Undergraduate Research Symposium

April 7th, 2023

U-M Chemistry Building Lower Atrium

930 N. University Ave, Ann Arbor, MI 48109

Undergraduate Research Symposium

Friday, April 7th 2023

10:00 AM - 4:00 PM

Chemistry Building Lower Atrium

University of Michigan

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Program Schedule

Note: *All presenters must check in 10 minutes prior to the beginning of their session.*

Time	Activity
10:00 AM -10:55 AM	Session A
11:00 AM -11:55 AM	Session B
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3:00 PM - 3:55 PM	Session F

SCHEDULE OF PRESENTATIONS

POSTER SESSION A

10:00 AM - 10:55 AM

Poster 1

Presenter: Prakhar Gupta
Contributing Authors: Gaurav Kaul
Advisor: Ada Eban-Rothschild (Psychology)
Developing Computer Vision Tools for Automatic Animal Behavioral Classification

Automating the classification of animal behavior is a major challenge in neuroscience. In recent years, machine learning and computer vision techniques have become part of the neuroscience toolkit for the high-throughput study of animal behavior. While progress has been made, existing strategies for behavior classification require the preprocessing step of keypoint prediction. Keypoints, which are 2D coordinates that describe locations of body landmarks (e.g., snout, hindlimb), are a useful abstraction scientists often go through because tools for keypoint estimation are accessible, and keypoints are a high signal to noise abstraction for describing an animal's position and locomotion–and are easy to represent. While keypoints carry a lot of relevant signals for reasoning about complex locomotion sequences, we hypothesize that the raw RGB video data itself could be invaluable for reasoning about behaviors since many behaviors of interest are visually indicated. We will compare behavior classification strategies that directly predict behaviors from RGB video (without the abstraction of keypoints), to existing methods that utilize keypoints. To do so, we will construct a dataset of animal behaviors, along with thorough validation of the various classification strategies on our behavior classification dataset. We anticipate that RGB video behavior classification models will perform competitively with models that go through the abstraction of keypoints when classifying behaviors.

Poster 2

Presenter: Sean Richards
Contributing Authors: Maximilian Hesselbarth
Advisor: Jacob Allgeier (Ecology and Evolutionary Biology)
Behavioral diversity increases primary production more than species diversity in a seagrass ecosystem

Primary production is driven by species-level attributes that dictate nutrient supply rates by consumers. Yet species-level traits are complex, thus understanding which traits most promote production is imperative to quantify the importance of biodiversity for ecosystem processes. Using a model artificial reef (AR) seagrass bed system we test species physiology and behavior's effects on seagrass production and how these two aspects of diversity interact at the community-level to drive production. ARs introduce three-dimensional structure to seagrass beds, initiating a feedback whereby fish excrete nutrients, alleviate nutrient limitations, and increase seagrass production. We quantified physiology and behavior's effects on ecosystem primary production by simulating two populations of reef fish under all combinations of physiology and behavior. Parameter swapping

indicated that behavior had a greater effect on production than physiology. Populations of exclusively recyclers had greater production than populations of exclusively foragers, but forager populations caused more production per nutrient excreted. We then simulated mixed behavior communities at all combinations for a population. Production was greatest when communities were diverse, at an optimal ratio of ~6 recyclers:1 forager. Our findings show that behavior is more important than physiology for mediating primary production in a nutrient poor ecosystem and that community diversity substantially enhances production.

Poster 3

Presenter: Alexa Goldstein
Contributing Authors: Jiayue Huang
Advisor: Anish Tuteja (Materials Science and Engineering)
Developing Icephobic Surfaces for Aircraft Industry Applications

Current deicing technology in aircraft industries includes both air and fluid methods. Thermal and bleed air technology utilizes heated air to remove ice from planes in order to minimize hazardous conditions on an aircraft surface. Commonly, antifreeze is applied repetitively to the aircraft which is both time intensive application and environmentally toxic. This study aims to improve the deicing process by using alternative surface solutions to both minimize the interfacial shear strength at smaller ice lengths and minimize the surface interfacial toughness to initiate crack propagation of larger area-independent ice sheets. By measuring the force required to remove various ice lengths from a surface, the relative ice adhesion strength can be calculated to a range where deicing technology becomes area independent. Surface design also allows for the possibility of using organic polymers which match the thermal hysteresis properties of antifreeze but are not environmentally toxic as shown by differential scanning calorimetry analysis. Product design improvements will limit ice adhesion strength and interfacial toughness while employing a fabrication process for surfaces with practical industrial applications.

Poster 4

Presenter: Michelle Song
Contributing Authors: Christina Capobianco, Easton Farrell, Alexis Donneys, Karen Kessell, Alexander Knights, Tristan Maerz
Advisor: Kurt D. Hankenson (Orthopaedic Surgery)
CD47 Deficiency Blunts the Early Immune Response Following Fracture

During fracture healing, immune cells are recruited to the injury site to debride damaged tissue and facilitate healing. CD47 is implicated in mediating macrophage polarization towards a pro-regenerative phenotype. We are interested in how CD47 facilitates the early fracture healing response. To interrogate this we used WT and CD47-null mice and performed bi-lateral transverse tibia fractures. Single-cell RNA-seq was used to profile immune cell populations in the fracture callus at 4 and 7 days post-fracture. We first performed unsupervised clustering (UMAPs) of all fracture callus samples using Seurat. We then isolated the immune populations to investigate differences in the WT and CD47-null conditions. In the absence of CD47, we observed an overall reduction in the immune response, evidenced by decreased proportions of several immune populations and a decrease in gene ontology terms involved in immune cell function across the populations. We identified a

decrease in macrophages at 4 days post-fracture and reductions in immune cell signaling pathways. We confirmed our scRNA-seq results with flow cytometry where we observed broad decreases in CD45+ hematopoietic cells, specifically denoting less Ly6+ neutrophils and CD11c+ F480- dendritic cells under a CD47 deficiency. Overall, our findings reveal that under CD47-null conditions, mice are unable to mount a robust initial immune response, which likely underpins the inferior fracture healing observed in these mice.

Poster 5

Presenter: Fiona Corcoran

Advisor: Elizabeth Tibbetts (Ecology and Evolutionary Biology)

Field-realistic exposure to neonicotinoid pesticide impairs visual and olfactory learning in paper wasps

Neonicotinoid pesticides impair learning and memory in non-target species such as Apis mellifera and Bombus bees, which can negatively affect their ability to forage. Previous work has primarily focused on assessing neonicotinoid effects on olfactory learning in harnessed bees. Less is known about effects in other taxa or in free-moving learning assays. Here we studied how an acute exposure of neonicotinoids influences olfactory and visual learning in free-moving Polistes fuscatus paper wasps. Wasps were exposed to a single, field realistic oral dose of either low dose imidacloprid (0.5 ng), high dose imidacloprid (2.0 ng) or sulfoxaflor (20 ng). Then, visual and olfactory learning was assessed. We found that neonicotinoids influenced learning, as sulfoxaflor and high dose imidacloprid wasps made fewer correct choices than control wasps. Notably, both visual and olfactory learning were similarly impaired by neonicotinoid treatment. Wasps treated with high dose imidacloprid were also less likely to complete the learning assay than wasps from other treatment groups. Instead, wasps remained stationary and unmoving in the testing area, consistent with imidacloprid impairing motor control. Finally, wasps treated with sulfoxaflor had lower survival than wasps in the other treatment groups. Our findings demonstrate that sub-lethal, field-realistic dosages of neonicotinoids can significantly impair learning and may have additional effects on survival and motor functioning.

Poster 6

Presenter: Mary Dwan

Contributing Authors: Brianna Dobbs

Advisor: Chin Hwa (Gina) Dahlem (Nursing)

Process and Outcome Evaluation of Recovery Opioid Overdose Team Plus (ROOT+): A Post-Overdose Community Outreach Program Utilizing Peer Recovery Coaches

Background: Post-overdose interventions have increased in popularity in response to rising overdose deaths. Programs utilizing Peer Recovery Coaches (PRC) to engage survivors through providing access to social services, harm reduction, recovery, and treatment resources have improved survivor outcomes.

Objective: Evaluate the process and outcomes of the Recovery Opioid Overdose Team Plus (ROOT+), a community post-overdose program led by PRCs in Washtenaw County.

Methods: After ROOT+ receives notification of an overdose, PRCs contact survivors within 72 hours in the hospital and follow up in the community. The RE-AIM (Reach, Effectiveness, Adoption, Implementation, Maintenance) Framework was used to evaluate ROOT+ data from December 1, 2020-August 31, 2022.

Results: ROOT+ responded to 335 unique overdose referrals. Clients were predominantly male(69%; n=229/331) and white(53%;n=176/265), with a median age of 37 years (range 18-81). From the 42.4% (n=142/335) engaged survivors, 10% (n=14) were engaged, 7% (n=10) were in recovery, and 10% (n=13) were in treatment after 90 days. The remaining survivors stopped engaging or had yet to engage (73%; n=103) or had deceased (1%; n=2).

Conclusion: The ROOT+ program successfully engaged individuals post-overdose to promote harm reduction and treatment uptake, demonstrating the impact of community based and PRC led quick response teams.

Poster 7

Presenter: Megan Coden
Contributing Authors: Kelly L. Sovacool, Sarah E. Tomkovich, Vincent B. Young, Krishna Rao
Advisor: Patrick Schloss (Microbiology and Immunology)
Predicting Clostridioides difficile infection severity based on the composition of the gut microbiome

C. difficile infection (CDI) can lead to adverse outcomes including ICU admission, colectomy, and death. The composition of the gut microbiome plays a role in determining colonization resistance and clearance upon exposure to C. difficile. We investigated whether machine learning (ML) models trained on gut microbiome compositions could predict which CDI cases led to severe outcomes. We collected 1,191 stool samples from CDI patients on the day of diagnosis and characterized their gut microbiomes via 16S rRNA gene amplicon sequencing. We processed and clustered the sequences into de novo OTUs, which we used to train ML models for predicting whether a severe outcome occurred according to three different severity definitions. We learned that our OTU-based random forest models perform best when predicting attributable severity, defined as an adverse outcome within 30 days of CDI diagnosis confirmed as attributable to CDI following clinical chart review. This suggests that chart review is valuable to verify the cause of severe outcomes. We used permutation importance to identify which OTUs contributed most to model performance and found that Enterococchus, which is known to be positively correlated with C. difficile colonization, was the largest contributor. In all, our results show that ML models can modestly identify patients at risk for CDI, which may allow healthcare providers to personalize treatment options to protect higher risk patients and ultimately improve CDI outcomes.

Poster 8

Presenter: Perla Fares
Contributing Authors: Ali Srour, Suvranta Tripathy
Advisor: Kalyan Kondapalli (Natural Sciences)
NHE9-mediated endosomal pH regulation impairs SARS-CoV-2 infection

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of the COVID-19 pandemic. Treatment options are currently limited. A thorough understanding of host cell factors involved in viral entry is essential to develop therapies. SARS-CoV-2 relies on the acidity of endosomes to infect cells, which is crucial for spike protein cleavage and fusion with the host endosomal membrane. Here, we describe a novel role for endosomal pH in trafficking SARS-CoV-2 from the cell periphery to the late endosomes, following endocytosis. Endosomal pH is maintained by the proton pump V-ATPase working in concert with counter-ion fluxes and proton leak pathways. Sodium proton exchanger NHE9, is an endosome-specific proton leak pathway. NHE9, encoded by the interferon-inducible gene SLC9A9, has been linked to an increased risk of severe COVID-19, indicating a possible involvement in the body's defense against SARS-CoV-2. Consistent with this, we observed a decrease in SARS-CoV-2 infection with an increase in NHE9 expression. We used total internal reflection fluorescence (TIRF) microscopy to track individual endosomes transporting spike protein bound to ACE2 receptors, in real-time. We found that luminal alkalization by NHE9 hinders directed motion of endosomes and promotes early detachment from microtubule tracks. In sum, NHE9 offers a unique opportunity for endosome-specific regulation of luminal pH and has potential as a therapeutic target for SARS-CoV-2 infection.

Poster 9

Presenter: Fairooz Oudeif

Contributing Authors: Sanat Modak, Siddhant Singh

Advisor: David Kwabi (Mechanical Engineering)

Nuclear Magnetic Resonance Characterization of Electrolytes in Organic Redox-Flow Batteries

Organic redox-flow batteries are projected to be safer, more cost-effective, and longer-lasting for grid energy storage in comparison to the present-day Li-ion systems. These batteries require the use of organic redox-active molecules such as quinoxalines. Current studies nevertheless indicate that many of these molecules undergo rapid degradation leading to capacity loss. Therefore, it is important to study and understand the degradation mechanism and its kinetics in order to devise strategies for its mitigation. In this work, we use a combination of electrochemical and spectroscopic techniques to discern the kinetics of quinoxalines decomposition. Specifically, proton nuclear magnetic resonance (H-NMR) is used to determine the kinetics of the degradation mechanism as a function of redox potential. H-NMR is used to enable inferences about their chemical structures of decay products present in solution over time. Our measurements enable us to infer rate constant of the degradation mechanism of 2,3-dimethyl-quinoxaline-6-carboxylic acid (DMEQUIC), which is known to result in a lower battery voltage, and thus a progressive loss in the energy density of a flow battery that deploys DMEQUIC as a positive electrolyte. We expect that our work will help to evaluate hypotheses that have been put forward in the literature about the relationship between rate of the degradation mechanism and a quinoxaline reduction potential.

POSTER SESSION B

11:00 AM - 12:00 PM

Poster 1

Presenter: Ellis Mason

Contributing Authors: Jennifer Goldschmied, Angela Jang

Advisor: Joshua Buss (Chemistry)

Soluble Silica: Targeting Silicate Ligand Structures as Models of Surface Organometallic Active Sites

Small molecule activation–the conversion of recalcitrant substrates to useful chemical feedstocks and fuels–is practiced on tremendous scales industrially, employing solid-state catalysts that typically operate at high temperatures and pressures. One of the most widely demonstrated catalytic supports is silica (SiO2), which forms strong surface to metal covalent linkages via a range of silanol moieties present on the silica surface. The harsh operating conditions and lack of structural uniformity complicate mechanistic studies of heterogeneous catalysts in operando. To garner insight into these critical industrial processes, this research targets the preparation of organic ligands that emulate a silica surface. Electronically, this requires electron-deficient silicon centers, enabled by exclusive Si–O connectivity. Sterically, large blocking groups are required to inhibit self-condensation reactions and the generation of heterogeneous silica. Through strategic molecular design, we seek to capture these key components of silica-supported heterogeneous catalysts. Subsequent coordination chemistry and reactivity studies will illuminate mechanism and structure/function relationships to inform the next generation of catalyst design. These observations are anticipated to enable more specific and efficient catalytic reactions.

Poster 2

Presenter: Claire McDermott

Advisor: Sandeep Pradhan (Electrical Engineering and Computer Science)

Minimum Finding Using the Quantum Singular Value Transformation

The quantum singular value transformation (QSVT), introduced in [GSLW19], is an algorithm that applies a polynomial transformation to the singular values of an arbitrary matrix block-encoded within a larger unitary. This algorithm was shown to unify multiple seemingly unrelated quantum algorithms, and provides a simple framework for the development of novel quantum algorithms. We present an overview of a QVST-based algorithm for finding the minimum element within an unstructured database, first describing a method to load and represent this data within a block-encoded matrix under the assumption of QRAM access, then discussing the polynomial used within QSVT to extract the minimum element. Finally, we analyze the time and space complexity and accuracy of this algorithm, and provide a discussion of areas for further research on this topic.

Poster 3

Presenter: Hassen H. Reda

Contributing authors: Siddika N. Radi, Molly R. Lesko, Sonya P. Merced, Dunia F. Abou-Ghaida
Advisor: Christopher Alteri (Natural Sciences)
Defining a Role for the Bacterial Type VI Secretion System during Territorial Conquest

Urinary tract infection is the second most common bacterial infection. Proteus mirabilis is a leading cause of catheter-associated UTI. P. mirabilis is also characterized by its swarming motility. During swarming, P. mirabilis will distinguish non-identical swarms by forming a boundary between populations known as a Dienes line. We have previously shown that Dienes lines result from the killing activity of the type VI secretion system (T6SS). We first used a catheter bridge model to assess P. mirabilis swarming on commercially available catheters, and found that colonization was similar across five catheter types. We used this catheter bridge model to assess any advantage conferred by the T6SS including the energetic cost of expressing the T6SS for the ability to take over agar territory following simultaneous crossing of separate catheter bridges. Three strains of P. mirabilis were used: wild-type HI4320 (killer and never a victim), 9C1 an immunity mutant (never a killer always a victim), and a T6SS mutant (never a killer and never a victim). Our findings indicate that the benefit of the T6SS may be conditional with respect to taking territory post-catheter and the benefit is significant when the target cell is unable to return fire. Interestingly, we found that to form a Dienes line, half of the total population at the boundary between swarms have to be killed. These findings also indicate that a killer bacterium is capable of eliminating up to 1,000 victim bacteria.

Poster 4

Presenter: Hattie Benedetti
Contributing Authors: Alexandru Lordan
Advisor: Dr. Patricia Reuter-Lorenz (Psychology)
Evaluating the Benefits of Verbal Working Memory Training in Individuals with Mild Cognitive Impairment

Working memory (WM) is a fundamental cognitive capacity that declines with age, and this decline is further exacerbated in older adults (OA) with mild cognitive impairment (MCI). Recent evidence suggests that training improves WM performance in healthy OA, but it is unclear whether similar effects are observed in individuals with MCI. In the present study, participants with amnestic-MCI (aMCI) completed a ten-day WM training program and additional neuropsychological (NP) tasks. During training sessions, participants completed six rounds of an adaptive verbal WM task, which adjusted based on performance. NP tasks were administered once before, and once after training. We predicted that training gains from the WM training task would be indicated by a significant increase in mean set size achieved from session 1 to session 10. Supporting this prediction, a large effect size for the aMCI group revealed significant WM performance improvements on the WM training task after ten training sessions. Cognitive training also has the potential to generate gains in additional cognitive domains, known as transfer. Our results suggest that the current training program was beneficial in improving WM performance for individuals with aMCI, but there were limited findings of transfer effects in this population. Investigating the real-world benefits of cognitive training in OA diagnosed with cognitive impairment is important to assess the ecological impacts resulting from training programs.

Poster 5

Presenter: Erica Griffin

Contributing Authors: Simi Neeluru
Advisor: Sarah Reeves (General Pediatrics)
Sickle Cell Disease: A Case for Racism and Disparities Within Healthcare

As stated by the CDC, sickle cell disease (SCD) affects an estimated 100,000 people in the United States. This genetic blood disorder can lead to several life-long health problems and reduced life expectancy. Individuals with SCD face many systemic barriers to care, such as structural racism, given that over 90% of persons with SCD are people of color. Despite this, the connection between racism and SCD is often not made. This project was conducted to understand the impact that racism and disparities can have on SCD care.

The project was informed by a literature review utilizing phrases relevant to SCD and racism in health care, such as "sickle cell disease", "health disparities" and "barriers to care". The literature review was conducted via various online databases such as PubMed and the University of Michigan Library Database.

People with SCD face barriers in almost every aspect of healthcare. Individuals suffer from the stigmatization of pain, low rates of preventive care, high hospital readmission rates, mistrust and provider bias, and low quality and limited access to care.

SCD is a condition that affects all aspects of life, and the added racial and healthcare disparities make it difficult to access equitable and trusting care that individuals with SCD deserve. Understanding health care utilization of those living with SCD and collaborating with the community is important in identifying gaps in treatment within the healthcare system and reducing barriers to care.

Poster 6

Presenter: Susan Hammoud
Contributing Authors: James Douglas Engel, Sharon A. Singh, Xiaofang Liu, Alejandra Sanchez-Martinez
Advisor: Sharon Singh (Pediatric Hematology)
Novel Pathways Contributing to Erythroid Failure in Diamond Blackfan Anemia

Diamond Blackfan Anemia (DBA) is a rare, inherited bone marrow failure syndrome that manifests as a variably penetrant macrocytic anemia, which can spontaneously enter remission. RPL5 is a commonly mutated gene in DBA and is associated with severe outcomes such as decreased spontaneous remission and morphological defects. Our previous work characterized a Rpl5 haploinsufficient (Rpl5Skax23-Jus/1/+) murine model and demonstrated an erythroid differentiation block at E12.5. To investigate pathways involved in erythroid failure in our model we performed bulk RNA-Seq on E12.5 fetal liver comparing mutant and WT mice. Differential expression analysis revealed several genes that exhibited significant up/down regulation, most notably Scd1. Gene ontology enrichment analysis demonstrated that dysregulated genes appear to be connected through role in metabolic function. To further validate findings in human cells, we generated RPL5 haploinsufficient HUDEP-2 cells using CRISPR. Beta actin was determined to be the most accurate housekeeping gene to normalize our data as it gave ~50% Rpl5 mRNA levels in mutant cells compared to WT. RT-qPCR was then

conducted to confirm preliminary RNA-Seq findings. Results show 50% downregulation of Scd1 levels in E12.5 mouse erythroid progenitors. Next, we'll measure SCD1 expression in our HUDEP-2 model. We will also validate other dysregulated genes and pathways significantly identified in RNA-Seq data that may be involved in DBA erythroid failure.

Poster 8

Presenter: Karan Kamath
Contributing Authors: Hanjoo Kim, Sara Moss-Pech
Advisor: Elizabeth Duval (Psychiatry)

Gender Differences in Social Anxiety Disorder Response

Social anxiety disorder (SAD) is characterized by a fear of social or performance situations and physical reactions (e.g., sweating). Physical symptoms can be measured through skin conductance response (SCR), an indirect measure of the body's unconscious fight-or-flight activity. It's important to understand whether factors such as gender or sex play a role in SAD. Previous literature shows that females show stronger responses to emotional faces than males (Killgore, 2001), and that females have a larger measured brain response than males to emotional faces (Orozco, 1998). In this study, we asked whether differences exist in physiological responses to affective faces between men and women with SAD, as measured by SCR. We predicted that women would have higher average SCR amplitudes than men. Participants included 44 adults with SAD, 30 women and 14 men, aged 19-60 (M = 27.02, SD = 9.45). Participants completed a face rating task, viewing happy, neutral, and angry faces, while SCR was collected via electrode disks. Independent t-tests were used to compare men and women's average SCR amplitudes for each affective face type. Results indicate there were no statistically significant differences between men and women when presented with happy faces (p=.145), angry faces (p=.370), and neutral faces (p=.949). Results suggest gender may not play a role in SAD responses. Future studies would benefit from a larger sample size, as this study may have been underpowered to detect results.

Poster 9

Presenter: Caitlin Hoyng
Contributing authors: Krisztina Fehervary, Megan Ewing

Night Sweats as Pillow Talk: Community Care for Sex Workers, Queer People, and Noncitizens in 1980s-1990s Berlin, AIDS, and a Little Bit of Context. A Multimodal and Oral History.

In 1980s East Berlin, sex workers, queer people, and noncitizens lived an uneasy existence under Stasi surveillance, or between double lives. Sex workers, who serviced international clientele and converted currency on the black market, lived in danger of exposing their work; officially, sex workers didn't exist in the East. Those who did became valued informants on clients for the Stasi. Queer people in East Berlin had more social leeway, but under a presumption: Don't talk about sexuality. Many gay men entered heterosexual marriages for

safety—a protective factor during AIDS. Noncitizens were alternatively barred from employment and recruited for work, while unable to bring family. For them, testing positive for HIV constituted deportation.

During the epidemic, these communities' stigmatized identities put them at higher risk for infection, while furthering the spotlight for surveillance or stigma. Post-Reunification, Eastern HIV activists sought to incorporate the viewpoints of queer socialists (who felt the GDR "obscured [their] ultimate wisdom" with surveillance) into mutual aid efforts—stigma against the East, however, created a barrier. Using German history, anthropological theory, and interviews with Berlin's sex workers, queer people, and noncitizens, this thesis will create an oral history on how everyday people determine what care means to them. My analysis focuses on mutual aid, art, and memories, and functions as an exploratory gathering of voices and locations.

POSTER SESSION C

12:00 - 1:00 PM

Poster 1

Presenter: Ahsan Ahmed
Contributing Authors: Wanqing Cheng
Advisor: Yu Leo Lei (Rogel Cancer Center)
We will assess whether morphine restricts the IFN-I system by promoting potassium efflux.

Recent findings show that chronic opioid use is associated with downregulation of IFN-I signatures. However, the mechanism of this observation remains unclear. Recent clinical data suggests that morphine medication is a significant risk for worse outcomes for patients receiving Immune checkpoint blockade (ICB). Thus, it is critical to characterize how opioids modulate the innate immune sensors. According to a centralized gene portal that aggregates an extensive array of gene annotation resources, BioGPS, the receptor for morphine, MOR, is highly expressed in macrophages, in agreement with earlier studies. The activation of MOR results in potassium efflux as a mechanism of its G protein coupled receptor activation. Recent evidence shows that potassium efflux restrains the STING-IFN-I pathway. Thus, we will assess whether morphine antagonizes the IFN-I system in a potassium-dependent fashion. We will also map the engagement of morphine with several classes of innate immune sensors to establish signaling specifically for the better targeting of morphine tolerance.

Poster 2

Presenter: Kayla Kaminski
Contributing Authors: Michael Kaminski
Lactate As More Than A Biomarker of Anaerobic Respiration in Critical Illness: Narrative Review

Background: In the context of critical care, lactate (La-) is often conceptualized as a by-product of anaerobic or ischemic conditions ---> high lactate=low oxygen which fails to acknowledge its complex, and often beneficial role in the human body.

Methods: A narrative review was conducted in December 2022 to explore the beneficial effects of lactate during critical illness. The PubMed and Cumulative Index of Nursing & Allied Health Literature (CINAHL) databases were queried.

Results: The astrocyte to neuron lactate shuttle triggers neuroplasticity associated pathways that encode for brain derived neurotrophic factor (BDNF). Antidepressant effects are associated with the peripheral administration of L-lactate: increased serotonin, neurogenesis, nitric oxide production, astrocyte function and cAMP signaling pathways. Administration of lactated ringers reduced muscle atrophy, depression, and cognitive decline; this effect was enhanced during caloric deprivation. Lactate is a neuronal energy source, affecting excitability, memory consolidation and neuroplasticity. Injection of lactate-releasing polymers (local or systemic) into mice with ischemic wounds improved angiogenesis and procollagen activation.

Discussion: The “high lactate, low oxygen” paradigm does not acknowledge the beneficial role of lactate as an energy source or signaling molecule, and fails to address its neuroprotective effects, contribution to ischemic wound healing and maintenance of circadian rhythm.

Poster 4

Presenter: Andres Bonilla

Advisor: Kristen Verhey (Cell and Developmental Biology)

Kinesin Motor Proteins and their Influence on Microtubule Modifications

The microtubule network is an integral part of cell structure and function, being responsible for maintaining structural integrity and playing a vital role in mitosis. Microtubules are composed of subunits called tubulin, which are found in two forms, alpha and beta.Alpha and beta tubulin can form a dimer, which are then strung together to create protofilaments. The arrangement of protofilaments in a cylinder then creates the microtubule. Tubulin subunits within a microtubule can also be subject to post-translational modifications, but how specific tubulins or microtubules are selected for modification is unknown.

Kinesin motor proteins are able to attach to cargo, and transport them utilizing two domains that ‘walk’ across microtubules in an anterograde direction utilizing an ATP-driven process. While microtubules have been known to play roles in regulation and other cell processes, the methods in which these multiple roles are managed is not well understood.

Recent studies have outlined the concept of the tubulin code, which states that modifications and changes within tubulin, the subunits for microtubules, are signals for functionality. Our hypothesis outlines that as kinesin motors come into contact with microtubules, the motors’ walking motion could possibly induce post-translational modifications, which, in turn, influence microtubule function. This project outlines a survey of kinesin motors and their influence on tubulin PTMs in cultured cells.

Poster 5

Presenter: Omar Abdalla

Contributing authors: Alexander Knights

Advisor: Kurt Hankenson (Orthopedic Surgery)

Modulation of Wnt signaling in osteoblast formation

According to the CDC over 32.5 million adults in the US suffer from osteoarthritis (OA), presenting a significant public health and economic burden(1). Post-traumatic osteoarthritis (PTOA), a subtype of OA, develops following joint injury and is a multifaceted disease that manifests as synovial inflammation, cartilage degradation, subchondral bone remodeling, and critically, formation of painful bony spurs in the joint, termed ‘osteophytes’.. Members of the bone morphogenetic protein (BMP) family are potent stimulators of bone formation agonist of interest to researchers studying PTOA, and there is growing evidence that the canonical Wnt signaling pathway is a pathological mediator of PTOA as well(2,3,4). It has been previously proposed that BMP and Wnt signaling may operate synergistically in bone formation (5) however the mechanisms

underpinning this interaction have not been defined. In this proposal, we look to assess the effect of modulating Wnt signaling on BMP-mediated differentiation of the cells that form bone – osteoblasts.

Poster 7

Presenter: Nadir Al-Saidi
Contributing Authors: Mita Varghese, Ramkumar Mohan, Simin Abrishami
Advisor: Kanakadurga Singer (Pediatric Endocrinology)

Investigating the role of sex in adipocyte and adipose tissue macrophage cross talk

Metabolic and non-metabolic comorbidities associated with obesity and diabetes have become more prevalent in both sexes, yet our understanding of the hormonal mechanism driving these diseases is still limited. Current therapies are being developed under the assumption that males and females respond to obesity in the same way, however more recent studies have found clear evidence regarding sex-specific differences, especially in obesity-induced inflammation. Sex is a factor driving differences in immune responses and, thus, should be accounted for when studying metabolic disease. While there are multiple factors that might influence sex differences including social, behavioral, sex-specific, and sex hormone-related differences, sex hormones specifically – primarily testosterone, estrogen, and the balance of the two – and their contribution to the pathology of obesity is less clear. This study aims to explore the importance of androgens' contribution to inflammatory responses associated with obesity and diabetes via in vivo studies with mice on a high-fat diet (HFD). Studies presented use androgen receptor knockout mice (ARKO) on HFD and as bone marrow donors in bone marrow transplants (BMTs). In addition to these animal models, this study implements in vitro experiments to understand the sex differences in the crosstalk between myeloid cells – which drive obesity-induced inflammation – and adipocytes.

Poster 8

Presenter: Emily Wallace
Contributing authors: Jacqueline Larouche, Bonnie Spence, Eric Buras, Carlos Aguilar
Advisor: Carlos Aguilar (Biomedical Engineering)

TGFβ inhibition engenders pro-regenerative immune and stem cell localization after volumetric muscle loss

Volumetric muscle loss (VML), the loss of a large mass of muscle, overwhelms skeletal muscle's innate regenerative ability, leading to inflammation, fibrosis, and reduced muscle function. To support the development of efficacious regenerative therapies for VML, we aim to better understand the molecular and cellular basis of regenerative dysfunction.

We recently observed that after VML, the transforming growth factor beta (TGFβ) signaling pathway is hyperactivated. To investigate this, we used immunohistochemical staining to spatially map cell localization in VML defects before and after TGFβ inhibition. We induced VML injuries in mice and administered ITD1, a TGFBR2 inhibitor, and saline (vehicle) in opposite limbs. Harvested tissues were stained with DAPI, laminin, and a cell type identifier for macrophages, fibro-adipogenic progenitors (FAPs), or MuSCs. We defined three morphological tissue areas – intact muscle, the defect, and a transition zone – then quantified cell presence in each.

This revealed that in VML, MuSCs and FAPs inhabit the transition zone, and macrophages and FAPs occupy the defect. Absence of MuSCs in the defect suggests that the local microenvironment facilitates their exclusion. ITD1 treatment increased mø defect infiltration and reduced FAP but improved MuSC presence in the transition zone. TGFβ inhibition also enabled MuSC infiltration into the defect, suggesting changes in the biochemical milieu that support MuSC-mediated regeneration.

Poster 9

Presenter: Sofia Dziechciarz
Contributing Authors: Stephen DeAngelo
Advisor: Yatrik Shah (Molecular and Integrative Physiology)

Investigating the Role of GPX4 in Colorectal Cancer

Glutathione peroxidase 4 (GPX4) is an enzyme whose primary function is to protect cells against oxidative stress and damage. GPX4 is expressed in a wide variety of tissues such as the liver, kidney, and colon. In colorectal cancer, GPX4 is upregulated, resulting in significant increases in cell proliferation and decreased levels of oxidative stress, demonstrating that GPX4 could have a promising therapeutic role in this disease. GPX4 has also been shown to regulate ferroptosis, a form of non-apoptotic programmed cell death dependent on high levels of iron and reactive oxygen species. To gain a deeper understanding of GPX4's role in ferroptosis and colorectal cancer we have created several doxycycline-inducible hairpins which selectively knock down GPX4. While colorectal cell lines are broadly sensitive to the GPX4 inhibitor RSL-3, we observe varied responses from direct GPX4 knockdown. As several family members of GPX4 also correlate with survival trends in colorectal cancer, we hypothesize that RSL-3 may have off-target activity towards one of these enzymes. To address this hypothesis, we are creating inducible knockdowns of other glutathione peroxidase family members to assess their potential roles in colorectal cancer.

POSTER SESSION D

1:00 - 2:00 PM

Poster 1

Presenter: Nicole Baalbaki

Contributing Authors: Misché A. Hubbard, Kody G. Whisnant, J. Scott VanEpps

Advisor: Nicholas Kotov (Chemical Engineering)

Chiral modulation of phenol soluble modulin self-assembly

Staphylococcus aureus biofilms have been implicated in numerous nosocomial and community associated infections worldwide. The virulence of S. aureus biofilms is dependent on the secretion of short, amphipathic peptides called Phenol-soluble modulins (PSM). PSMs provide a structural scaffold for S. aureus biofilms through fibrillation into amyloid-like fibers. Besides biofilm structuring, PSMs have other biological functions including triggering an inflammatory response, lysing mammalian cells, and show antibacterial activity towards other microbes. In this work, chiral carbon nanoparticles (CNPs) are explored for their enantioselective effect on the self-assembly process of PSM peptides. We assess the physicochemical properties of PSMα1-4 after co-incubation with chiral CNPs both as individual peptides and mixed together. With this, the fibrillation kinetics of nanoparticle-treated PSMs are assessed and the secondary structure is analyzed using circular dichroism. TEM images reveal asymmetrical hierarchical self- assembly of PSMs and chiral CNPs into supramolecular structures.

Poster 2

Presenter: Gabriela Ivonne Lopez-Salgado

Geogrid reinforcement can reduce the execution cost of road construction projects in Michigan

In the state of Michigan, wire mesh is used for concrete reinforcement in road and sidewalk construction, sometimes having embedded systems. While it has always been used in industry, it is a material that requires much work to handle and that can be a significant additional expense. It is tedious studying materials that can provide concrete with reinforcement in accordance to state specifications, be easy to work with, and not increase the square footage construction expense. Thus, I conducted break tests to measure the flexural strength and calculate the compressive strength between concrete utilizing wire mesh reinforcement versus geogrid reinforcement at 3, 6, and 62 days of age utilizing a personally designed and built embedded system to simultaneously study vibrations and temperature within concrete, as well as the effects of collecting data with epoxy coated and non-epoxy coated electronic components. During each break test, one of the slabs had wire mesh while the other had geogrid reinforcement, and one would have epoxy coated sensors while the other had non-epoxy coated sensors. This study could help the Michigan Department Of Transportation (MDOT) and construction companies in the state of Michigan have a better production of construction projects at a lower cost, given that currently a small fraction of owners utilize reinforcement because it increases expenses per square footage in flatwork.

Poster 3

Presenter: Cesar Martinez

Contributing Authors: Ali Kutlu, Andrew Skurer, Angela Zhang, Audrey Hoelscher, Dana Beseiso, Gyan Farrell Culag

Advisor: Rachel Niederer (Biological Chemistry)

Translational control of gene expression by 5' untranslated regions of mRNA in yeast

Gene expression is regulated through multiple levels including the transcriptional, translational, and post-translational level. Translational control is an important mechanism for modulating gene expression and thus protein output. One of the key translational regulators of gene expression is the 5' untranslated region (5' UTR) of mRNA. Previous research has shown that genes have different promoters that result in mRNAs containing alternate 5' UTRs of different lengths. Furthermore, it was shown the expression of these genes was affected by these alternate 5'UTR isoforms. However, the specific features of these 5' UTR isoforms that cause these differences in gene expression require further investigation.

In this project, we aimed to identify regulatory features of 5' UTRs responsible for translational control of the YJR034W gene. To achieve this, we generated recombinant plasmids containing a luciferase reporter, and alternate 5' UTR isoforms of our gene of interest. We then made systematic mutations throughout the unique sequence of the long 5' UTR. Next we utilized a luciferase reporter assay to measure protein expression in yeast and determine how mutated 5' UTRs affected gene expression. By mutating the 5' UTR, this experiment will provide insight into the mechanisms of translational control of gene expression by 5' UTRs.

Poster 4

Presenter: Livia Fredrick

Contributing Authors: Christina Capobianco

Advisor: Kurt Hankenson (Orthopaedic Research Laboratories)

Absence of CD47 correlates to an increase in endothelial cells in the early fracture callus

Angiogenesis, the development of new blood vessels, is essential for proper fracture repair. Previous studies have demonstrated that inhibition of new blood vessel growth leads to delayed bone healing. Importantly, CD47, a ubiquitously expressed transmembrane protein, has been implicated in the regulation of blood vessel formation. Further, a CD47 deficiency leads to increased angiogenesis and non-bone tissue repair. We hypothesized that during bone healing, CD47ko will lead to increased blood vessel formation in the fracture callus. To interrogate this, we performed immunofluorescence staining to look at the blood vessel markers, CD31 and endomucin (EMCN). Here, we characterize the blood vessels involved in the fracture healing process and blood vessel density in different regions of the fracture callus. CD31+ or EMCN+ cell density in regions proximal and distal to the fracture site were compared in wild-type and CD47ko mice. Representative images from each region were analyzed using the Vessel Analysis plugin in ImageJ. Two to four images per region were taken due to callus morphology. We observed a significant increase ($P<.05$) in CD31+ and EMCN+ cell density in the CD47ko mice in distal regions. This difference was not found in proximal regions. Further analysis at later time points (day 7) will reveal the growth of these vessels as the callus develops. Identification of CD31/ EMCN double-positive cells will also help to identify the blood vessels and their functions.

Poster 5

Presenter: Zeinab Bezih

Contributing Authors: Perla Fares, Habiba S. Shamroukh, Muaaz Akhtar, Kalyan C. Kondapalli

Advisor: Suvranta Tripathy (Natural Sciences)

Luminal pH regulates the force kinetics of motor proteins on phagosomes

Microtubule based transport enables phagosomes to fuse with endocytic organelles. This leads to acidification of phagosomes essential for degradation for entrapped microbial pathogens. Our recent published research showed that the luminal pH of phagosomes regulated by sodium proton exchanger, NHE9, can impact transport of phagosomes. Specifically, we demonstrated that an increase in luminal pH leads to significant decrease in the processive movements and run length without effecting the velocity. To expand on these observations and characterize the impact of luminal pH on the kinetics of the motor protein generated forces, we engineered stable overexpression of NHE9 in the well-established macrophage cell line, RAW264.7 and conducted optical trapping experiments at single-molecule resolution on 800 nm carboxylate-coated polystyrene beads, phagocytosed by RAW 264.7 cells. Here we present that increased luminal pH by NHE9 overexpression caused significant impairment in generating larger forces on late phagocytosed beads and a reduction in the average binding time of dynein. In addition, the average force generated by kinesin motors towards cell periphery was enhanced. These observations imply that increased luminal pH of phagosomes inhibits phagosome maturation process by modifying the mechanics of motor proteins. These findings have significant implications for our understanding of macrophage mediated immune response.

Poster 6

Presenter: Brandon Hutchison

Contributing Authors: Amelia Felkowski, Kale Stahl

Advisor: Aditya Viswanathan (Mathematics and Statistics)

Edge Detection from Phaseless Measurements

We consider the problem of edge detection from phaseless measurements, a question that occurs in a variety of applications such as optical microscopy and speech processing. Traditionally, the process of recovering a complex-valued specimen (vector, signal, function, etc.) given access to magnitude-only measurements is referred to as phase retrieval. Edge detection is the discrete analog to finding jump discontinuities within functions of a continuous variable. Solving either problem is a nontrivial endeavor, and it is our goal to solve them simultaneously. We present a method which detects edges directly from phaseless data via semi-definite programming. By appealing to the sparse structure that a vector of edges should possess, we are able to identify jumps within a discretized, piecewise smooth function without having to recover the entire function first.

Poster 7

Presenter: Danielle Moon

Contributing Authors: Han Kyoung Choi, Shuqun Qi, Jun-Lin Guan

Advisor: Fei Liu (Biologic and Materials Sciences and Division of Prosthodontics)

Role of autophagy in osteoblast activity of femur bone development in Fip200-4A knockin mice

Fip200 is an autophagy-essential gene with both autophagy-dependent and independent functions. Despite its understood function in many cell types, its role in osteoblasts in skeletal and craniofacial bone development is unclear. Our previous work showed the deletion of Fip200 gene in osteoblasts leads to osteopenia; however, it is unclear to what extent the loss of Fip200's functions decreases bone mass. To address this, we generated a novel FIP200-4A mutation in which residuals of FIP200 were mutated to disrupt its autophagy-dependent function but preserve its autophagy-independent functions. We used a novel mating scheme to generate conditional Fip200 knockout (CKO) mice and FIP200-4A knockin (CFKI) mice, collected at 2 months. Cortical area, TMD, BMD, body weight, and femur length showed a significant decrease in CKO and CFKI mice, suggesting cortical bone relies on autophagy-dependent functions. Trabecular BV/TV of CKO female mice had a significant decrease compared to the control, with a significant increase in trabecular spacing in CKO versus CFKI mice, suggesting that loss of female trabecular bone is impacted by Fip200's autophagy-independent function. No significant difference was seen in the trabecular BV/TV of male mice among the groups. In conclusion, Fip200's autophagy-dependent function has differential contributions to femur phenotypes, and will further our knowledge of bone development-related issues, perhaps providing a mechanistic basis for new therapeutics.

Poster 8

Presenter: Tara Tekkey

Advisor: David Kohn (Dental School and Biomedical Engineering)

Impact of Exercise on Perilacunar Remodeling and the Osteocyte Lacunar Canalicular Network in Bone

Bone is a dynamic and complex tissue capable of modeling and remodeling its structure in response to sustained mechanical loads. Understanding how exercise contributes to bone strength and quality provides a basis for developing treatments toward improving bone constitution. In bone, remodeling is heavily influenced by the osteocyte lacunar canalicular network (OLCN), which consists of osteocytes and their dendritic extensions that facilitate intercellular communication. Previous studies in diabetic disease models have shown decreased bone strength, as well as diminished network connectivity, increased lacunae sphericity, and decreased number of osteocyte dendrites as well as lacunae and canaliculi, despite a lack of change in bone mineral density. Although there is prior research on how exercise mediates perilacunar remodeling and bone composition, the impact exercise has on the OLCN remains unknown. Using an exercise mouse model, changes in the OLCN were quantified and analyzed, including lacunae morphology and osteocyte connectomics.

Poster 9

Presenter: Anya Singh

Contributing Authors: Eryn Arble, Andrew Giles

Advisor: Jody Lori (Global Affairs Office at the School of Nursing)

Preparing Nursing Students for an International Immersion Experience Program

The UMSN and Salokaya College partnered in 2012 as a realization of the needs of a global-minded education. While the program was interrupted in 2020, the next program will begin July 2023. The paper explores the

planning of the clinical, experiential 4-week program.. It will encompass the development process, orientation, cultural-education considerations, and program itinerary.

The development process had major considerations: pre-program education, addressing clinical, academic and cultural exposure goals. The program was developed to 1) give UMSN students orientation, 2) allow students to experience differences between healthcare systems through observations in clinical fields like hospitals, community health centers, and NGOs, 3) allow students to learn about the Indian nursing education system by pairing UMSN students with Salokaya students, 4) allow students to explore culture and society through historical sites and community tours.

The program development and orientation materials are nearly completed; the Orientation will occur in mid-April.

In an increasingly interconnected society, global considerations are critical in developing culturally competent nurses. While COVID-19 interrupted the global exchange of ideas and people, partnerships have been restored and are working to improve past programs through the incorporation of more structured programs to emphasize learning goals and targets for UMSN students.

POSTER SESSION E

2:00 - 3:00 PM

Poster 1

Presenter: John Yin
Contributing Authors: John Moldovan
Advisor: John Moran (Gastroenterology)
Embedded Alu sequences can facilitate processed pseudogene formation

Processed pseudogenes (PPs) are non-functional copies of genes that are generated through the reverse transcription of messenger RNA (mRNA) by the Long INterspersed Nuclear Element (LINE-1) reverse transcriptase protein, ORF2p. LINE-1 is a retrotransposon that can insert copies of itself into new genomic locations by a copy-and-paste mechanism termed retrotransposition. The LINE-1 ORF2p protein can also mobilize short interspersed nuclear element (SINE) RNAs (e.g., Alu) and to a lesser extent other cellular RNAs (e.g., mRNA). Evidence suggests that Alu RNA can localize to ribosomes that are actively translating L1 RNA, which allows Alu RNA to effectively compete with the L1 RNA for ORF2p binding. However, how mRNAs and other cellular RNAs are able to gain access to ORF2p remains unclear. Using cultured cell retrotransposition assays, we show that a human AluY RNA sequence embedded within a larger mRNA transcript can promote the retrotransposition of an enhanced green fluorescence protein (EFGP) mRNA transcript. Additional retrotransposition assays show that an embedded AluJ sequence can also promote the retrotransposition of EGFP mRNA. In sum, our data suggest that Alu sequences embedded within larger mRNA transcripts can promote the formation of PPs. PPs play an important role in genetic diversity with some PPs playing essential roles in human development and tumor formation. This study could help future studies identify host factors that are important for PP formation.

Poster 2

Presenter: Nathaniel White
Contributing Authors: Steven Havens
Advisor: Wenjing Wang (Chemistry)
Computational Optimization of Receptor-Ligand Complexes

The Rosetta suite of bioinformatics and structural biology software holds significant promise in optimizing nanobody structure and various other tools employed by the Wang lab. It will be used in conjunction with the great lakes supercluster to compute the binding energies of various protein structures. These calculations are used in conjunction with experimental methods to identify and test the best structures as predicted computationally. Current results indicate significant improvement in the binding stability MOR-Opioid peptide complex, serving as proof-of-concept for the method.

Poster 3

Presenter: Katherine Morrissey
Contributing Authors: Siqi Li
Advisor: Bart Bartlett (Chemistry)
Photochemical Alcohol Oxidation with Inorganic Mediators in Ambient Conditions

Increasing energy consumption and the reliance of industrial processes on petrochemicals lead to heavy demands for nearly exhausted fossil fuels. Photocatalytic bio-alcohol oxidation is a tool that can be used as a replacement for these demands by generating value-added products from biorenewable resources under solar irradiation. However, prevention of overoxidation of aldehyde products remains a key challenge. Halogen mediators like chloride are candidates to combat this challenge. It has been previously demonstrated that the selective electrochemical oxidation of ethanol to 1,1-diethoxyethane (DEE) can be carried out using a chloride mediator that provides a faster rate and requires a lower energy input. Additionally, the mediated oxidation of alcohols using CdS has been previously reported using nitrate ion as a mediator. Such observations provided the impetus to investigate using the CdS photocatalyst for chloride-mediated oxidation of bioethanol to DEE. With an adapted solvothermal reaction, CdS nanowire has been prepared. To couple alcohol oxidation with hydrogen gas generation, CdS-1%NiS heterojunction material is prepared via a microwave synthesis. XRD measurement confirmed the purity and phase of the Wurtzite CdS. With GC analysis, it is found that the presence of chloride significantly accelerates the formation of DEE and H2. Current efforts focus on the kinetic and mechanistic study of such AOR-HER reaction.

Poster 4

Presenter: Evan Hall
Contributing Authors: Rogerio Pinto
Advisor: Gideon Bradburd (Ecology and Evolutionary Biology)
Checking the Temperature: The Evolutionary Explanations and Drug Resistance Prevalence for Dolutegravir for HIV Treatment

Drug treatment advancements for HIV have dramatically increased since the virus' identification in the early 1980s. Integrase strand transfer inhibitors (INSTIs) are one of seven HIV treatment drug classes currently utilized to create viral suppression among people living with HIV (PLWH). First generation INSTIs see low barriers of genetic resistance, and with the introduction of dolutegravir, a second generation INSTI, there is optimism that higher barriers of genetic resistance will reduce drug resistant mutations to INSTIs and the overall effectiveness of this class of HIV treatment. Therapy naive and previously treated (successfully or unsuccessfully) patients for HIV report different levels of drug resistant mutations or actual resistance to dolutegravir, 0.4-31% and 0.1-67.2% respectively. Evolutionary considerations point to both non-polymorphic and polymorphic mutations for these drug resistant mutations with such arising from substitutions and epistatic interactions. The limited characterization of evolutionary explanations and drug resistant prevalence explain a pertinent need for more investigative research to improve the widespread effectiveness of second generation INSTIs and future treatment options for HIV treatment for PLWH.

Poster 5

Presenter: Jolie Greenbaum

Contributing Authors: Soo Jung Lee
Advisor: Michael Wang (Veteran Affairs)
Quantifying Conformational Aberrancy of NOTCH3 Protein Mutated at Position 146 to Determine Pathogenicity of CADASIL

NOTCH3 protein function and activity contributes to the pathogenesis of CADASIL – a common cause of stroke, vascular dementia, and small vessel disease. Considering the importance of cysteine residues in disulfide bond linkages, my lab is looking to quantify the difference in activity levels between NOTCH3 wildtype proteins and NOTCH3 mutants at locations in the DNA of CADASIL patients where a cysteine has undergone a point mutation. My lab recently provided sufficient evidence to support the claim that the pathogenicity of NOTCH3 mutations in EGF domains 1-3 is correlated to an upshift on a gel mobility shift assay and seeks to use a new method to quantify the degree of difference between activity levels of wildtype NOTCH3 and mutant. To quantify this difference Dr. Michael Wang implemented the idea to introduce mutations at cysteine residue locations in the EGF1-3 repeats of NOTCH3 that have been cloned between SBT and LBT, vital components of LSL backbone whose activity will be determined by NOTCH3 conformation of our experimental design. In order to test activity levels of various mutations, I have been assigned to introduce missense mutation in position 146 in EGF3 using standard laboratory techniques while other lab members focus on cloning different regions. The key impact of this research is to uncover the pathogenicity conferred by specific NOTCH3 mutations in a position of the protein that is associated with cerebral small vessel disease, CADASIL.

Poster 7

Presenter: Jasmin Lee
Advisor: Karen Downing (American Culture and U-M Library)
Mixed-Race Literature Database Project

The Mixed Race Literature Database is a project conducted by LSA senior Jasmin Lee to compile literature surrounding mixed-race identity in the humanities and social sciences. The purpose of the database is to surface and gather together conceptual and empirical literature on a topic of growing importance/interest across many social science and humanities disciplines, but is often difficult to find and access due to language ambiguities, poor/inconsistent indexing, and the interdisciplinary nature of the topic.

Jasmin is developing this literature search/discovery strategy with social science and digital scholarship librarians at the University Library and the American Culture department. She is sequencing the search and retrieval of the resources, browsing results, and choosing articles to read, analyze, and enter into the database. Jasmin has also created her own dictionary of tags and inclusion criteria for this database. For each database entry, she includes standard bibliographic information, whether the piece is empirically or conceptually based, what research methods were used (if empirical), the research question(s), any theoretical/conceptual frameworks used, sample type, and important findings. While this project is ongoing, Jasmin is looking forward for the release of the database upon its completion.

Poster 8

Presenter: Kelly Deng
Advisor: Stephen Ragsdale (Biological Chemistry)
Investigating heme acquisition properties of heme oxygenase-1

Heme, an iron-containing biomolecule synthesized in the mitochondria of mammalian cells, plays an important role in gas exchange and signal transduction in the human body. In addition, the CO and biliverdin resulting from the degradation of heme each have crucial cellular functions as a vasodilator and antioxidant, respectively. Heme oxygenase (HO) is the only known mammalian enzyme that can catalyze the degradation of heme, and its two isoforms, HO1 and HO2, have a high degree of homology. As free heme can potentially damage cells by creating reactive oxygen species (ROS), its transport throughout the cell is mediated by chaperones. We hypothesize that HO1 and HO2 utilize the same chaperones to acquire and degrade heme. Many proteins, such as glyceraldehyde 3-phosphate dehydrogenase (GAPDH) and Hsp90β have recently been demonstrated to be involved in the chaperoning of heme to heme binding proteins. Using chemical crosslinking, fluorescence quenching titrations, and UV-vis kinetic heme transfer assays, I aim to investigate whether HO1 acquires heme through these proteins.

Poster 9

Presenter: Brett Arenberg
Advisor: Scott Denstaedt (Internal Medicine)
Investigating the Role of CLP Monocytes in Altering Epithelial Immune Function

We have established that mice that survive sepsis have enhanced lung injury responses to lipopolysaccharide (LPS) as compared to naïve mice, and that enhanced lung injury is associated with persistent inflammation. Alveolar epithelial cells and mononuclear phagocytes interact in ways that can be damaging to the alveolar epithelial barrier. Therefore, given that we see enhanced inflammatory responses in post-CLP monocytes in response to LPS, we hypothesized that primed monocytes that are recruited to alveolar spaces are interacting with the epithelial cells in a way that is detrimental to the alveolar barrier and promotes lung injury. We sought to develop a model of monocyte and epithelial co-culture to study the influence of post-CLP monocytes on alveolar epithelial function.

Monocytes were isolated from mice 3 weeks out from cecal ligation and puncture. MLE12 cells were cultured to confluence in 12 well plates, and then co-cultured with and without monocytes in trans wells. Cells were stimulated for 5 hours with and without LPS. The cell culture supernatant was removed, and RNA was isolated from the epithelial cells. Quantitative PCR and ELISA were performed for MIP-2 from the RNA and supernatant respectively.

We found that epithelial cells exposed to CLP monocytes and LPS expressed twice as much MIP-2 as the epithelial cells exposed to naïve monocytes and LPS. This suggests monocytes play a role in enhancing lung injury in response to infection after septic shock.

POSTER SESSION F

3:00 - 4:00 PM

Poster 1

Presenter: Eleanor Mills
Contributing Authors: Charles Ryan, Yao Tsan, Samantha Regan
Advisor: Stephanie Bielas (Human Genetics)
Understanding genetic contributors of congenital microcephaly: a polycomb perspective

Congenital microcephaly is a cause of shortened lifespan and significant morbidity in young children. The increasing accessibility of whole exome sequencing has brought to light pathogenic variants in polycomb group proteins that underlie defects in neural development, such as mutations in the paralogues RING1 and RNF2, both of which facilitate the monoubiquitination of histone 2A (H2AUb1) in Polycomb Repressive Complex 1 (PRC1). Despite the identification of genetic contributors, mechanistic understanding of how these variants lead to disease remains poor. PRC1-dependent H2AUb1 is thought to play a significant role in DNA damage repair. To investigate whether disruption of this PRC1 function contributes to human microcephaly, we assessed the effect of pathogenic variants in RING1 and RNF2 on DNA damage repair in human neural progenitor cells (NPCs). We found that NPCs harboring RING1 and RNF2 pathogenic variants displayed delayed double strand DNA break repair. In light of this, we propose that RING1 and RNF2 play key roles in ubiquitination and DNA damage repair during neurogenesis, a capacity that is necessary for the production of a normal sized brain.

Poster 2

Presenter: Sanjana Kumar
Contributing Authors: Ranjit Mehta
Advisor: Mukesh Nyati (Radiation Oncology)

Malignant melanoma remains one of the fastest-growing cancers worldwide. About 99,780 new melanomas will be diagnosed in the US in 20221. While primary cutaneous melanoma can be excised via surgery, metastatic melanoma requires advanced therapies to be managed. Approximately 50 percent of metastatic melanoma patients have a mutation in the BRAF gene.2 The mutation of BRAF causes its persistent activation, leading to subsequent activation of downstream signaling and cancer cell phenotypes. While BRAF antagonizing therapies such as vemurafenib exist, patients acquire resistance to vemurafenib and other therapeutics. Thus, a new therapeutic is required to treat drug-resistant mutant-BRAF metastatic melanoma. We hypothesize DPI-503 causes tumor cytotoxicity via EGFR ablation leading to fewer xCT and SGLT1 nutrient transporters. The aim of this study was to investigate the mechanism by which DPI-503-induced loss of EGFR and associated nutrient transporters affect cellular metabolism and cause cytotoxicity.

Poster 3

Presenter: Mukund Jayaraju

Contributing Authors: Sreeja C Sekhar, Michele Cusato, Sandra Orsulic, Pilar de la Puente, and Analisa DiFeo

Advisor: Analisa DiFeo (Pathology)

Therapeutic targeting of miR181a to modulate Tumor Immune Response in HGSOC

The most common subtype of ovarian cancer, high grade serous ovarian cancer (HGSC), is the most lethal due to high recurrence rates and late-stage diagnosis. Targeting microRNAs (miRNAs) has emerged as a strategy in cancer therapeutics and our lab has established the aberrant expression of miR-181a in chemotherapy resistant HGSC patient tumors. Functionally, we found that patient tumor cells with high miR-181a activity have increased survival and tumor initiation capacity. miR-181a exerts such effects on cancer cells through the regulation of several cancer regulatory pathways such as TGFβ, Wnt, and IFN signaling, indicating miR-181a as a drug target in HGSC therapeutics. We are validating miR-181a as a target through its ability to reactivate the interferon signaling pathway.

This study shows that inhibition of miR-181a reverses various tumorigenic phenotypes, promotes tumor cell death, and blocks metastasis in vivo. We found that knockdown of miR-181a in HGSC cells resulted in activation of the STING pathway, stimulating both IRF-3 and NFKB dependent interferon signaling, causing apoptosis. Additionally, our data revealed that miR-181a loss increases immune cell infiltration and enhanced the intensity of STING signaling when activated with a STING agonist ADUS100. Given the role of miR-181a in oncogenic transformation and HGSC development, our studies focus on identifying small molecules that can effectively target miR18a and be used as a therapeutic lead to treat HGSC.

Poster 4

Presenter: Ashley LaPlant

Contributing authors: Hanjoo Kim

Advisor: Elizabeth Duval (Psychiatry)

How low can you go? Relationships between depression symptoms and reactivity during emotion processing and regulation in social anxiety

Individuals with Social Anxiety Disorder (SAD) often have comorbid depression that can impact their emotions and reactivity. Existing research on the correlation between depression and emotional processing and regulation points to depression resulting in lower emotional reactivity; however, there is a lack of research on how differences in depression symptoms may affect the level of reactivity. We hypothesized that higher levels of comorbid depression would be associated with lower reactivity during emotion processing and regulation. Data were collected from 18 individuals (mean age = 24.78, 12 women) who completed the Shifted-Attention Emotion Appraisal Task (SEAT). Over the course of the task, reactivity was measured with skin conductance response (SCR) count (the number of times a reaction was observed) and SCR average (the average magnitude of their reactions). A correlation was performed with SPSS to analyze this data. There was not a significant correlation between depression scores and SCR count ($r = 0.11$, $p = 0.65$) or depression scores and SCR average ($r = 0.09$, $p = 0.73$). This suggests that individuals with SAD and depression react similarly during emotional processing and regulation regardless of their level of depression. However, as these findings are preliminary,

further research is needed in a larger sample to better investigate relationships between depression symptoms and emotion processing and regulation in people with SAD.

Poster 5

Presenter: Anna Chiara Russo

Advisor: Rachel Reinert (Metabolism, Endocrinology, and Diabetes)

Endoplasmic Reticulum Associated Degradation impacts PC2 function and glucagon production in α-cells

Pancreatic islets rely on cellular protein quality control to maintain glucoregulatory hormone production. Islet α-cells predominantly convert proglucagon to glucagon through prohormone convertase 2 (PC2). To understand how protein quality control affects proglucagon processing in α cells, we inactivated the highly conserved Sel1L-Hrd1 endoplasmic reticulum-associated degradation (ERAD) system using Cre-loxP recombination in mice. Compared to littermate controls, Sel1LΔGcg mice showed an age-related decline in glucagon secretion in vivo, associated with a 43% decrease in pancreatic glucagon content and a 37% reduction in α cell mass. Expression of the prohormone form of PC2 (proPC2) was increased in Sel1L knockout α-cells, while there was no change in mature PC2 levels, suggesting accumulation of misfolded peptide and/or impaired maturation. To investigate the mechanism underlying these changes, we used CRISPR to delete Sel1L in αTC cells. ERAD-deficient αTCΔSel1L cells showed 1.75-fold higher expression of proPC2, in addition to appearance of a novel truncated (~56 kD) form of proPC2. Though expression of the mature (64 kD) PC2 form was unchanged in αTC-Sel1L cells, PC2 activity was reduced in half by enzyme assay. Altogether, these data demonstrate that Sel1L-Hrd1 ERAD is required to ensure PC2 maturation and glucagon production in α cells, thus maintaining classic α cell identity.

Poster 6

Presenter: Caleb Steeby

Contributing Authors: Cory Laman, Alyssa Fan, Arthur Zhu, Caroline Zubieta, Sana Shaikh, and Jennifer Pierce

Advisor: Caroline Zubieta (Anesthesiology)

Predictors of willingness to engage in nonpharmaceutical interventions for chronic low back pain

Chronic pain research studies are important for both finding new treatments and improving existing treatments for individuals with chronic pain. In order for clinical trials to be effective, participants need to be engaged and willing to participate in treatment groups. Our research aims to investigate how attitudes toward treatments affect willingness to participate in nonpharmaceutical interventions for chronic low back pain, specifically acupressure and Mindfulness Based Stress Reduction (MBSR). We hypothesize that positive attitudes toward the specific intervention would be associated with greater willingness to participate. Patients with chronic low back pain from Michigan Medicine were recruited via DataDirect and completed a single online survey. Results are pending. With this knowledge we hope to increase the awareness of factors that influence willingness to participate and improve the effectiveness of future research studies.

Poster 7

Presenter: Christopher Oshana

Contributing Authors: Marcia Sampaio Campos, Jocelid Carreño, Taylor Cezon, George Eckert, Susan E. Flannagan, Carlos Gonzalez-Cabezas, Elisabeta Karl, Steven Levy, Kristin Miller, Amr M. Moursi, Elizabeth Pitts, Mona Riaz, Livia Maria Andaló Tenuta, Emily Yanca, Shelby Yesney.

Advisor: Margherita Fontana (Cariology, Restorative Sciences, and Endodontics)

Investigating Reasons for Cavitated Lesion Withdrawal From a Phase III RCT on SDF

A Phase III multicenter Randomized Controlled Trial (RCT) testing the effectiveness of Silver Diamine Fluoride (SDF) in arresting cavitated caries lesions in children with severe early childhood caries in the U.S. enrolled 831 subjects, each followed for 8 months. This sub-study examines reasons for lesion withdrawal..

The analysis utilized data extracted on June 20th, 2022 for a DSMB report. Frequency and reasoning behind study lesion withdrawal was summarized from the three sites—University of Michigan (UM), New York University (NY), and University of Iowa (UI).

Of 1,926 lesions included in the study across all sites, 437 lesions were withdrawn. Reasons included: Study lesion treated restoratively: 129(30%); Study visit out-of-window due to COVID-19 shutdowns: 76(17%); Loss to follow-up: 70(16%); Parent decision: 62(14%); Abscess formation/pulpal exposure: 72(16%); Other Adverse Events (AEs): 19(4%); Other (uncooperative child, exfoliated tooth, etc.): 9(2%).

Comparing among sites ($p<0.001$), UM lost proportionally more lesions due to abscess formation/pulpal exposure (UM=24%; NY=8%; UI=4%), while NY lost more lesions due to AEs (NY=11%; UM<1%; UI=0%). UI lost more lesions due to parent decision (UI=39%; NY=11%; UM=14%) and loss to follow-up (UI=36%; NY=22%; UM=10%).

Over the course of the RCT, 23% of the lesions were withdrawn. Dental treatment outside the study was the most common reason for lesion withdrawal, followed by COVID-19 shutdowns and loss to follow-up.

Poster 8

Presenter: Taylor Culinski

Contributing Authors: Sarah Johnson

Advisor: Gergana Kodjebacheva (Public Health)

Influence of telehealth use on the health and quality of care among children living with disabilities during the COVID-19 pandemic: a systematic literature review

Telehealth includes virtual appointments, phone visits, and e-mail/text exchanges. Telehealth use greatly increased during the COVID-19 pandemic. Research on telehealth use among children living with disabilities during the COVID-19 pandemic is limited. This systematic review analyzed the influence of telehealth use on health and quality of care among children living with disabilities during the COVID-19 pandemic. The databases PubMed, ScienceDirect, PsycINFO, and CINAHL were searched, with 12 articles meeting the inclusion criteria. Telehealth use had a positive influence on both physical and mental health among children

living with disabilities in clinical and at-home settings. Specifically, telehealth services improved the quality of life as measured by greater family function, shorter hospital stays, and decreased anxiety for patients. Across care types, telehealth allowed children in rural areas to receive the necessary medical, behavioral, or psychological care they needed that would otherwise have been inaccessible. This also allowed medical providers to assess home environments to ensure that children living with disabilities could meet their health goals. Telehealth may have positive influences not only on the convenience factors but also on the health and quality of care among children living with disabilities. Future research may explore the influence of longitudinal use of telehealth beyond the COVID-19 pandemic on the health of children living with disabilities.

Poster 9

Presenter: Anna Vogel

Advisor: Peter Freddolino (Biological Chemistry)

Determinants of Hfq-mediated silencing of lambdoid prophages

Cryptic prophage regions in the Escherichia coli (E. coli) bacterial genome have long been associated with multiple roles, including stress tolerance, biofilm formation, and antibiotic resistance, as well as the generally attributed role of protection from phage infection. Proteins such as Fis and Hfq often regulate these regions, along with regions associated with virulence in bacteria. Loss of Fis and Hfq in E. coli lead to cell death due to de-repression of genetic cryptic prophage region Qin. Our aims in this study are twofold. The first is to determine which regions of Qin are associated with lethality. Knowing that ΔfisΔhfq mutants are non-viable, we can selectively delete sections of Qin in ΔHfq strains, then use standardized P1 phage transductions to remove fis. Colony counting on a selective plate will give us data for respective region lethalities, as well as information on intermediate phenotypes. Our second aim is to find the Hfq-mediated determinants of prophage repression. Using our system of selectivity via prophage lethality, we can replace Hfq with specific mutants, and use standardized P1 transduction to remove Fis and test the ability of the mutant Hfq to silence prophage regions. Understanding the regulatory mechanisms of prophage regions in ways such as these gives us insight into ways in which we could kill virulent E. coli using their own genetics.

Poster 10

Presenter: Katherine Ellis

Contributing Authors: Tobias Dwyer, Philipp Schönhöfer

Advisor: Sharon C Glotzer (Chemical Engineering)

Navigation of Bacteria-Like Colloidal Robots In Ordered Environments

Bacteria-like colloidal robots have been studied in random porous environments and their diffusion in those environments are well understood. Less understood are how these colloidal robots move in ordered environments such as crystals or liquid crystals. Ordered environments such as these also allow the study of these robots diffusion in a preferred direction. In order to move in preferred directions, colloidal robots need simple rules that allow them to only swim in the chosen direction. Such mechanisms have already been observed in E. Coli swimming in liquid crystals. Here we present a simple model of a bacteria-like colloidal robot in an ordered environment to show how changing the rules of when the bacteria can swim influences its movement in the preferred direction.