Arts E
Abstract Title: Optimization of an external-nested PCR approach to SARS-CoV-2 variant of concern surveillance in wastewater: A new model for early outbreak detection

Abstract:
Introduction: COVID-19, caused by the SARS-CoV-2 virus, has resulted in millions of deaths in Canada and was the third leading cause of death in 2022. As new variants of SARS-CoV-2 continue to evolve and spread, wastewater surveillance (WWS) has emerged as a valuable tool for detecting viral loads within communities as the utility of clinical reporting is limited due to underreporting of asymptomatic cases. Previous research also suggests that SARS-CoV-2 variants of concern (VOC) can be detected in wastewater approximately 2 weeks before first clinical detection highlighting the benefits on WWS for public health initiatives.

Methods: This study introduces a novel approach for VOC detection by isolating and amplifying a select region of the receptor-binding domain (RBD) for the SARS-CoV-2 spike (S) gene, rather than reconstructing sequences from fragmented RNA. Wastewater samples collected in London, Ontario (2021–2023) and stock samples of known VOCs, including Delta and Omicron, were used to optimize external-nested polymerase chain reaction (PCR) conditions. These PCR amplicons will then be sequenced using next-generation sequencing (NGS) to determine the different VOC profiles in the wastewater over time and assess the ability for early VOC detection.

Results: Preliminary findings show that in stock samples of Wuhan, Delta, and Omicron variants, our external and nested primer sets demonstrated selective binding and amplification of the target RBD region. However, when tested on wastewater samples, primer dimerization was observed, leading to nonspecific amplification at ~100 base pairs. Further optimization, including the design of alternative primers, is in progress to mitigate dimerization and enhance amplification specificity before proceeding to sequencing.

Discussion: By refining this confirmatory approach, we aim to enhance the accuracy and reliability of VOC detection in wastewater, improving early warning capabilities well before clinical case identification. This method has the potential to provide critical insights for public health responses during emerging outbreaks.

PATHOLOGY

Presenter's Name: Mihele, Maria
Additional Authors: Khan ZA
Abstract Title: Identification and characterization of stem cell transcripts in mouse bone marrow

Abstract:
Introduction: Stem cells are characterized by their ability to self-renew and differentiate, playing an essential role in tissue regeneration and repair. In adults, bone marrow is the most accessible and abundant source of stem cells. Current approaches to identify stem cells in the bone marrow have relied on known hematopoietic and mesenchymal stem cell markers such as Ptprc, Csf3r, and Pdgfra. This study aims establish a comprehensive expression footprint of stem cell-associated genes in postnatal mouse bone marrow.

Methods: Using total RNA isolation and RT-qPCR, we analyzed a list of 96 genes associated with stem cell function, differentiation, and pluripotency. Further characterization will be performed through immunohistochemistry to identify the spatial localization of these cells within bone marrow tissue. Additionally, spatial transcriptomics and functional differentiation assays will help determine the specific stem cell type and their functional properties.

Results: Although the study and analyses are still in progress, we have made a number of interesting observations. First, and not surprising, is the observation that the most robust transcripts in bone marrow flush samples are known housekeeping genes such as 18S, Gapdh, and Hprt1. Interestingly, we found transcripts associated with pluripotent stem cells (Sox2 and Nanog) in postnatal bone marrow samples as the most robust stem cell-related genes. Genes regulating cell proliferation and differentiation such as Eef1a1 and Ctnnb1 were also found to be highly expressed. In terms of extracellular matrix genes, we noted high expression of Fn1 and Col1a1. Once complete, our results will lay the foundation to examine how this molecular architecture changes during ageing and in chronic conditions associated with bone marrow and stem cell alterations.

Discussion: These findings highlight molecular components essential for bone marrow stem cell function. The expression of Sox2 and Nanog suggests persistence of cells with pluripotent differentiation capacity in postnatal tissue. Further, identification of additional membrane and intracellular antigens may complement traditional surface marker-based approaches to identify and study bone marrow-derived stem cells, providing supplementary tools to distinguish stem cells from other bone marrow cells. Further characterization will clarify their roles in stem cell identification and function, aiding future research and potential therapeutic applications.

Presenter's Name: Moran, Devon
Additional Authors: Greasley A, Zheng X
Abstract Title: Regulation of Ischemia Reperfusion Injury in Cardiomyocytes via Sodium Thiosulfate Treatment

Abstract:
Introduction: Cardiovascular disease is the leading cause of death worldwide and often involves heart transplant as the primary therapeutic intervention. Postoperative complications leading to high early mortality including poor graft function and failure are a direct result of ischemic onset during static cold storage (SCS) and subsequent reperfusion injury during transplant. Ischemia-reperfusion injury (IRI) is an inevitable process during the transplant procedure and current remedies beyond SCS in preservation solutions like University of Wisconsin (UW) solution fail to improve the condition. Sodium thiosulfate (STS) is a promising therapy that through hydrogen sulfide (H2S) generation, has been shown to reduce the effects of IRI. We hypothesize that STS will decrease IRI in cardiomyocytes to improve early mortality associated with heart transplant and increase static cold storage time.

Methods: To test this hypothesis, we first cultured AC16 human cardiomyocytes in a CoCl2 chemical hypoxia model to assess the effectiveness of STS treatment in vitro. Following validation, STS treatment with UW solution at varying administration times will be evaluated in a hypoxia-reoxygenation assay. Finally, STS will be administered in a syngeneic, heterotopic mouse transplant to measure heart function and graft integrity.

Results: Treatment with sodium thiosulfate is expected to decrease cell death in chemical induced hypoxia as well as during the hypoxia-reoxygenation assay. Heart function, fibrosis, ischemic injury, and cell death are expected to improve in mice that receive STS at various timing during transplantation.

Discussion: This study will provide novel insight into the ability of STS to mediate IRI during heart transplant. Ability to increase graft function and alleviate tissue injury after transplant could hopefully improve the high early mortality due to static cold storage ischemia-reperfusion injury.

PATHOLOGY

Presenter's Name: Morrone, Alex
Additional Authors: Dick FA
Abstract Title: The Effects of Inhibiting Known Cancer Dormancy Pathways on Ovarian Cancer Spheroid Viability

Abstract:
Ovarian cancer is the most lethal gynecological malignancy, with a 5-year survival of less than 30%. Chemotherapy-resistant aggregates of tumour cells known as spheroids play an important role in the spread and recurrence of high-grade serous carcinoma (HGSC) – the most common and most deadly form of ovarian cancer. Spheroids extracted from patient ascites have been observed to be dormant. Changes observed in dormancy include increases in stemness, epithelial to mesenchymal transition, and autophagy. These changes are mediated by the Wnt, TGFβ, and ULK1 pathways, respectively. The Netrin signaling pathway has emerged as a novel pathway underlying HGSC dormancy, but single gene knockouts have demonstrated that it is not essential to dormancy – individual knockouts only cause moderate reductions in spheroid viability. However, the effects of inhibiting multiple dormancy pathways have yet to be explored. I hypothesize that treating Netrin knockout cells with inhibitors for other known cancer cell dormancy pathways will result in a greater decrease in spheroid cell viability. Spheroids from Netrin-1, UNC5B, and Luciferase knockout cell lines generated from the iOvCa147 ovarian cancer cell line will be exposed to varying concentrations of LY-2109761, WntC59, and MRT68921 to inhibit TGFβ, Wnt, and ULK1, respectively. A crystal violet assay will be used to quantify the effect this has on HGSC spheroid viability. Next, a series of assays will be performed to confirm on-target action of the inhibitors and validate impacts on HGSC viability. I expect the cells treated with inhibitors to have lower viability than untreated cells, and cells with a component of the Netrin signalling pathway knocked out in addition to a second pathway inhibited to have the lowest viability. Additionally, I expect that all reductions in viability will be due to inhibitors acting on-target. This study will address a gap in knowledge concerning the implications of simultaneously inhibiting multiple dormancy pathways in HGSC spheroids. It can also inform the development of treatments that target spheroids, which has the potential to significantly improve patient outcomes.

Presenter's Name: Picard, Spencer
Additional Authors: Leung Z, Kawa DT, Kiser PK
Abstract Title: Differentiating Donor vs. Recipient Cells in an Embryogenesis Model

Abstract:
Introduction: Embryonic stem cell (ESC)-derived teratomas are a useful model to study embryogenesis and tumor development by mimicking early cell differentiation. However, no previous study has investigated which host-derived structures are involved in the development of these teratomas. Previous studies have found that p66Shc knockout (p66ShcKO) ESCs exhibit impaired differentiation and abnormal cell replication. Understanding the interactions between donor- and host-derived components could provide deeper insights into the mechanisms underlying teratoma development. We hypothesized that a FISH-based assessment would provide a more precise determination of host-derived contributions compared to morphological assessment alone.

Methods: Female NSG (XX) mice were injected subcutaneously in the inguinal region with male (XY) wild-type (WT) or p66ShcKO ESCs. Through histological assessment, we identified and quantified the prevalence of differentiated and undifferentiated tissues, along with their germ-cell lineage (ectoderm, endoderm, mesoderm). Currently, we are applying fluorescence in-situ hybridization (FISH) using X and Y chromosome probes to distinguish donor (XY) from host (XX) structures in WT and p66ShcKO teratomas. Data will then be qualitatively compared to morphological assessment findings to determine host vs. donor contributions.

Results: Histological analysis of teratomas revealed a higher percentage of undifferentiated tissues compared to WT teratomas. Preliminary FISH results are expected to confirm the distinction between host- and donor-derived structures, aligning with morphological assessment findings. It is also presumed that there will be consistency in host- vs. donor-derived status across similar cell types in all investigated teratomas.

Discussion: Preliminary findings suggest that p66Shc plays a critical role in cell differentiation patterns during early embryonic development. This study is the first to investigate host- vs. donor-derived contributions to ESC-derived teratomas. By elucidating these interactions, our findings will enhance our understanding of both embryogenesis and tumor development. Furthermore, these results will clarify the role of p66Shc in cell differentiation and improve the translational relevance of teratomas models for embryologic and cancer research. Identifying specific host-derived components could also inform targeted therapeutic strategies for tumor progression.

PATHOLOGY

Presenter's Name: Rana, Emaan
Additional Authors: Kum J
Abstract Title: Qualitative Exploration of the Histopathological Atlas of Laboratory Mouse Tissues

Abstract:
Introduction: Open educational resources (OERs) alleviate financial burdens on students due to rising textbook costs and tuition. Virtual OERs are often used in histology education to support student learning. However, most histology OERs tend to focus on human tissue and lack comprehensive information on mouse tissues. The histopathological atlas of laboratory mouse tissues bridges this gap and serves as a tool for students working with mouse tissues that require staining interpretation. This study aims to evaluate the educational benefit and usability of the histopathological atlas of laboratory mouse tissues.

Methods: A survey was conducted to quantitatively and qualitatively assess the histopathological atlas of laboratory mouse tissues. Graduate students within the Pathology and Laboratory Medicine department were recruited. The Technology Acceptance Model (TAM) was adapted to assess interface usability and the Strengths, Weaknesses, Opportunities and Threats (SWOT) framework structured feedback on potential improvements for the OER. These frameworks were adapted through Likert scale and open-ended questions, respectively. Thematic analysis was used to analyze the open-ended question responses.

Results: Our results show that both naïve and students with histology experience preferred the inclusion of both Pentachrome and H&E stains as they were beneficial in identifying different structures. The interface was reported to be easy to navigate and the students appreciated the descriptions associated with each tissue. Suggested improvements include incorporating tissue stains for pathologies and creating a searchable database to filter tissue types based on the user's interest.

Discussion: These findings indicate that the histopathological atlas of laboratory mouse tissues is a beneficial educational tool for both naïve and experienced histology students. Its effectiveness can be enhanced by diversifying the tissue slides and incorporating more details regarding the labelled structures, which would further enhance user experience and educational value.

PATHOLOGY

Presenter's Name: Rath, Advika
Additional Authors: Kum JJY, Khan ZA
Abstract Title: Elucidating the potential association between bone marrow neuropathy and enhanced adipogenesis in diabetes.

Abstract:
Introduction: Diabetes mellitus is a chronic disease characterized by impaired glucose regulation, leading to systemic complications such as neuropathy and bone marrow dysfunction. Diabetic autonomic neuropathy may disrupt neuronal signaling to reduce circulating CD34-positive cells for vascular repair, while hyperglycemia-induced suppression of TGFβ1 promotes adipogenesis, impairing bone marrow stem cell mobilization. Although these phenomena are documented, the relationship between neuropathy and adipogenesis in diabetic bone marrow remains unclear.

Methods: To investigate this relationship, bone marrow tissue samples from streptozotocin-induced diabetic C57BL/6 mice are being analyzed in this study. Immunohistochemistry using antibodies against RBFOX3 (neuronal marker) and PLIN1 (adipocyte marker) will characterize neuronal density and adipocyte presence in the target region. Sequential tissue sections will be aligned to visualize both tissue types, and image analysis will be conducted using QuPath software. Neuronal marker staining will be evaluated at varying distances from adipocytes to spatially characterize potential connections between adipocyte presence and nerve degeneration.

Results: To date, we have optimized immunohistochemical staining of decalcified mouse bone tissues for RBFOX3 and PLIN1. The feasibility of sequential section alignment using QuPath was evaluated, validating its application for tissue co-localization. Data collection and quantification of neuronal size in relation to adipocyte proximity are in progress.

Discussion: This study establishes a feasible approach to study the interrelationship between neuropathy and adipogenesis in diabetic bone marrow using spatial analysis. Future evaluation can highlight if neuron tissue density is affected by adipocyte proximity, contributing to our understanding of diabetes-induced bone marrow dysfunction.

Presenter's Name: Schreier, Evan
Additional Authors: Barua E, Barr S
Abstract Title: Developing Enhanced Interferons for Improved Viral Defence

Abstract:
Interferons (IFNs) play a critical role in the innate immune response against viruses and tumours; however, their clinical application is limited by toxicity and poor pharmacokinetics. While advances in engineered IFN therapies have shown promise, the precise structural modifications that balance enhanced antiviral activity and reduced cytotoxicity remain poorly understood. Bats, which tolerate high viral loads without severe disease, provide a unique model for studying interferon biology and may offer insights into safer, more effective therapies. This study aims to generate and characterize human and bat interferon mutants that exhibit enhanced antiviral efficacy and decreased cytotoxicity. It is hypothesized that specific mutations in human and bat interferon proteins will enhance antiviral responses while minimizing toxicity through structural changes that modulate receptor interactions and signalling. To test this hypothesis, we used a PCR-based mutagenesis to generate a library of mutants for human IFNα2, human IFNβ1, Black Flying Fox bat (BFF) IFNα1, BFF IFNβ1 and BFF IFN. These mutants were screened for antiviral activity with HIV as a model system and cytotoxicity in cell-based assays. Further validation of candidates will be done with repeat dilution series assays and structural predictions of the mutants will be performed using AlphaFold to identify key structural alterations linked to enhanced activity and reduced toxicity. We hope to identify interferon mutants that show improved antiviral activity against HIV-1 and decreased cytotoxicity. Structural analysis will reveal how specific mutations influence 3D protein structure and receptor interactions, providing a better understanding of the relationship between interferon structure and receptor binding. These findings could lead to the development of more effective and safer interferon-based therapies for viral infections and cancers, ultimately improving patient outcomes and broadening the therapeutic potential of interferons.

Presenter's Name: Selimi, Brent
Additional Authors: Shin EH, Morin AL, Win PW, Chen S, Castellani CA
Abstract Title: Characterization and Optimization of Cell Line Models of Mitochondrial DNA Variation

Abstract:
Introduction: DNA polymerase gamma (POLG) and mitochondrial transcription factor A (TFAM) are key regulators of mitochondrial DNA (mtDNA) replication. We previously introduced D1135A and D198A mutations into two separate tetracycline (tet) inducible POLG cell lines to decrease mtDNA copy number (mtDNA-CN) and increase heteroplasmy, respectively. D1135A showed reduced mtDNA-CN upon induction but lacked a strong dose-dependent response, while D198A did not survive characterization, likely due to basal tet level exposure in standard FBS. Separately, the lab generated TFAM heterozygous knockout (KO) cell lines via CRISPR-Cas9, leading to mtDNA reduction. Comparison of the TFAM KO lines to controls revealed differential methylation and gene expression, for which we are currently characterizing off-target mutations.

Methods: To optimize dose-dependent responses, POLG D1135A and D198A cell lines will be cultured in tet-free FBS. Cell lines will be treated with different concentrations of tet for 48 hours to elicit a dose-dependent response. Heteroplasmy of the D198A line and mtDNA-CN of the D1135A line will be quantified via sequencing and qPCR, respectively. A citrate synthase assay will evaluate mitochondrial function. TFAM KO models will undergo PCR to amplify and barcode off-target regions. Agarose gel electrophoresis and gel extraction will be used to prepare targets for Illumina MiSeq Sequencing.

Results: Using tet-free FBS to culture the D198A line led to increased stability, more consistent growth, and increased confluency (~35% vs 100% after 4 days), reflecting a passaging interval that matches previous D1135A observations. For TFAM KO off-target analysis, primers successfully amplified off-target regions; we are currently preparing these targets for indexing and sequencing. Extending incubation time to 48 hours, in conjunction with the use of tet-free FBS is expected to enhance dose-dependent responses. Citrate synthase assays should reveal reduced mitochondrial function in both tet-induced POLG variant lines. TFAM KO models are predicted to have minimal off-target mutations in loci of interest after PCR and sequencing.

Conclusion: Optimizing inducible mtDNA-CN variation and heteroplasmy models will advance mechanistic research and uncover links to the nuclear epigenome. Confirming low off-target effects in the TFAM KO model would validate findings of nuclear epigenetic modifications and differential gene expression as a result of mtDNA-CN reduction.

PATHOLOGY

Presenter's Name: Sooklall, Jason
Additional Authors: McCord C, Khan ZA
Abstract Title: An in-depth analysis of the microbial basis of refractory osteomyelitis of the jaws

Abstract:
Introduction: Chronic osteomyelitis of the jaws (COMJ) is a rare condition in which bacterial colonization of the mandible leads to inflammation and bone necrosis. A small subset of these cases refract following surgical removal of the infected bone and treatment with antibiotics, necessitating additional treatment rounds. Recently, our laboratory detected presence of bacterial transcripts in decalcified bone tissues from patients with refractory and non-refractory osteomyelitis using pan-bacterial 16S rRNA gene qPCR. Since these results found no difference in bacterial load between refractory and non-refractory samples, the aim of our present study is to determine whether bacterial species and strains can distinguish between refractory and non-refractory osteomyelitis. Therefore, we hypothesize that the microbiomes of these lesions will differ between refractory and non-refractory samples, providing an indication of a worse disease phenotype.

Methods: To evaluate the species of bacteria present, we first isolate RNA from N=24 samples of COMJ, with 12 cases being refractory and 12 non-refractory. We then process this RNA into cDNA for use in qPCR with species-specific primers, targeting bacteria previously identified in microbiological and molecular studies of COMJ. We will then verify our platform against known bacterial standards and microbiology reports.

Results: To date, our platform has been able to make a positive identification of two bacterial species (F. nucleatum and S. anginosus) in our samples. Also, we determined that the prevalence of these species differs between groups, with F. nucleatum being more prevalent in refractory cases, S. anginosus being more prevalent in non-refractory cases. Due to the success of these trials, we are currently pursuing further investigations, searching for known pathogenic bacteria such as P. gingivalis and A. actinomycetemcomitans.

Discussion: Our findings show that individual bacterial species can be detected using molecular biology techniques, despite fragmentation of RNA during the decalcification process. These findings open-up new avenues in COMJ research such as next generation sequencing of archival patient samples, as enough material remains to positively identify bacterial species present.

Presenter's Name: Taylor, Kathryn
Additional Authors: Ugilini S, Dhanvantari S
Abstract Title: Stathmin-2 Regulates Lysosomal Exocytosis in Pancreatic Alpha Cells as a Mechanism of Hyperglucagonemia in Diabetes

Abstract:
Introduction: Hyperglucagonemia, or the excessive secretion of glucagon, is an emerging yet underexplored contributor to hyperglycemia in diabetes. Previous work from our lab has shown that, in pancreatic alpha cells, the protein Stathmin-2 negatively regulates glucagon secretion by redirecting it to degradative lysosomes. In diabetes, decreased Stathmin-2 expression disrupts this pathway, leading to excessive glucagon release. Our preliminary findings have shown that in diabetic alpha cells, glucagon colocalizes with LAMP1+ lysosomes at the periphery, suggesting lysosomal exocytosis as a mechanism for glucagon hypersecretion. Arl8, a lysosome-kinesin adapter protein, facilitates the anterograde movement of lysosomes. We hypothesize that glucagon is trafficked to Arl8+ secretory lysosomes, driving the hyperglucagonemia observed in diabetes.

Methods: Pancreatic tissue sections from control and streptozotocin-induced diabetic mice were immunostained for glucagon, LAMP1, Arl8, and Stathmin-2 to assess changes in glucagon's spatial distribution relative to secretory lysosomal markers. Additionally, siRNA-mediated knockdown of Stathmin-2 was performed in cultured αTC1-6 cells. These cells were stained for Arl8 to examine changes in its expression and distribution in response to Stathmin-2 depletion.

Results: Diabetic pancreatic tissues exhibited colocalization of glucagon with Arl8 and LAMP1, along with increased expression intensity of LAMP1 compared to controls. Stathmin-2 knockdown resulted in increased fluorescence intensity of Arl8. These findings suggest enhanced anterograde trafficking of lysosomes to the periphery for glucagon secretion, supporting the role of lysosomal exocytosis in glucagon hypersecretion in diabetes.

Discussion: Glucagon's contribution to hyperglycemia in diabetes is overlooked and underestimated. With diabetes affecting over 500 million people worldwide, understanding the intracellular mechanisms of hyperglucagonemia is crucial to better understand pathogenesis and progression of diabetes. In addition, highlighting the mechanism of glucagon secretion through secretory lysosomal pathways may offer novel therapeutic strategies for managing hyperglycemia, potentially improving outcomes for diabetes patients.

PATHOLOGY

Presenter's Name: TenHag, Kayla
Additional Authors: AlMutawa F
Abstract Title: Advancing Rapid Diagnosis in Bloodstream Infections: Direct Identification and Antimicrobial Susceptibility Testing

Abstract:
Introduction: Bacterial bloodstream infections (BSIs) are severe conditions requiring rapid diagnosis. Traditional blood culture workflows require an 18–24-hour incubation period before identification and antimicrobial susceptibility testing (AST). Direct testing from positive blood cultures could shorten turnaround time (TAT), by replacing the incubation process with an approximate 20-minute centrifugation step. Previous studies have demonstrated the potential for direct identification and AST, but further validation is needed to ensure accuracy across different bacterial species seen in our specific laboratory. This study evaluates the accuracy of direct testing compared to conventional methods. We hypothesize that bypassing plate inoculation and performing direct identification and AST from positive blood cultures will maintain accuracy while reducing TAT, facilitating faster clinical decision-making and improved patient management.

Methods: Four centrifugation procedures were tested on positive blood cultures representing gram-positive cocci and gram-negative bacilli, the most common bacterial groups in our laboratory. Matrix-Assisted Laser Desorption/Ionization – Time of Flight (MALDI-TOF) was used for organism identification, and the BD Phoenix system for AST. The best-performing method, involving sodium dodecyl sulfate (SDS) treatment and three 1-minute centrifugation periods, was selected for further validation on 150 samples, with 50 completed to date.

Results: Preliminary findings show high accuracy for gram-negative organisms, with 96% correct MALDI identification (24/25) and >99% categorical agreement in AST. Gram-positive identification accuracy was lower (79%, 19/24), with AST completed on 9 samples. SDS may interfere with gram-positive growth, preventing AST in some cases. For the 9 gram-positive samples with AST results, categorical agreement remained high (>98%), though adjustments to SDS concentration or an alternative method may be needed for consistent testing.

Discussion: Direct testing offers potential for faster BSI diagnosis, improving clinical decision-making and reducing broad-spectrum antibiotic use. Reducing TATs is essential in combating antibiotic resistance by enabling earlier initiation of targeted therapies. Our findings will help refine microbiology workflows, enhancing patient care and antimicrobial stewardship.

Presenter's Name: Wilson, Scott
Additional Authors: Kum J
Abstract Title: Students' Perspectives of Teaching and Learning in an Undergraduate Pathology Classroom

Abstract:
Introduction: Universities around the globe predominantly employ didactic instruction. Didactic instruction involves lectures, where instructors provide information, and students receive the information without any student-instructor engagement. Active learning is a novel method of instruction that prioritizes interaction and engagement between students and instructors. Undergraduate pathology is taught using didactic lectures and are well-liked among students. There has been a recent pedagogical shift from didactic learning towards active learning in university education to increase student performance and satisfaction, which may have applications in undergraduate pathology. The study aims to investigate the students' perspectives on teaching, learning, and engagement in an undergraduate pathology classroom.

Methods: Pathology 3500–Introduction to Human Pathology–The Study of Disease, is Western's largest undergraduate pathology course. A Qualtrics survey was distributed to students who completed Pathology 3500 between 2017-2023. Students are asked to anonymously self-report demographic information, final grades, course engagement, overall experience, and suggestions for improvement. Student questionnaires on courses and teaching were collected and provided by Western's Registrar's Office (RO) for pathology courses from 2016-2024. Qualitative coding and grounded theory were used to draw results from written responses. Codes were grouped into four categories: Course Improvement Suggestions; Struggles with Course Engagement; Challenges in Course; Course Materials Feedback.

Results: Our preliminary findings suggest that the proportion of RO responses about course materials decreased following the COVID-19 pandemic. However, an apparent increase in the proportion of RO responses relating to course engagement was observed following the pandemic. It should be noted that the comments received regarding the course materials were almost exclusively negative.

Discussion: The decrease in negative feedback relating to the course materials following the pandemic may indicate students preferring the in-person materials over the online delivery during the lockdowns. With the shift to in-person learning, the apparent increase in the proportion of responses regarding course engagement following the pandemic may indicate an increase in student interest in active learning. These findings are significant in supporting that students are favorable towards active learning.

PATHOLOGY

Presenter's Name: Xu, Wei Jia
Additional Authors: Lalonde E, Mohseni Meybodi A
Abstract Title: Prognostic Value of Copy Number Variations Detected by SNP Microarray in B-Cell Acute Lymphoblastic Leukemia

Abstract:
Introduction: B-cell acute lymphoblastic leukemia (B-ALL) is the most common pediatric cancer, and detection of genetic abnormalities is critical for accurate patient diagnosis and prognosis. The clinical gold standard for cytogenetic techniques, karyotyping and fluorescence in situ hybridization (FISH), have limited resolution and scope, often missing submicroscopic alterations like copy number variations (CNVs). Single nucleotide polymorphism (SNP) microarray offers high-resolution genome-wide analysis, detecting changes unidentifiable by karyotyping and FISH, but cannot detect balanced chromosomal changes, limiting its standalone diagnostic use. At London Health Sciences Centre (LHSC), SNP microarray is not yet clinically used for routine diagnostics in B-ALL. We hypothesize that integrating SNP microarray with karyotyping and FISH will enhance diagnostic accuracy and risk stratification for B-ALL patients.

Methods: Bone marrow samples were collected from 50 B-ALL patients (aged 1–77) between 2021 and 2025. Karyotyping and FISH data were available for 45 patients, whose samples were subsequently analyzed using SNP microarray following standard protocols. Microarray data were interpreted using BlueFuse Multi. Whole gene/partial deletions in 8 genes from the UKALL-CNV classifier as well as in TP53 were recorded and used for risk stratification. Patients were stratified into risk groups using both WHO cytogenetic (karyotyping + FISH) and UKALL-CNV (microarray) classifiers as prognostic indicators.

Results: Relevant gene deletions were identified in 21 patients (47%). When comparing WHO cytogenetic risk classifications with UKALL-CNV-based risk groups, 30 patients (67%) were reclassified into different prognostic categories, while 15 patients (33%) showed no change. Specifically, 7 patients (16%) were moved to a higher-risk category, including all 3 patients with TP53 deletions, whereas 23 patients (51%) were reclassified into a more favorable risk group.

Discussion: Although SNP microarray cannot replace routine cytogenetic tests due to its limitations, this study demonstrates its value as a complementary diagnostic tool. The observed reclassification between WHO cytogenetic and UKALL-CNV risk groups highlights microarray's ability to detect novel genetic markers that can impact prognosis. Our findings will support the validation of SNP microarray for routine clinical use in B-ALL, potentially improving patient stratification and treatment outcomes.

Presenter's Name: Rayevskiy, Stanislav
Additional Authors: Ali A, Garcia OE, Castellani CA
Abstract Title: Deciphering the Role of Mitochondrial DNA and MicroRNA in Knee Osteoarthritis Progression

Abstract:
Introduction: Osteoarthritis (OA) is a chronic joint disorder marked by tissue degeneration and joint dysfunction. MicroRNAs (miRNAs) have been implicated in OA pathogenesis, including in mitochondrial function. This study investigates the potential role of miRNAs as potential mediators between mitochondrial DNA (mtDNA) variation and OA severity, as well as their direct influence on OA-related outcomes. We hypothesize that miRNAs mediate the relationship between mtDNA features (haplogroup, haplotype, and cumulative mtDNA distance) and OA phenotypes (symptomatic and structural) and that specific miRNAs are associated with OA severity.

Methods: A total of 502 patients from the Osteoarthritis Initiative Cohort (OAI) were analyzed. miRNA counts were obtained from baseline plasma and serum samples. mtDNA haplogroups were generated using haplogrep3, haplotypes via the HTRX R package, and mtDNA distances via FastTree. High-dimensional mediation analysis (HDMA) was conducted using hdmed, incorporating age, BMI, mtDNA distance, haplogroup, and haplotype as exposure variables and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores, joint space narrowing, and Kellgren-Lawrence grades as outcomes. MiRNAs showing significant mediation or direct associations across at least two outcomes underwent individual regression analysis ($p < 0.05$). miRNA that were significant for at least one of the possible outcomes during individual analysis were retained ($p < 0.05$, BH). Gene targets were predicted using mirDIP, and pathway analysis was performed with DisGeNET, Disease Ontology, Gene Ontology, KEGG, and Pathway Commons databases.

Results: A panel of 59 miRNAs were identified as potentially involved in OA pathogenesis, with 9 previously linked to OA in the literature. Of these, 24 miRNAs were mediators of relationships involving mtDNA variables. Pathway analysis indicated that these miRNAs regulate molecular pathways associated with arthritis or broader arthritis mechanisms (osteoarthritis, polyarthritis, arthritis).

Discussion: This study highlights the regulatory role of miRNAs in OA and their connection to mtDNA, demonstrating their combined influence on OA progression. Further validation in larger cohorts is necessary to confirm clinical relevance.

PATHOLOGY