Research Day Abstracts

2023

4th Year Honours Specialization Students

Presenter's Name: Huang, Zi Huai
Additional Authors: Liu Q, Hu P
Abstract Title: cGAN – Driven Radiomic Prediction of Mutation Status Based on MR Images of Breast Cancer

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

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

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

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

Presenter's Name: Janarthanan, Sugitha
Additional Authors: Dima DC, Mohsenzadeh Y
Abstract Title: Action Categorization in the Mind Across Vision and Language

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

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

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

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

MEDICAL BIOINFORMATICS

Presenter's Name: Jin, Bernie
Additional Authors: Poon AFY
Abstract Title: Comparing Intrinsic Disorder of Core and Accessory Viral Proteins

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

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

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

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

Presenter's Name: Liu, Amber
Additional Authors: Shooshtari P
Abstract Title: Benchmarking BABEL Deep Learning Method Against Various Cell Types in Humans and Mice

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

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

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

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

MEDICAL BIOINFORMATICS

Presenter's Name: Nguyen, Julia
Additional Authors: Morin A, Castellani CA
Abstract Title: Association between mitochondrial DNA haplogroups and nuclear DNA methylation in cardiovascular disease and aging

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

Presenter's Name: Zahid, Danish
Additional Authors: Poon AFY
Abstract Title: Assessing the Robustness of Episignature-Based Disease Prediction Methodology to Random Variation: A Feasibility Study on Artificially Forging an Episignature in the Absence of Disease

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

MEDICAL BIOINFORMATICS

Presenter's Name: Choudhary, Farhan
Additional Authors: McKinley G
Abstract Title: Using the One Health Approach to Investigate the Extent of Human Health Impacts due to Climate Change on Walpole Island First Nations and the Broader Southwestern Community

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

Presenter's Name: Gendron, Laura
Additional Authors: Haagsma J, Shepherd T
Abstract Title: A One Health Approach to Examining Potential Reprogramming Events Causing Neoplastic Change in Oviductal Cells

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

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

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

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

ONE HEALTH

Presenter's Name: He, Francine
Additional Authors: Frisbee, SJ
Abstract Title: One Health Approach on the Pharmacotherapy of Carcinoid Heart Disease in Neuroendocrine Tumours

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

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

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

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

Presenter's Name: Panjwani, Samina
Additional Authors: Princz-Lebel O, Saksida L, Bussey T
Abstract Title: Exploring the neurocircuitry mechanisms underlying stimulus-response learning in mice, and its relevance to Parkinson's disease

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

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

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

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

ONE HEALTH

Presenter's Name: Pavlovic, Milica
Additional Authors: Frisbee SJ, Fleet J
Abstract Title: Diabetes and the Relationship Between Post-Stroke Cognitive Impairment and Falls

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

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

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

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

Presenter's Name: Ramnarine, Jordan
Additional Authors: Williams L
Abstract Title: Who Speaks for the River?: An Indigenous Feminist Approach to the One Health Impacts of Climate Colonialism on Two-Spirit Peoples in Deshkan Ziibi

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

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

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

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

ONE HEALTH

Presenter's Name: Tapp, Brandon
Additional Authors: Jessani A
Abstract Title: Questionnaire Design for the Identification of Oral Health Status and Oral Health Service Utilization Among Rwandan Pregnant Women

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

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

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

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

Presenter's Name: Vora, Sachee
Additional Authors: Wathens CN
Abstract Title: Applying a One Health Approach to Investigating Refugee Health Models and Evaluating the Efficacy of the Newcomer Clinic and Integration Program

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

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

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

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

ONE HEALTH

Presenter's Name: Wang, Isabel
Additional Authors: Gibson C
Abstract Title: What We Can Learn From the Victorians: A Comparison of Modern and Victorian Epidemic Response and Prevention

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

Presenter's Name: Boles, Helen
Additional Authors: Greasley A, Zheng X
Abstract Title: Understanding Circular RNA Back-splicing Regulation and Efficiency

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

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

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

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

Presenter's Name: Chen, Tony
Additional Authors: Stevic I, Knauer M
Abstract Title: Investigating the Effects of Timing, Accelerometry, and Temperature of Pneumatic Tube Systems on Blood Samples

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

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

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

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

PATHOLOGY

Presenter's Name: Cogghe, Joni
Additional Authors: Zhang ZX
Abstract Title: AIM2 as an Endogenous DNA Sensor and a Potential Player in Post-Heart Transplantation Organ Viability

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

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

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

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

Presenter's Name: Dabrowski, Gabriela
Additional Authors: Knauer MJ, Richardson K
Abstract Title: Evaluation of the Roche Cobas® Pulse Glucose Monitoring System

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

Presenter's Name: Dabrowski, Natalia
Additional Authors: Khan ZA
Abstract Title: Differential Expression of Myeloid and Lymphoid Lineage-Associated Genes in the Adipocytic Bone Marrows of Ageing Mice

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

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

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

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

PATHOLOGY

Presenter's Name: Dan, Angela
Additional Authors: Ding M, Gunaratnam L
Abstract Title: Understanding the KIM-1 shedding function in renal cell carcinoma

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

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

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

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

Presenter's Name: Ghantous, Dominic
Additional Authors: Corneil BD
Abstract Title: Single-trial analysis of express visuomotor responses in Parkinson's Disease

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

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

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

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

PATHOLOGY

Presenter's Name: Imran, Aansah
Additional Authors: Chang N, Dhanvantari S
Abstract Title: Islet Hormone Regulation of Glucagon Secretion Occurs Through Increased Trafficking to the Endolysosomal System Mediated by STMN2

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

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

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

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

Presenter's Name: James-McDonald, Christian
Additional Authors: Larsen F, Asfaha S
Abstract Title: Investigation of the Effects of DNA Demethylating Drugs on DCLK1+ Cell Derived Tumor Organoids

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

PATHOLOGY

Presenter's Name: Jeong, Jessica
Additional Authors: Figueredo R, Maleki S
Abstract Title: Assessing the Presence of Bacterial Cas9 in MLH1-knockout Neuroblastoma Cells

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

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

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

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

Presenter's Name: Kawa, Daniel
Additional Authors: Jackson-Boeters L, Kiser P
Abstract Title: Assessing in Vivo Off-Target Binding of a Novel Oral Antibody Vaccine Developed to Prevent Colonization of Enteric Pathogen E. Coli O157:H7

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

PATHOLOGY

Presenter's Name: Kuczek, Jakub
Additional Authors: Zhang Q
Abstract Title: Investigating Nuclear Morphometry in Diffuse Astrocytic Gliomas

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

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

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

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

Presenter's Name: Lin, Sherman
Additional Authors: Tran C et al
Abstract Title: 1000 Mitoses Project: An International Consensus on Mitotic Figures

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

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

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

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

PATHOLOGY

Presenter's Name: McCullagh, William
Additional Authors: Bhattacharjee RN, Ravichandran S
Abstract Title: Immunological Impact of Carbon Monoxide Releasing Molecules on In-Vitro Renal Ischemia Reperfusion Injury.

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

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

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

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

Presenter's Name: McLoughlin, Allison
Additional Authors: Taray-Matheson D, Diao H, Min W
Abstract Title: CircHUWE-1 as a Regulator of Prostate Cancer Growth

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

PATHOLOGY

Presenter's Name: Pan, Nachuan (Harrison)
Additional Authors: Wang E, Wang H, Chakrabarti S, Chen S, Feng B
Abstract Title: The role of miR-9 in diabetic cardiomyopathy

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

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

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

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

Presenter's Name: Parikh, Prey
Additional Authors: Parikh P, Hamilton DW, Darling M
Abstract Title: The Characterization of a 'Scar Tissue' Phenotype of Fibrous Proliferations of the Oral Mucosa and Gingiva

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

PATHOLOGY

Presenter's Name: Prasad, Kendra
Additional Authors: McCord C
Abstract Title: Characterizing Human Papillomavirus Associated Oral Epithelial Dysplasia: An Evaluation of Biomarkers

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

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

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

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

PATHOLOGY

Presenter's Name: Raina, Neha
Additional Authors: de Chickera S, Sidahmed AM
Abstract Title: Identifying non-HLA antibodies and their role in kidney transplantation outcomes

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

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

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

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

Presenter's Name: Vytlingam, Kevin
Additional Authors: Ji X, Peng T
Abstract Title: Determining the interaction between junctophilin-2 and junctin by the bimolecular fluorescence complementation (BiFC) assay

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

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

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

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

Presenter's Name: Wang, Shirley
Additional Authors: Khan ZA
Abstract Title: Unlocking cellular potency in human cells through chemical reprogramming

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

PATHOLOGY

Presenter's Name: Yang, Ha Ryun
Additional Authors: Nichols M, Hsia C, Chin-Yee B, Bhayana V, Chin-Yee I
Abstract Title: Anemia associated with Decreased Plasma Zinc Levels is Likely Secondary to Acute Inflammation

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

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

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

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

PATHOLOGY

Presenter's Name: Yu, Manus
Additional Authors: MohdWessam AJ, French A, Cameron L
Abstract Title: IL-21 and TGFβ Influence Glucocorticoid Insensitivity in Th2-Th17 double-positive cells.

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

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

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

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

Presenter's Name: Zemingui, Angela
Additional Authors: Kiser P
Abstract Title: Characterizing the Impacts of Lifelong Western Diet Exposure on Maternal and Fetal Renal Tissues

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

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

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

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