

Research Day Abstracts

2021

**4th Year Honours
Specialization Students**

Presenter's Name: Callaghan, Paige

Additional Authors: Baxter J, Olea-Popelka FJ

Abstract Title: An interdisciplinary approach to attitudes towards wind turbine health risks in Canada

Abstract: Although designed as a safer and more sustainable energy source to meet carbon emission targets, wind turbine development in Canada has come to a near complete stop, due in part to strong pushback from concerned citizens regarding wind turbine impacts to human health and well-being. Social acceptance of wind turbines has shown to be an influential factor in turbine development, yet perceived health risks are often not considered. Wind turbine health impacts are highly debated, as are the pathways in which these impacts may occur. However, several studies examine this epidemiologically, and assume a direct cause-effect relationship between exposure and health outcomes. Consequently, this study presents a novel approach to negative wind turbines health outcomes through an interdisciplinary, one health analysis of perceived health concerns and causal exposure pathways. One health is a holistic approach to health that considers animal, human, and environmental perspectives, while emphasizing multidisciplinary stakeholder collaboration. As a component of a one health approach to wind turbines, we offers stakeholders an opportunity to voice their opinions on concerns related to negative health outcomes from wind turbine exposure, taking the pulse of how wind turbines are perceived in light of information that often seems inconsistent or conflicting.

Our research goal is to identify predictors of perceived wind turbine health concerns, including perceptions of causal exposure pathways, as well as create an interdisciplinary stakeholders map to emphasize one health connections and opportunities for future collaboration across Canada and specifically at Western University. It is hypothesized that those who perceive a direct causal exposure path will be most concerned about all health outcome categories in question. To test this, a Canada-wide questionnaire was distributed via quota sampling to self-identified urban and rural residents (n=212 and n=199, respectively), conducted by a Qualtrics(XM) paid panel service. Questions were presented on a 7-point Likert scale to enable a quantitative analysis of a qualitative questionnaire, with predictor variables selected from current wind turbine health risk debates and discussions in the literature, as well as basic socio-demographic factors. Data analysis is ongoing in SPSS software using bivariate and multivariate correlation, subsequently followed by linear regression with variable inputs selected via a stepwise elimination procedure. The one health stakeholders map was created in kumu.io software to demonstrate multidisciplinary connections with key individuals involved in any aspect of wind turbines.

Although analysis and interpretation are currently ongoing, we are confident our results will be completed by the presentation day, and may convey the importance of considering health risk perceptions as an influential factor in social acceptance of wind turbines. Our study findings may serve to improve wind turbine risk communication to effectively address and mitigate potential health concerns, ultimately promoting social acceptance of wind energy in Canada's continued transition to a low carbon economy. It may also serve to increase awareness and opportunity for interdisciplinary collaborations in the creation of sustainable solutions to the unintended consequences wind turbines pose, highlighting the possible benefits of a one health approach.

Presenter's Name: Chaplin, Ava

Additional Authors: Simon A, Kohalmi S

Abstract Title: Impact of the COVID-19 Pandemic on Undergraduate Research in the Department of Biology at the University of Western Ontario: Effect on project types, learning outcomes, and student perceptions.

Abstract:

Introduction: The COVID-19 pandemic has prompted academic institutions across the world to adopt online or blended models of learning. As a result, laboratory and research-based classes, which play a pivotal role in the undergraduate experience of students in the fields of science, technology, engineering, or math (STEM), have been heavily constrained. This study aims to assess how restricted access to laboratories due to the COVID-19 pandemic has impacted: (1) the number and types of undergraduate research projects performed in the Department of Biology at the University of Western Ontario, (2) the experience and satisfaction-levels of students performing these projects, and (3) students' perceived learning outcomes.

Methods: A literature review, an examination of administrative documents, and a survey of over 60 students who completed an undergraduate research project in Biology in the 2020/2021 academic year or in the 4 years prior was conducted to assess the impact of the COVID-19 pandemic on undergraduate research. As well, in keeping with the One Health approach, a stakeholder map was constructed.

Results: Data analysis, which consists of both quantitative and qualitative methods, is still underway although it is expected to be completed in time for the Pathology Research Day.

Discussion: Results from this study will allow for a greater understanding of the impact of the COVID-19 pandemic on post-secondary education and undergraduate students' research experience. Findings may be of use to other departments and educational institutions that are seeking to improve their own undergraduate research courses amidst the COVID-19 pandemic or looking to incorporate experiential-based learning techniques into existing online courses.

Presenter's Name: Grove, Rachael

Abstract Title: Sensitivity of Ontario's Mercury Fish Consumption Guidelines to Methylmercury Variability

Abstract:

Exposure to methylmercury through the consumption of contaminated fish can lead to a variety of neuromuscular disorders in adults and can increase the risk of still birth and development issues for infants who are exposed in the womb. The Ontario Guide to Eating Fish presents guidelines for the safe consumption of fish in Ontario based on measured tissue contaminant levels, including mercury. These guidelines are calculated using the assumption that all mercury is in the form of methylmercury, however, a 2018 study by Lescord et al. found this assumption to be incorrect for smaller fish which often had lower proportions of methylmercury. Based on this finding, my project investigated the degree of sensitivity of current Ontario mercury fish consumption recommendations to different proportions of methylmercury. A critical analysis was conducted to determine how the tolerable daily intake (TDI) values used in the consumption guidelines were calculated, and to determine if these values were still current. A sensitivity analysis was also conducted on fish consumption guidelines for white sucker and walleye from several Ontario lakes to determine if lower methylmercury proportions changed the recommended number of meals per month. It was found that current TDI values primarily draw on data from two studies conducted approximately 20 years ago. It is recommended that further research should be conducted on the human health effects of mercury/methylmercury to determine if these TDI values are still appropriate for use today. The sensitivity analysis revealed that in many lakes, the recommended number of meals per month increased as the percentage of methylmercury decreased, although the degree of change varied among fish species and lakes. Stakeholders who work on topics relating to ecosystem contaminants and human health were also analyzed and many key stakeholders throughout the province were identified. Many individuals in Ontario, especially First Nations communities in Ontario's Far North, rely on fish for a large portion of their diet. The findings of this study should be taken into consideration when creating future fish consumption guidelines to ensure that the guidelines are based on the most recent information available, and to ensure that the recommended number of meals per month are not being over-restricted due to conservative assumptions.

Presenter's Name: Khando, Pema

Additional Authors: Bauer GB

Abstract Title: Survey sex/gender as a proxy measure for uterine or ovarian status: Assessing measurement bias in sexual and reproductive cancer research

Abstract:

Background: There is increasing support for distinguishing between the multiple dimensions of sex and gender which exist. However, most survey data continue to classify respondents according to a single, unclearly defined dimension of sex/gender, which can have the effect of masking critical health findings. Hysterectomy-corrected reproductive cancer research has demonstrated how deleterious this assumption can be, having revealed an underestimation of cervical cancer rates among Black and elderly women. Sex biases within animal models have also contributed validity issues in reproductive cancer research. Canines, in particular, are potentially at high risk of unacknowledged proxy measurement of sex and cancer risk due to the high prevalence of hysterectomy within this population. The purpose of this study is to examine the validity of administrative sex/gender as a proxy for uterine and ovarian status and assess whether and how this may vary across age and ethnoracial groups. Furthermore, we aim to identify and connect key stakeholders to advance sex/gender.

Methods: Sensitivity and specificity were calculated to estimate the validity of administrative sex/gender as a proxy for uterine status and ovarian status across age and ethnoracial groups using data from two large data sets from the U.S. – the National Health and Nutrition Examination Survey (NHANES) and the Behavioral Risk Factor Surveillance System (BRFSS) study. Positive and negative predictive values for the populations have also been calculated. A literature review was conducted to investigate canine hysterectomy research, with attention to the measurement of sex and reproductive cancer risk in canine species. A visual diagram of key stakeholders in reproductive cancer was constructed.

Results: Initial work has been conducted and analysis is currently in progress, but we are confident that results will be ready to be presented on April 7, 2021. We expect to generate base information that can be incorporated by reproductive cancer researchers, including the total proportion of the U.S. population with hysterectomy and oophorectomy among those classified female for survey sex/gender identity, as well as across intersections of race/ethnicity and age.

Discussion: Results from this study will contribute to promoting proxy evaluation to advance understanding of sex and gender multidimensionality.

Presenter's Name: Marginean, Teodora

Additional Authors: Gibson CJ, Olea Popelka FJ

Abstract Title: Emerging from the 'fog of war' – communications and the role of media during COVID-19

Abstract:

The rapid emergence and spread of COVID-19 has led to the greatest global disruption to daily life in the 21st century. During this pandemic, decision-makers have relied on media outlets such as television networks and newspapers to disseminate information about health risks and personal protective directives to concerned citizens. The public looks to these media outlets for clear and concise communication, but messaging from multiple, conflicting sources and authorities have led to mass confusion and frustration. This project examines communications during the pandemic in Ontario to elucidate what messages worked, what went wrong, and what authority or expert groups dominated COVID-19 discourse as sources of information. The research particularly aims to gain deeper insight on the effects of media messaging on public perception and understanding of mask-wearing and restriction directives. An analysis of articles from newspapers representing local and national perspectives will allow for a better understanding of messaging relayed to the public from different authorities, while the creation of a stakeholder map and identification of colleagues working on similar research topics will highlight areas for improvement during this pandemic and future crises. Factiva and Canadian Business and Current Affairs, two news databases, were used to search for and select articles from the Toronto Star (n = 4680) and Globe and Mail (n = 1220). Key information such as headlines, experts mentioned, and tone will be extracted and categorized in Excel. Using grounded theory principles, the content of these articles will be analyzed and coded to identify overarching themes and sub-themes.

Acknowledging the multitude of experts involved in this issue, Kumu.io software will be used to map key stakeholders identified from the database analysis and will elucidate cross-discipline collaborations and involvement in decision-making. Colleagues from Western University will also be identified, and connections will be established to share resources and create potential knowledge translation tools.

These findings will allow us to produce a list of lessons learned that can aid in improving media communications during future crises. Gaps, errors, and successes in messaging will be useful knowledge not only for media outlets, but for public health experts and government authorities. A One Health lens is applied throughout the research project for a multisectoral understanding of messaging regarding human health, animal health, and environmental health.

Presenter's Name: Marshall, Jacklyn

Abstract Title: Duntroon Highlands Golf Club Water Conservation Plan

Abstract:

Golf courses impact many aspects of their surrounding environment including the air, water, soil, landscape, ecology, social aspects, economics, and resources. Pesticide use is common, and although regulated, these pesticides continue to migrate to ponds, groundwater, and nearby streams and ditches. Here, they can pose damage to native aquatic and insect life, and potentially pose a danger to our drinking water and human health. Duntroon Highlands Golf Club is situated within the Blue Mountains Watershed, and water from the course frequently makes its way into Georgian Bay. Due to increasing precipitation events driven by climate change, greater volumes of water are projected to leave the course and enter into Georgian Bay. To mitigate this effect, the amount of water leaving the course must be reduced because this contaminated water is threatening the Georgian Bay ecosystem. A scoping review was conducted to evaluate our current understanding of the threats that golf courses pose to our surrounding environment and the way that these threats are perceived by the public. A list of key stakeholders in this issue were identified and mapped using Kumu.io software. The main goal of this project was to determine how much water would need to be recycled to wash the golf carts. Field work was executed measuring the volume of water that is required to perform this task at Duntroon Highlands Golf Club. These results were then presented along with a scoping review and stakeholder map to the Duntroon Highlands Golf Course as well as Greenland Engineering, a company that designs smart water cisterns and focuses on water recycling. This has promoted the development of a construction plan to capture some of this water and redirect it for practical use, thereby reducing both the overall water use and effect of heavy precipitation of flooding and nutrient run-off. This will conserve water use and reduce the course's run-off into the Georgian Bay ecosystem. Further, this will create a positive shift from the perspectives of the course as both a business and a part of the local ecosystem. Because of Duntroon Highlands' location within the Blue Mountain Watershed, the results of this study provide an example for how other businesses along Georgian Bay can decrease their negative impacts on the people, plants, animals, and shared environment of Georgian Bay.

Presenter's Name: Nichols, Vanessa

Additional Authors: Frisbee, SJ

Abstract Title: Socioeconomic Characteristics in Patient Use of Virtual Cardiac Rehabilitation During COVID-19

Abstract:

Cardiovascular disease (CVD) is the second leading cause of death in Canada and puts a significant burden on our health care system. Cardiac Rehabilitation and Secondary Prevention (CRSP) Programs teach patients how to be more active and make lifestyle changes that can lead to a stronger heart and better health. In response to the COVID-19 pandemic, CRSP programs across Canada have suspended in-person services and have been forced to rapidly transition to remote-only care. This rapid transition means that all aspects of treatment including exercise training, therapeutic education and communication with the care team, are through digital means only. Resumption of patient intake requires a screening and triaging process to maximize limited resources and social return. Patients were subsequently assigned to one of four priority categories [Red, Yellow, Green, Blue] using clinical judgement to assess patient risk and determine eligibility for virtual care.

This is a retrospective cohort study using summary tables of demographic and clinical information from a single CRSP site in Ontario, Canada.

The primary aim of this paper is to analyze the demographic and socioeconomic factors associated with each triage category of patients who utilized CRSP services during the pandemic. These findings can be used to identify vulnerable patient populations who may not engage with virtual programming, yet still require medical care in a changing health care delivery landscape.

Presenter's Name: Nova, Olga

Additional Authors: Olea-Popelka FJ, Kiser P

Abstract Title: A One Health Approach to Human-Altered Environment Enrichment Effects on Stress Response in Laboratory Rodents

Abstract:

Stress and Environmental Enrichment (EE), the stimulatory supplement to animal housing, have been believed to be closely intertwined for several decades. EE has been found to alleviate symptoms and improve health outcomes. However, with the lack of a consensus in defining 'stress', and given the gap in research, it has not yet been established whether EE, as it pertains to and affects stress, can impact study outcomes. The animal stress model is directly impacted by human intervention and environmental influence, thus this interdisciplinary issue benefits greatly from a One Health approach, of which a key focus is the connection of stakeholders. As such, this thesis aims to a) study whether environment-associated stress alters experimental outcome and b) identify relevant stakeholders within and outside of the Western University (WU) community. These objectives are satisfied with a targeted literature review exploring stress and EE in publications that study laboratory rodents, a detailed list of identified stakeholders, and a map that visualizes the connections between these individuals and organizations. Relevant publications are identified through a database search of papers published between 1995 and 2020, then categorized by methodology and results. Relevant stakeholders are identified through Google searches and connections within the WU community, then organized using Excel and mapped using Kumu.io software. The results are currently undergoing analysis and are not yet available but will be ready to be shared at the Pathology and Laboratory Medicine Research Day. The completion of this thesis yields an up-to-date review of current understanding that introduces the human component and highlights the One Health connection. This thesis will contribute to an underrepresented topic and introduce a vital but novel One Health approach, thereby encouraging collaboration between stakeholders and assisting in bridging the gaps between siloed disciplines.

Presenter's Name: Obetta, Chikaodili

Additional Authors: Olea-Popelka FJ

Abstract Title: Knowledge, Attitude and Practices Associated with Zoonotic Tuberculosis in Southwestern Nigeria

Abstract:

Zoonotic tuberculosis (ZTB) is a neglected form of the tuberculosis (TB) disease in humans caused by the bacillus *Mycobacterium bovis*. *M. bovis* is the traditional causative agent of bovine TB (BTB) in cattle and other animals. The negative impacts of ZTB are harmful to public health and the livestock industry worldwide. In 2019, Nigeria accounted for approximately 4.4.% of the estimated TB incident cases worldwide. Challenges posed by ZTB in Southwestern Nigerian communities include a lack of adequate surveillance systems for the pathogen *M. bovis*, poor sanitary and environmental health conditions, lack of knowledge about zoonotic TB and the prevention strategies and the TB associated economic losses in many communities. ZTB depends on the interconnection of humans, animals, and their shared environment; thus, a One Health approach is necessary to address the diagnosis, prevention and treatment challenges of the disease. The main goal of this research project is to evaluate the knowledge, attitude and practices about ZTB in Southwestern Nigeria. Reviewing the awareness, attitudes and risk factors of zoonotic diseases is very critical in facilitating a collaborative One Health approach towards the development and successful implementation of appropriate ZTB prevention and control strategies in communities. To do this, firstly, I will be conducting a literature review of published research articles on ZTB in Southwestern, Nigeria. Secondly, based on the literature review findings, I will be developing an interviewer-administered knowledge, attitude and practices (KAP) survey to be used for the One Health Initiative Project in the Ibarapa Meje region, Oyo State, Nigeria. I will also be identifying and visually 'mapping' key ZTB stakeholders. In doing this, I hope to further understand the complex factors driving the spread of ZTB in Southwestern Nigerian communities as well as to provide base information that will be disseminated to the vital ZTB stakeholders in Nigeria across different disciplines and can be used to promote collaboration aimed at addressing the ZTB challenges.

Presenter's Name: Postill, Gemma

Additional Authors: Olea-Popelka FJ, Daley M

Abstract Title: The Earliest Indication of the COVID-19 Pandemic's effects on Suicides in Ontario

Abstract:

Introduction: The COVID-19 pandemic has impacted mental health through both the uncertainty it creates and the social isolation response. Suicide rates can be used to understand such impacts and if available in real-time, would improve mental health outcomes during the pandemic. Ontario's digital cremation records, which include 70% of all deaths in Ontario, provide a real-time source of mortality data and has been used to estimate all-cause mortality early in the pandemic. The goal of this thesis was to address this need by analyzing cremation data to identify the changes in the number provincial suicides in 2020 compared to the baseline and contextualized these results with a One Health approach.

Methods: The suicide records were identified from the cremation data by manner or cause of death variable in the record utilizing the interpreter Python. The 2020 suicide records were also be assessed for mention of 'COVID-19' in the cause of death text. The records were first separated by year as either 2020 or baseline data (2017-2018). The suicides in 2020 were compared to the baseline in terms of month, sex, age, and geospatial location. A review of scientific and 'grey' literature related to mental health and suicide was conducted to assess the human, animal, and environmental variables that influence suicide rates and the relevant stakeholders who work to reduce suicide rates.

Results: Overall, the results indicated that the pandemic had a protective effect on the number of provincial suicides with 961 suicides in 2020 compared to the 2017-2019 average of 1134 suicides. The only month that showed an increase was September (+5.9% increase over the baseline), with most of the increase occurring the week following Labour Day, which had a +63.2% increase over the baseline. The demographic analysis revealed that the only sex/age groups that showed a percentage increase in the number of suicides were females aged 19-29 years (+5.8%) and females aged 30-44 years (+25.7%). The literature review emphasized the complex mixture of risk factors (unemployment, divorce, and isolation) and protective factors (collective action, companion animals, and social support programs) that contributed to these results. The stakeholder map highlighted the need for integrated action to address the multiple risk factors.

Discussion: This was the first study to utilize cremation data to estimate, in near real-time, changes to the number of suicides in Ontario. These findings demonstrated the utility of cremation data to provide timely mortality information during a public health emergency. These early estimates of suicides are critical for understanding the mental health impact of COVID-19 and also for enabling evidence-based mental health resource allocation. The results are consistent with other literature, which highlights that the pandemic adversely affected women's preferred coping strategies (social support and emotional-focused coping) more than men's preferred coping strategies, making women more vulnerable to the negative mental health impacts of the pandemic. Additionally, the association of suicide rates with economic variable found with the One Health literature review necessitate that cremation records continue to be used to the monitor the effects that continued economic effects of the pandemic such as the discontinuation of CERB.

Presenter's Name: Weppler, Natasha

Additional Authors: McKinley G, Olea Popelka FJ

Abstract Title: Land-Based Therapy: How it Affects Indigenous Well-Being and Mental Health in Canada, New Zealand, and Australia

Abstract:

Purpose: Indigenous peoples face significant health disparities, especially regarding mental health. Mental health policy and programs need to be informed by a One Health approach that understands not just epidemiological evidence, but also community ideals. Land-based healing opportunities are a common practice in Indigenous communities. Land-based healing intertwined Indigenous traditions and culture to address mental health in conjunction with an environmental approach that acknowledges the profound relationship between Indigenous peoples and the Land. By critically analysing evaluated programs, this scoping review identifies the strength of these programs. This review looks at each program and evaluation critically to identify not only the results of the land-based therapies but also to identify research gaps.

Methods: To describe how land-based technology affects the mental health of indigenous peoples a scoping review will be performed to identify key research within the scientific literature. We will use key inclusion criteria to identify the success of these evaluated programs.

Results: Our results show that overall, there is a lack of research being done on Indigenous mental health in general, as well as how land-based therapy affects Indigenous mental wellbeing. The scoping review included searches across 15 different scientific websites and less than 20 articles evaluating land-based programs were identified.

Discussion: These findings show a significant gap in scientific research regarding Indigenous mental wellbeing. The general results of these evaluated programs showed success in land-based therapies but since so few scientific evaluations have been performed and the large variety in programs, it is difficult to come to a complete consensus on the success of land-based therapies.

Keywords: Mental Health, Mental Illness, Mental Wellness, Land-Based Therapy, Pedagogy, First Nations, Indian, Indigenous, Spirituality, Colonization

Presenter's Name: Al Jawhri, MohdWessam

Additional Authors: Kim SJ, Dick FA

Abstract Title: Effects of p38 Mitogen-Activated Protein Kinase induction on RB phosphorylation at the non-CDK sites, S838 and T841

Abstract:

Introduction: The retinoblastoma tumor suppressor protein (RB) is an important cell cycle regulator. The canonical model of RB regulation states that cyclin-cyclin-dependent kinases (CDK) complexes inactivate RB by phosphorylation and permit cell entry into the S phase. Mono-phosphorylation of RB (phosphorylation of a single phosphorylation site) has been shown to impact RB function. Recently, our lab has investigated two non-CDK phosphorylation sites in Jurkat cells, Serine 838/Threonine 841, and discovered that these phosphorylation events are required for Condensin II release from chromatin, a cell-cycle independent/non-canonical role. We hypothesized that conditions of cellular stress will elicit RB phosphorylation at these sites in a p38-dependent manner.

Methods: Jurkat cells will be cultured in suspension and treated under conditions of osmotic shock, oxidative stress, genotoxic stress, and with nocodazole (microtubule destabilizing agent). Whole-cell lysates were prepared after treatment using RIPA lysis. GST-E7 pulldown was performed on the whole-cell lysates to isolate RB. Isolated RB and p38 activation were assessed using immunoblot. RB phosphorylation at the Serine 838/Threonine 841 sites and the effects p38 inhibition on RB phosphorylation will be assessed.

Results: This work will reveal the breadth of circumstances where p38 regulates Condensin II through RB phosphorylation. We anticipate that phosphorylation at the Serine838/Threonine841 sites is p38-dependent under these circumstances, and inhibition of p38 will result in reduced phosphorylation.

Discussion: The results of this study will aid in gaining insight into the breadth of cellular stresses that activate this regulatory effect on RB and Condensin II. This study may then contribute towards characterizing the relevance of p38 signaling to broader RB functions that could be involved in modulating chemotherapeutic sensitivity.

Presenter's Name: Cheong, Ian

Additional Authors: Edmond P, Hildebrand D, Yang L, Rutledge A

Abstract Title: Validation of an enzyme-linked immunosorbent assay for assessing serum B-cell maturation antigen levels in patients with multiple myeloma

Abstract:

Introduction: Multiple myeloma (MM) is a cancer that results from the abnormal proliferation of plasma cells which normally reside in the bone marrow and secrete antibodies. Patients generally present in a premalignant stage, such as monoclonal gammopathy of undetermined significance (MGUS) or smouldering MM (SMM). Currently, serum monoclonal antibody levels are used to monitor patients for progression from MGUS or SMM to full-blown MM as well as their response to treatment. Unfortunately, patients with non-secretory MM cannot be monitored using monoclonal antibody levels and require more invasive procedures to monitor their disease status. Serum B-cell maturation (sBCMA) is an emerging alternative biomarker with the potential to monitor disease status in secretory and non-secretory MM patients. We are looking to: (i) validate an sBCMA enzyme-linked immunosorbent assay (ELISA) for use with the automated EUROIMMUN Analyzer I instrument, and (ii) assess the stability of sBCMA in stored patient serum samples.

Methods: Validation of the EUROIMMUN instrument was done by generating three sets of pooled patient serum as quality control (QC) samples. The QC samples were run on the EUROIMMUN instrument as per the ELISA kit manufacturer's instructions and a standard curve was generated using the BCMA standards provided with the kit. Coefficients of variation (CVs) of the QC samples and recoveries of the standards were calculated to assess precision and accuracy, respectively, of the instrument. BCMA stability was assessed by performing ELISAs on fresh and stored serum samples.

Results: The EUROIMMUN's precision was acceptable, with both the within-run and between-run CVs meeting our target of 20% or less. In terms of accuracy, the instrument generally met our target recovery range of 100% \pm 20%, although the recovery of the lower concentrations was outside of this range. Meanwhile, performing the ELISA manually resulted in improved recovery of the standards. Assessment of BCMA stability is still ongoing, as there were inconsistencies and issues with the quantification of the samples.

Discussion: The EUROIMMUN Analyzer I provides acceptable precision when performing a BCMA ELISA. However, issues with our BCMA stability experiment and the out-of-range recoveries indicate that more work needs to be done in order to improve the accuracy of the instrument.

Presenter's Name: Courchesne, Marc

Additional Authors: Khazaei R, Nygard K, Cumming R

Abstract Title: Examining the Spatial Expression of P66Shc within Brain Tissues of Healthy and Transgenic Alzheimer's Disease Mice

Abstract:

Introduction: Alzheimer's disease (AD) is a neurodegenerative disorder resulting in gradual cognitive dysfunction and memory loss. A major pathogenic factor in AD is oxidative stress triggered by the progressive deposition of toxic amyloid-beta (A β) plaques. The p66Shc adaptor protein has been implicated in potentiating A β -induced oxidative stress by increasing reactive oxygen species generation and repressing antioxidant defense. In this study, we are attempting to determine the cell type specificity, subcellular localization, and regional distribution of p66Shc expression and activation in the rodent brain.

Methods: The spatial expression of p66Shc in transgenic AD mice and healthy mice will be determined using p66Shc specific, cell-type specific, and mitochondrion-specific antibodies combined with immunofluorescence (IF) microscopy. IF staining and imaging of healthy and AD brain tissues from both sexes have been completed. The levels of p66Shc that are colocalized with cell-type and mitochondrion-specific signals are currently being quantified.

Expected Results: We expect that p66Shc expression and activation will be elevated in the brains of AD mice compared to healthy mice for all cell types, especially in neurons due to higher susceptibility to oxidative stress. The localization of p66Shc within the mitochondria is also expected.

Discussion: The results of this study should reveal which cell types in the brains of healthy and AD mice are involved with p66Shc activity, as well as subcellular localization. This study could then provide novel insight into the mechanism of p66Shc in healthy and transgenic AD mouse brains. Elucidating the role that p66Shc plays in the pathogenesis of AD for both sexes could validate p66Shc as a potential therapeutic target.

Presenter's Name: Day, Brooke

Additional Authors: Feng B, Chakrabarti S

Abstract Title: Role of ANRIL in Diabetic Nephropathy

Abstract:

Introduction: Diabetes is a growing health and socioeconomic crisis. Noncoding RNAs (ncRNA) play important roles in diabetic complications, however, the role of these ncRNAs in diabetic kidney fibrosis is not clear. The long ncRNA ANRIL is located at the CDKN2A/B locus, which is a highly susceptible region to human cancers and metabolic disease. Previous work in our lab has reported elevated ANRIL expression in the kidneys of diabetic animals. Here, ANRIL was demonstrated to mediate structural and functional alterations in the kidneys. Further, ANRIL-knockout (ANRILKO) has demonstrated to protect against renal fibrosis. In other systems, including atherosclerosis and cancer, ANRIL is regulated by transcription factors E2F1 and CTCF. A reciprocal relationship between ANRIL and these transcription factors has also been hypothesized. Here, we explored whether ANRIL modulates renal fibrosis in diabetic nephropathy (DN) through the regulation of E2F1 and CTCF transcription factors.

Methods: Renal tissues from ANRILKO and wild-type (WT) mice, both with and without streptozotocin-induced diabetes were used. Real-time quantitative reverse transcription PCR was used to measure mRNA expression of E2F1 and CTCF. The mRNA expression of the extracellular matrix (ECM) protein Collagen 4a1 (Col4a1) was measured as an indicator of renal fibrosis.

Results: Our results showed that Col4a1 expression was significantly increased in WT diabetic mice compared to WT nondiabetic mice. Elevated Col4a1 expression was prevented in ANRILKO diabetic mice. E2F1 expression was significantly reduced in ANRILKO nondiabetic and ANRILKO diabetic mice compared to WT nondiabetic mice. E2F1 expression was also reduced in WT diabetic mice compared to WT nondiabetic mice. Further, CTCF expression was significantly increased in ANRILKO nondiabetics compared to WT nondiabetic mice. CTCF expression was also increased in WT diabetic mice compared to WT nondiabetic mice and reduced in ANRILKO diabetic mice compared to ANRILKO nondiabetic mice.

Discussion: Our results demonstrate that ANRIL regulates mRNA expression of ECM components in renal tissues of diabetic animals and that ANRILKO is protective against renal fibrosis. In addition, the results suggest that ANRIL may play a protective role in regulating E2F1 and CTCF expression in renal tissues in a nondiabetic state. However, the ability of ANRIL to regulate E2F1 and CTCF in renal tissues may be altered during diabetes. These results contribute to our understanding of the regulatory networks through which ANRIL contributes to renal fibrosis. A greater understanding of such networks can assist in the identification of early-stage biomarkers for diagnosis and treatment of DN.

Presenter's Name: Gaur, Amish

Additional Authors: Van Hedger S, Johnsrude IS

Abstract Title: The Effects of Degraded Speech on Long-Term Memory in Individuals with Mild-Moderate Sensorineural Hearing Loss

Abstract:

Introduction: Sensorineural hearing loss (SNHL) is a common form of hearing impairment in which individuals have difficulties in understanding speech sounds. These difficulties are especially prevalent in challenging listening environments (e.g., speech in background noise). It has been suggested that an increased effort required to understand speech in these challenging listening environments may result in a depletion of cognitive resources and can manifest as cognitive decline in the long-term (Rabbit, 1968; Wingfield et al., 2005). This 'effortfulness hypothesis' would thus provide a direct link between hearing loss and cognitive decline. However, research supporting this theory has for the most part been limited to simple materials (e.g., spoken digits). Speech in real life is often more descriptive and meaningful to a listener. Therefore, an increased amount of effort required to understand degraded meaningful speech may actually facilitate a more semantic form of processing (Craik & Lockhart, 1972). In fact, recent research in our laboratory has shown that long-term memory (LTM) for degraded meaningful speech is greater than that for clear speech in normal hearing individuals, provided the speech remains intelligible. Moreover, we have found that the memory benefit for degraded sentences is greater than that for degraded words—suggesting that contextually rich meaningful speech is more available to a greater depth of processing. This study looks to extend these findings by investigating LTM for perceptually degraded speech compared to clear speech in individuals with SNHL.

Methods: We are currently recruiting participants with mild-moderate SNHL and an age matched normal-hearing control group to take part in an online behavioural experiment. In this experiment, participants will listen to two blocks of 48 sentences and 48 words as part of the encoding phase. Half of the materials in each block are degraded with background noise, and the other half is presented in the clear. Intelligibility for the speech materials is assessed in the encoding phase via self-report. Participants are then asked to complete a memory recognition task in which they are presented visually with two blocks of 48 sentences and two blocks of 48 words, half of which are presented for the first time (i.e., "foils"). They are to report if they recognize each presented stimulus from the encoding phase. Memory recognition scores will then be analyzed using a three-factor mixed ANOVA: (noise/clear), (sentence/word), and (SNHL/control).

Results: As of now, 11 SNHL and 11 age-matched control participants have been recruited for this study. We expect that memory for degraded speech will be greater than that for clear speech in individuals with SNHL. We also expect to see a greater memory benefit for contextually rich degraded sentences compared to words. In addition, we do not expect to see a significant difference in results in individuals with SNHL and control participants.

Discussion: These results would suggest that individuals with SNHL may process degraded speech in a similar manner to individuals without clinical hearing loss. Furthermore, these findings would be in contrast to the effortfulness hypothesis and may provide alternative insight on the link between hearing loss and cognitive decline. Thus, we hope that this research will provide valuable knowledge that can be used in the management of hearing loss and cognitive function in the clinic.

Presenter's Name: Goldberg, Polina

Additional Authors: Duennwald M, McDonald D

Abstract Title: Aberrant Mitochondrial Transfer-RNAs contribute to the Pathogenesis of Neurodegenerative Diseases

Abstract:

Introduction: Mitochondria are semi-autonomous organelles as they contain their own circular genomes. Previous research implicates variant mitochondrial tRNA (mt-tRNA) in a number of human pathologies, mainly those involving post-mitotic cells such as neurons. Mutated tRNA-modifying enzymes have also been implicated in human disorders, and the presence of mutated tRNA-modifying enzymes has been shown to cause protein aggregation in yeast cells. These findings have led our lab to investigate the potential role of mistranslating mt-tRNAs and mutated tRNA-modifying enzymes in the pathogenesis of neurodegenerative diseases. Neurodegenerative diseases are a group of disorders that result in a progressive loss of neural structure and function. Protein aggregation is a hallmark pathology of all neurodegenerative diseases, and a mitochondrial role for this pathology has been proposed.

Methods: The organization of mt-tRNAs in mitochondrial genomes (mitogenomes) of several key model organisms will be compared to establish that mt-tRNAs are evolutionary conserved. The incidence of polymorphisms in tRNA-modifying genes and tRNA-specific aminoacyl synthetases will be investigated in clinical cases of neurodegenerative diseases. Finally, we will investigate whether four mistranslating tRNA variants cause protein aggregation in *Saccharomyces cerevisiae* using the Hsp104-YFP reporter system.

Results The number and relative organization of mt-tRNAs in mitogenomes of key model organisms are conserved. Furthermore, there are numerous identified mutations in both mt-tRNA-modifying genes and mt-tRNA aminoacyl synthetases that have been implicated in human neurodegenerative diseases. Finally, no significant increase in protein aggregation in *S. cerevisiae* was observed when co-expressing any of the four mistranslating tRNA variants.

Discussion: This study is an in-depth investigation into the role of both variant tRNAs and variant tRNA-associated enzymes in the context of neurodegenerative diseases. This study also investigates whether or not mistranslating tRNA may contribute to protein misfolding, a hallmark feature of neurodegenerative diseases.

Presenter's Name: Hong, Megan

Additional Authors: Raveendraraj J, Liang O, Abdolmaleki D, Cameron L

Abstract Title: Effect of glucocorticoids on Th2 cell metabolism and mitochondrial ROS production

Abstract:

Introduction: Reactive oxygen species (ROS) have been associated with asthma severity by promoting T helper 2 (Th2) cell-driven inflammation. This elevation in ROS may be attributed to mitochondria dysfunction observed in asthmatics. We have shown that while glucocorticoids (GC) suppress Th2 cell-driven inflammation, they may also counterintuitively promote the expression of some pro-inflammatory genes. Furthermore, GCs may be less effective in women as estrogen can potentiate the pro-inflammatory effects of GCs. The underlying mechanism(s) for these occurrences are not well understood. However, GCs and estrogen could potentiate mitochondria dysfunction seen in asthmatics by altering cell metabolism and lead to increased ROS production. Despite ROS having an important role in T cell function, the effect of GCs on Th2 cell metabolism remains elusive. We hypothesize that GCs will promote mitochondria dysfunction in Th2 cells by shifting metabolism toward oxidative phosphorylation and result in increased mitochondrial ROS production, an effect that will be potentiated by estrogen.

Methods: Immortalized CD4+ T cells (CCRF-CEM) exhibiting a Th2 cell phenotype were treated with dexamethasone, hydrocortisone and/or estrogen receptor alpha agonist, propyl pyrazole triol, for 24 h (n=3-6). Total intracellular ROS was quantified using a CM-H2DCFDA ROS probe with flow cytometry for detection. Expression of mRNA for genes involved in metabolism and redox homeostasis (GSTM3, CYC1, CAT, TXNIP, MYC, LDHA, and SLC38A1) were measured using RT-qPCR.

Results: ROS production was increased in response to GC and potentiated by estrogen. GC decreased mRNA expression of LDHA and MYC that promote glycolysis. Whereas GC increased the expression of TXNIP mRNA that negatively regulates glycolysis. The level of CYC1 mRNA, a gene encoding for complex III of the electron transport chain, decreased in response to GC. The effect of GC on LDHA, TXNIP, and CYC1 mRNA levels was enhanced by estrogen.

Discussion: These results suggest that GCs may increase mitochondrial ROS production by promoting the use of oxidative phosphorylation over glycolysis and/or impairing the efficiency of electron transfer along the electron transport chain. Estrogen was shown to potentiate the metabolic effects of GCs. These findings suggest a possible mechanism of mitochondria dysfunction resulting in increased ROS production from changes in T cell metabolism. This mechanism may explain the paradoxical nature of GC therapy and suggests that estrogen levels may influence the efficacy of GCs.

Presenter's Name: Hu, Xiangtian (Shawn)

Additional Authors: Diao H, Liu Q, Min WP

Abstract Title: DLC1 beta-mediated Regulation of Cardiac Ischemia-Reperfusion Injury in Heart Transplantation

Abstract:

Introduction: Heart transplantation is the gold standard therapy for end stage cardiac diseases. However, donor hearts are susceptible to ischemia-reperfusion (I/R) injury, which may lead to surgical failure and mortality of the recipient. Increased apoptosis, hypertrophy, and deregulated angiogenesis are primary manifestations of I/R injured hearts. Injury progression is directed by PI3K/Akt1, ROCK/Rho kinase pathways; for instance, increased RhoA activity is associated with increased expression of apoptotic proteins. Detailed signalling mechanisms in these pathways remain uncharacterized. One such multi-domain protein, DLC1 beta, is downregulated after I/R injury. This study will investigate the signaling pathways and role of DLC1 beta in cardiac I/R injury. We hypothesized that overexpression of DLC1 beta will reduce the severity of I/R injury.

Methods: H9c2 rat myocardium cell lines will be cultured in vitro with DMEM and FBS; then, DLC1 beta adenoviral vectors will be transfected for DLC1 beta overexpression. GENBAG Anaerobics will be used to simulate ischemia/reperfusion environment by inducing hypoxia. qPCR, Western blot and SYTOX green nucleic acid stain will be used to determine protein expression and cell death under hypoxia.

Results: Our results show cells overexpressing DLC1 beta under hypoxia had decreased apoptosis. It is expected to see decreased RhoA activity in cells overexpressing DLC1 beta.

Discussion: These findings suggest overexpression of DLC1 beta provides protection for cardiomyocytes in hypoxic environments by reducing apoptosis. Reduced apoptosis is likely attributed to DLC1 beta's RhoGAP activity.

Significance: For the first time, this study will define the role and signaling mechanism of DLC1 beta in I/R injury. The results may lead to the exploration of therapeutic potentials of DLC1 beta-targeted I/R therapy.

Presenter's Name: Lee, Wen Shen

Additional Authors: Chin-Yee I, Chin-Yee B, Lazo-Langner A, Iansavitchene A, Istasy P

Abstract Title: Examining the Impact of Artificial Intelligence on Health Equity in Oncology: A Scoping Review

Abstract:

Artificial intelligence (AI) draws from fields such as computer science, linguistics, psychology, and philosophy to develop technology with human-like cognitive functions. The applications of AI are numerous and broad, with some of the most promising benefits occurring in the healthcare sector, especially with regards to cancer diagnosis and patient care. There are also risks to consider, such as the potential for AI to be hacked, the ethical liabilities of AI decision-making, and the widening of health disparities. The literature discusses such advantages and benefits of AI but is limited in elucidating the impact of AI technology on health equity in cancer patients. We hope to address such knowledge gaps and provide insight into how current AI technologies could impact equitable care for cancer patients. We will perform a scoping review to map out the current literary landscape of AI in cancer care and explore its impact on health equity. Literary searches with the electronic databases Medline, EMBASE, and arXiv will be done using keywords relevant to AI, socioeconomic inequity, gender/racial bias, and oncology. Finalized articles will be analyzed and our results will be presented in a qualitative and iterative manner to address project aims. We expect heterogeneous literature, providing evidence for bias in AI technology contrasted with other applications that address health disparities. Currently, we have only screened 2019 article abstracts/titles from Medline, with 93 moving forward to the full-length review. To better prepare for a seamless transition and adoption of AI technology, it is crucial for society to understand the impact of this promising technology. Our study aims to provide a framework for mapping out and identifying trends in the literature on AI and its impact on health equity in cancer patients. In doing so, we hope to also identify knowledge gaps in the literature for future research.

Presenter's Name: Matyashin, Maxim

Additional Authors: Chin-Yee I, Chin-Yee B, Hsia C

Abstract Title: The Impact of SGLT2 Inhibitors on Secondary Erythrocytosis: A Report of Three Cases

Abstract:

Introduction: SGLT2 Inhibitors are a new class of antihyperglycemic pharmacological agents that are used in second-line therapy for the treatment and management of Type 2 Diabetes Mellitus. Increasing use of SGLT2 Inhibitors has created a need to identify and manage potential adverse effects associated with this class of medication. Recent case studies have implicated SGLT2 inhibitors in the development of erythrocytosis that warrants additional investigation. The Division of Hematology at London Health Sciences Centre has further noticed increased referrals of patients on SGLT2 inhibitors presenting with erythrocytosis, and laboratory data from this cohort was collected for review.

Cases: Three patients were include in this series, a 78-year-old male, a 61-year-old female, and a 66-year-old male, all referred to the hematology clinic for erythrocytosis. Two individuals presented with an increase in hemoglobin values following the initiation of their SGLT2 inhibitor. All three cases showed a resolution of the erythrocytosis within 3 months after discontinuation of the SGLT2 inhibitor.

Discussion: The discontinuation of SGLT2 inhibitors is associated with the resolution of the patient's erythrocytosis in three cases. Patients further underwent Next Generation Sequencing testing for myeloproliferative neoplasms, all of which were negative for JAK2 mutations. SGLT2 inhibitor use should be considered part of the differential diagnostic criteria and investigations for erythrocytosis. Physicians need to be aware of this association with these commonly used class of drugs to avoid unnecessary investigation for polycythemia and may consider discontinuation of SGLT2 inhibitors in individuals with elevated hemoglobin.

Presenter's Name: Parlatan, Lara

Additional Authors: Meng D, Kingsley J, Frisbee SJ

Abstract Title: The Impact of Smoking on Achieving Exercise Goals in Patients Participating in a Cardiac Rehabilitation and Secondary Prevention Program

Abstract:

Cardiac rehabilitation and secondary prevention (CRSP) is an evidence-based, cost-effective outpatient program intended to improve health and functioning and reduce risk of future disease events for patients diagnosed with cardiovascular disease (CVD), including those who have recently experienced a cardiac event (i.e., heart attack, surgery or device implantation). Two fundamental pillars of CRSP programs are supported smoking cessation (SSC) and increasing the achievement of exercise capacity and activity, defined as an increase in 0.5 metabolic equivalents and an achievement of 150 minutes of physical activity per week, respectively. Despite the importance of achieving both of these therapeutic goals, little is understood about the relationship between smoking and exercise and attaining successful outcomes by patients participating in CRSP. Therefore, the goal of this current study is to examine the role smoking plays in the achievement of exercise goals in CRSP.

To investigate this research goal, we conducted a retrospective-observational-cohort study of patients participating in CRSP at the Central East Local Health Integration Network in Ontario, Canada, between 2012-2019. REB approval was obtained, at both the Scarborough Health Network and the Western University HSREB, to conduct a secondary data analysis of patient health information maintained in the region-wide patient management system. It is estimated that approximately forty-thousand patients were referred to CRSP between 2012-2019 and will form the basis of the analysis in this current study. As part of their intake evaluation, patients self-reported their smoking status; this information will be used to stratify patients into smoking and non-smoking patients, and smoking patients will be further stratified into those who accept SSC and those who refuse. The proportion of patients who achieve the measured exercise outcomes by the end of the CRSP program will be analyzed for each group (non-smoking patients, smoking patients involved in SSC, and smoking patients not involved in SSC). Additional patient factors, including socio-demographic and health factors, will also be evaluated. It is hypothesized that patients who accept SSC as part of their six-month CRSP program will have better exercise outcomes than those patients who participate in CRSP but do not accept SSC. As well, non-smoking patients will have better exercise outcomes than smoking patients.

The significance of this research lies in understanding if and how SSC can improve CRSP outcomes for care decision making. For example, it may be necessary to invest resources to develop more individualized care plans for smoking patients within CRSP, so that they are better able to achieve successful exercise outcomes and overall improvements to their health. Better CRSP outcomes will reduce the likelihood of CVD progression, leading to a better quality of life for the individual. At a societal level, better CRSP outcomes lead to a decrease in the financial and health care burden of CVD.

Presenter's Name: Prajapati, Rahil

Additional Authors: Toyon A, Chang-Kit B, Frisbee SJ

Abstract Title: Evaluating Quality Indicators (QIs) and Outcomes of Care in Diabetic and Non-diabetic Patients enrolled in Cardiac Rehabilitation and Secondary Prevention (CRSP) programs within the Central East Local Health Integration Network (LHIN)

Abstract:

Diabetes mellitus is one of the world's largest global health challenges of the 21st century. Patients with diabetes have increased risk factors for cardiovascular disease (CVD), resulting in elevated morbidity and mortality. Cardiovascular Rehabilitation and Secondary Prevention (CRSP) programs are known as the "standard of care" for CVD patients and effectively reduce CVD morbidity and mortality. However, CRSP is generally underutilized and importantly, the care is not standardized resulting in a lesser benefit to morbidity and mortality rates. Quality indicators (QIs) and outcome measures have been developed by Grace et al., 2014 to aid in standardizing CRSP patient care by evaluating the quality of care which can be used to bridge gaps in CRSP patient care to further reduce CVD morbidity and mortality. This study aims to evaluate the quality and outcomes of care provided specifically to diabetic patients enrolled in a CRSP program to evaluate whether patient care matches the increased risk faced by these patients. We will characterize the health profile of diabetic patients in CRSP programs and identify variation in outcomes of care compared to non-diabetic patients through a comprehensive literature review. Data collected from the Scarborough Health Network (SHN) CRSP program in Central East Local Health Integration Network (LHIN) will be used to compare quality indicators and outcome measurements between diabetic and non-diabetic patients enrolled in CRSP to evaluate their quality of care. Variation in QIs and outcome measurements over time between the two populations will also be considered. Data will be analyzed through various statistical methods including student's t-tests, analysis of variance (ANOVA), and multivariable linear regression. Although we expect quality indicators to suggest that the quality of care between diabetic and non-diabetic patients is similar, it is expected that outcomes of care are overall lower in diabetic compared to non-diabetic patients. This is implicated by a sedentary lifestyle and higher BMI, characteristic of diabetic patients. A decrease in quality of care over time in diabetic patients is also expected due to the increasing prevalence of diabetes worldwide resulting in an increased workload on healthcare providers. Although there has been extensive research into specific outcome measures in diabetic patients such as exercise capacity, or specific CVD conditions such as coronary heart disease, there are few to none evaluating quality of care and a wide variety of outcome measures. This study will be the first to holistically evaluate quality indicators and outcome measures in a diabetic population enrolled in CRSP. Results from this study may be used to target areas of weakness and to improve the quality of CRSP care in the diabetic population, with the goal of significantly reducing morbidity and mortality from diabetes and CVD. This study may also spark interest from other groups worldwide to evaluate quality of care and improve CRSP programs for better patient outcomes.

Currently, primary no data from SHN has been evaluated yet, thus most of the presentation may instead be relevant to a scoping review of the current literature regarding diabetic patients' outcomes in CRSP our team is conducting.

Presenter's Name: Qian, Yu Chen

Additional Authors: Ni R, Peng T

Abstract Title: Developing novel ssDNA aptamers targeting receptor binding domain of SARS-CoV-2 S-protein for potential diagnosis and therapy uses

Abstract:

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), more commonly known as COVID-19, is a novel contagious respiratory virus discovered in 2019. The spike proteins of SARS-CoV-2 bind to angiotensin-converting enzyme 2 (ACE2) on human cell membranes and allow for viral entry into the host's cells. Currently, therapeutic interventions are non-specific, and detection methods remain costly and time-consuming, but DNA aptamers may potentially solve these problems. ssDNA aptamers spontaneously fold into unique 3D structures and can bind target proteins with high affinity and specificity. We have created, PCR-amplified, and purified an ssDNA library composed of random oligonucleotides 90 base pairs in length. Using systematic evolution of ligands by exponential enrichment (SELEX) technology, we will isolate the aptamers with the greatest affinity and specificity for the SARS-CoV-2 S-protein. Interaction of ssDNA aptamer with SARS-CoV-2 S protein RBD will be determined using Enzyme-Linked Aptamer Assay (ELAA) and Western Blot. Finally, we will determine whether ssDNA aptamer(s) targeting SARS-CoV 2 S-protein RBD inhibits the virus from binding to ACE2. Using antibodies and Western Blot, we will evaluate the effects of ssDNA concentration on SARS-CoV-2 S-protein RBD interaction with ACE2. These aptamers have the potential to be developed into low-cost and precise novel diagnostic and therapeutic tools for COVID-19.

Presenter's Name: Ryan, Sarah

Additional Authors: Sidahmed A

Abstract Title: Cytokine and Chemokine Levels in Immunocompromised and Immune-Competent Covid-19 Patients and Correlation to Clinical Outcomes

Abstract:

The Coronavirus disease 2019 (Covid-19) is caused by respiratory infection by severe acute respiratory syndrome coronavirus 2. Previous studies have shown that cytokine release syndrome (CRS) may be implicated in the pathophysiology of Covid-19. CRS is caused by the elevation of pro-inflammatory cytokines and chemokines. It is unknown whether immunocompromised Covid-19 patients experience elevations in cytokine and chemokine levels. We hypothesize that chemokine and cytokine levels will be lower in immunocompromised Covid-19 patients compared to immune competent Covid-19 patients. Furthermore, we hypothesize that cytokine and chemokine levels will be correlated to disease severity and clinical outcomes. We will conduct a literature search on PubMed and Western Library's Omni databases. Included will be observational studies which include patients receiving treatment for rheumatological conditions, patients with solid organ transplants, or patients with hematological malignancies. Studies involving patients in registered clinical trials for Covid-19 therapeutics or vaccines will be excluded. We expect immune competent patients to exhibit higher levels of cytokines and chemokines than immunocompromised patients. We then expect that elevated inflammatory biomarker levels be correlated to clinical outcomes and disease severity. The findings of this study could contribute to finding pharmacological therapeutics to target the Covid-19 immune response and elucidate the pathophysiology of Covid-19. The findings could also translate to clinical practice to identify at-risk patients for Covid-19 complications or more severe disease.

Presenter's Name: Tong, Jaryd

Additional Authors: Lazo-Langner A, Chin-Yee B, Chin-Yee I

Abstract Title: Improving Diagnostic and Epidemiologic Detection of SARS-CoV-2

Abstract:

SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) is an RNA virus that has infected people in over 200 countries and territories dating back to December 2019. The virus belongs to a family of coronaviruses which have a zoonotic origin and it is thought that the virus originated from bats and made the jump to humans. The virion consists of many structural proteins, the main one being the spike protein which facilitates entry of the virus into our cells, allowing the RNA virus to be released into the cytoplasm of our cells. Due to the infectious nature of the disease, it is essential for rapid and accurate testing to be conducted. Currently, the gold standard for testing is Nucleic Acid Amplification Testing (NAAT), which relies on laboratory techniques such as RT-PCR. Although testing has been successful, there are still issues such as costs and sensitivity that need to be addressed. Our study aims to create a diagnostic algorithm, combining clinical information, laboratory information and serological tests, to create different risk categories for SARS-CoV-2 positivity, using the NAAT as the gold standard. The clinical and laboratory information was analyzed using two-tailed T tests and 2x2 contingency tables to determine if there are significant differences between patients that are positive for SARS-CoV-2 and those that are negative based on the NAAT. Serological values were used in comparison to the NAAT test to create Receiver Operating Characteristic (ROC) curves. Logistic regression models are currently being created using SPSS to construct a model that can accurately create risk groups to determine if a patient is positive for COVID-19. We expect to be able to create a model combining clinical, laboratory and serological values that can predict COVID-19 positivity. We are currently in the stages of testing different models in SPSS and some serological cut-off values have shown some results that could be applicable to a model; however, we are continuing to run statistical models to create one that is feasible and accurate. COVID-19 is still very prevalent and the costs of doing PCR testing can be fairly expensive.

Therefore, by creating a diagnostic algorithm that can be close to as accurate as PCR testing, it can be used as a preliminary step to determine if a patient is at high risk for COVID-19, where a confirmatory PCR test would be done, or if they are low risk and no further testing would be needed at the time.

Presenter's Name: Wang, Tan Ze

Additional Authors: Warsi A, Rong K, Greasley A, Li S, Lin K, Zheng X

Abstract Title: Differential expression of circular RNAs in septic peripheral blood mononuclear cells

Abstract:

Sepsis is the leading cause of death in intensive care units (ICU), characterized by a dysregulation of the immune system in response to infection. Sepsis is associated with alterations in genomic expression in leukocytes, which can potentially be the basis for novel interventions. Circular RNAs (circRNAs) are a class of highly stable, covalently closed single-stranded RNA that is implicated to alter gene expression and contribute to many diseases. Previous research has established the upregulation of circRNAs in blood leukocytes of sepsis patients compared to healthy controls, yet specific circRNAs that contribute to the development of sepsis remain unknown. The current study seeks to identify circRNAs in peripheral blood mononuclear cells of sepsis patients that are differentially expressed between ICU admission and discharge, and to investigate their biological functions. PBMCs were isolated from three sepsis patients before and after intensive care. Total RNA was extracted from PBMCs with Trizol and subjected to RNA sequencing. Differentially expressed circRNAs were identified using circRNA annotation programs. We found 94 up-regulated and 3 down-regulated circRNAs in PBMCs collected at ICU admission compared with ones at discharge. Gene ontology analysis revealed that the altered circRNAs were associated with immune cell activation and regulation, specifically the Fas and RAS pathways. Looking at the ratio of circRNA to linear RNA expression, we found 56 up-regulated and 13 down-regulated circRNAs after normalization to the expression of their linear counterparts. We then validated 4 of the most significantly altered circRNAs by qRT-PCR. It was found that circular RNA S100A9 (circS100A9, which is back-spliced from the S100A9 gene) is the most differentially expressed circRNA in PBMCs of sepsis patients between ICU admission and discharge, and significantly upregulated at ICU admission, which is consistent with the RNA sequencing results. The precise role of circS100A9 in sepsis is under investigation. Furthermore, we compared different circRNA annotation programs used to analyze our RNA-seq data. We found that different programs generated significantly different expression profiles. The results generated by bowtie and STAR were more consistent with qRT-PCR results. In conclusion, circRNA expression profiles are strikingly different in septic PBMCs between ICU admission and discharge, suggesting that circRNAs may participate in sepsis. These findings support the role of circRNAs as potential targets for novel genome-based treatments for sepsis.

Presenter's Name: Xu, Yili

Additional Authors: Xu Y, Figueredo R, Krishnamoorthy M, El-Hajjar M, Gerhardt L, Maleki S

Abstract Title: Effects of mismatch repair deficiency on MHC class I expression and interferon signalling in neuroblastoma and melanoma cells

Abstract:

Introduction: Highly immunogenic tumors often have higher tumor mutational burden (TMB) and respond better to immune checkpoint blockade immunotherapy. DNA mismatch repair (MMR) deficiency is a common cause of increased TMB and can be induced in cancer cells by knocking out components of the DNA MMR pathway, such as MLH1. By inducing MMR deficiency in cells, it may be possible to increase the immunogenicity of tumors and sensitize them to immunotherapy. However, it is currently unknown how antigen presentation in tumor cells is affected by induced MMR deficiency. Recent work in our lab showed that the induction of MMR deficiency in Neuro-2a mouse neuroblastoma cells resulted in an increase in the surface expression of MHC class I. Here, we aim to further elucidate which components of the MHC-I and interferon signalling pathway are affected in tumors with induced MMR deficiency. We hypothesize that MMR-deficient cells express higher levels of MHC class I molecule components and have increased activation of the interferon response pathway compared to their MMR-proficient counterparts.

Methods: Neuro-2a neuroblastoma and B16-F10 melanoma cells, as well as their respective clones with MLH1 gene knockout to induce MMR deficiency, were used. MMR-deficient (dMMR) and MMR-proficient (pMMR) cells were cultured for two different time periods (8 weeks and 14 weeks for Neuro-2a cells, 8 weeks and 16 weeks for B16-F10 cells) to allow for the accumulation of mutations. Cells were lysed and intracellular levels of MHC class I, TAP1, JAK1, JAK2, phospho-JAK1, and phospho-JAK2 were determined by western blot analysis.

Expected Results: We expect to see higher levels of MHC class I, TAP1, JAK1, JAK2, phospho-JAK1, and phospho-JAK2 in dMMR cells from both cell lines compared to pMMR cells. In addition, we expect that cells cultured for longer periods of time (14 weeks for Neuro-2a, 16 weeks for B16-F10) will also have higher levels of MHC class I, TAP1, JAK1, JAK2, phospho-JAK1, and phospho-JAK2 compared to cells cultured for a shorter duration of time.

Discussion: Findings from this project will help characterize the response of cancer cells to induced MMR deficiency and may help further our understanding of potential mechanisms that contribute to higher immunogenicity in MMR-deficient tumors. This project contributes to the exploration of induced MMR deficiency in tumor cells as a strategy to improve immune checkpoint blockade.

Presenter's Name: Zhang, Ruo Hao

Additional Authors: Khan ZA

Abstract Title: Carboplatin induces Wnt Signalling in Angiogenesis-Mediated Ovarian Cancer Resistance

Abstract:

Introduction: Despite significant improvements in the prognosis of many solid cancer types, survival rates post-high grade serous ovarian cancer (HGSOC) diagnosis have remained low over the last 30 years. Chemotherapy resistance is prevalent and particularly common in recurrent disease. Both the Wnt/ β -catenin developmental pathway and angiogenic signalling are known to be upregulated in chemoresistant HGSOC cells, contributing to resistance to its standard treatment: carboplatin. However, the connection between Wnt and angiogenic signalling in the development of resistance is yet to be elucidated. We thus hypothesize that carboplatin treatment induces the Wnt pathway, changing angiogenic factor expression in a mechanism that promotes the survival of epithelial ovarian cancer cells.

Methods: To investigate Wnt induction, we used immunofluorescence microscopy to identify nuclear β -catenin staining in HGSOC tissues before and after treatment with carboplatin. Additionally, carboplatin induction of the Wnt pathway in HGSOC was measured by culturing cells from the COV362 line with carboplatin treatments (0, 25, 50 μ g/mL). qPCR analysis of Wnt pathway proteins AXIN2, WISP1, and CCND1 was conducted. As well, pro-angiogenic factor expression in the cells will be quantified using qPCR analysis.

Results: We expect to see increased β -catenin nuclear reactivity in chemotherapy-treated tissues. It is also expected that the Wnt pathway will be upregulated after carboplatin treatment, as shown by an increase in key Wnt pathway gene mRNA levels. Furthermore, it is expected that mRNA levels will increase for pro-angiogenic genes in response to Wnt pathway activation.

Discussion: The results of this study can contribute towards identifying the mechanism of chemoresistance in HGSOC, integrating current knowledge about Wnt/angiogenesis induction. Results may indicate novel targets for tumour surveillance and therapy and suggest future avenues for research in other tumours treated with carboplatin.