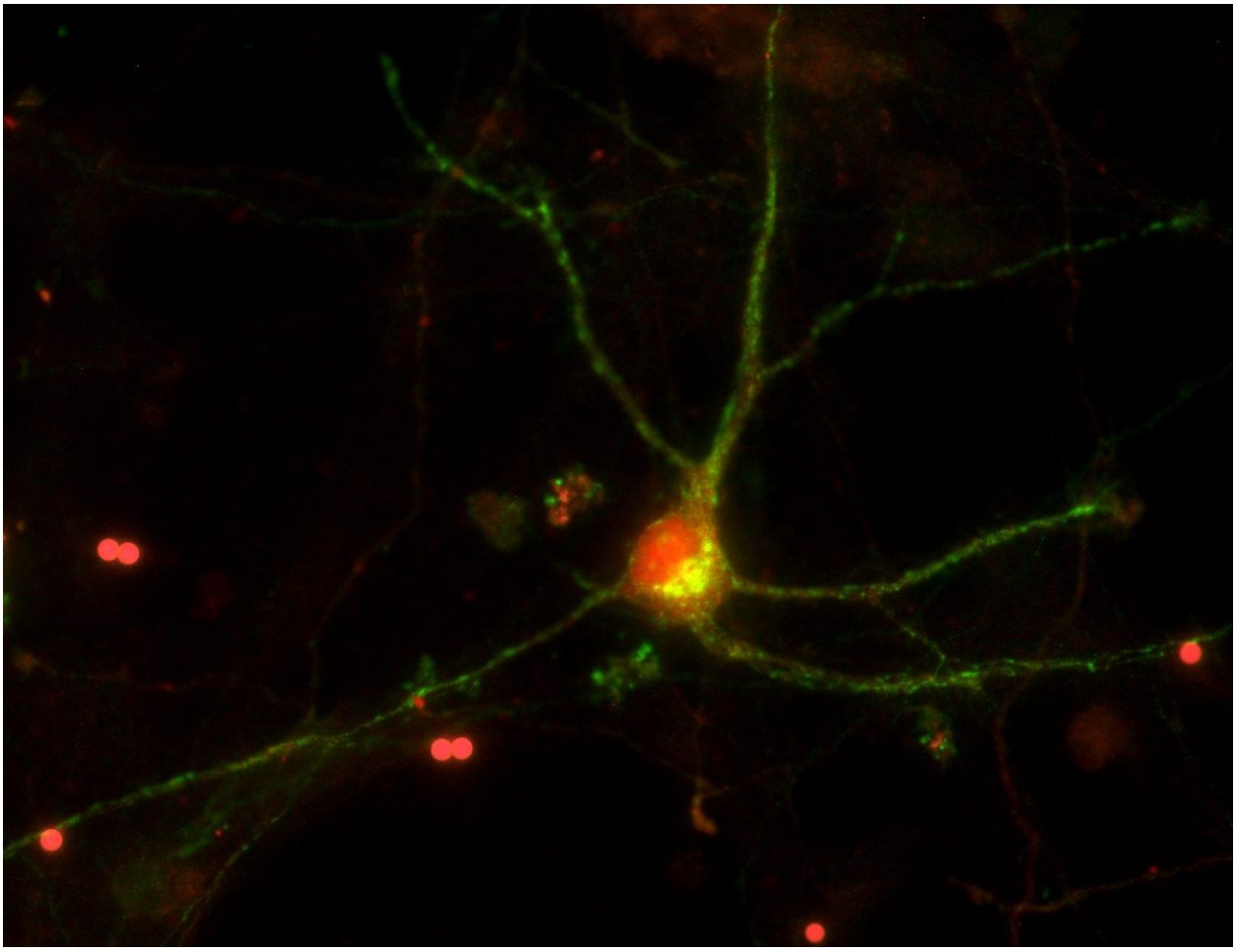

27th Annual Wayne State University School of Medicine

CHUAN-PU LEE, PH.D.

Endowed Graduate Student
Research Presentation Day

Cover Image: By Rima Rana

Image Caption: Neuron Bead Assay. Cortical neurons from day 0 DSCAM flox pups cultured and electroporated with Cre-mCherry and Cdh3-GFP (Cadherin 3-GFP) give DSCAM mutant neurons expressing Cdh3 (red and green merged image). Neurons are then incubated for 1 hour with beads coated with cadherin-3 and DSCAM (Down Syndrome Cell Adhesion Molecule).

In Honor of C.P. Lee

Dr. Chuan-Pu Lee (known as “C.P. Lee” by her friends), passed away on July 20, 2016. C.P. Lee was the strongest advocate for graduate students at Wayne State University. She reminded students that diligence and determination were the only limits to achieving their success. C.P. Lee also generously offered pre- and post-doctoral travel awards to aid the cost of national and international conferences. Before her passing, C.P. Lee worked with the GSRPD committee to set up cash prize endowments for exceptional presentations each year at GSRPD. Her life and memory will continue to serve graduate students through this much-anticipated annual event:

The Chuan-Pu Lee, PhD Endowed
Graduate Student Research Presentation Day.

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Schedule of Events

Event	Time	Venue	Speakers
Registration	8:00 – 8:30 am	Margherio Conference Center	
Breakfast and Poster Setup	8:00 – 8:45 am	Scott Hall Cafeteria	
Welcoming Remarks	8:45 – 9:00 am	Margherio Conference Center	Rima Rana and Margaret Sena Akpo *GSRPD 2023 Co-Chairs* Dr. Linda Hazlett, PhD *WSU Vice Dean of Research and Graduate Programs*
Oral Session 1	9:00 – 10:15 am	Margherio Conference Center	Five 10-minute presentations with 5-minute Q&A
Poster Session 1	10:15 – 11:20 am	Scott Hall Cafeteria	Poster presentations
Oral Session 2	11:20 – 12:35 pm	Margherio Conference Center	Five 10-minute presentations with 5-minute Q&A
Lunch	12:35 – 1:25 pm	Scott Hall Cafeteria	
Oral Session 3	1:25 – 2:30 pm	Margherio Conference Center	Five 10-minute presentations with 5-minute Q&A
Poster Session 2	2:30 – 3:45 pm	Scott Hall Cafeteria	Poster presentations
Coffee Break	3:45 – 4:15 pm	Margherio Conference Center (Outside)	
Keynote Lecture	4:15 – 5:15 pm	Margherio Conference Center	Dr. Gil Mor, MD, PhD *Director for C.S Mott Center for Human development*
Awards Ceremony	5:15 – 5:30 pm	Margherio Conference Center	Dr. Daniel Walz, PhD *WSU Associate Dean of Research and Graduate Programs*

Welcome Message

Welcome to the 27th Annual Graduate Student Research Presentation Day at the Wayne State University School of Medicine! GSRPD is a student-run event that showcases biomedical research across many disciplines. We are happy to have GSRPD 2024 as an in-person event that affords the School of Medicine community an opportunity to see our faculty and peers' participation and enthusiasm for scientific progress! We are excited to feature **65 (15 oral and 51 poster)** presentations given by graduate students from both the medical and main campuses at Wayne State University and appreciate those which, due to time constraints, could not be experienced in previous years.

We are delighted to have you in person with us and hope you can see as many research presentations as possible. Additionally, we extend wishes for the health and safety of all involved and hope that we can experience this event with you again next year.

Acknowledgments

We thank all faculty members who volunteered their time and experience and the student presenters who shared their research with us. Furthermore, we extend our greatest appreciation to the Office of Graduate Scholars at the Wayne State University School of Medicine for their endless efforts to help execute the procedural aspects of this event. Lastly, we thank all the graduate students who presented their exciting research to the Wayne State community. GSRPD would not have been possible without you are finest researchers. We look forward to seeing you next year!

Special thanks to Dr. Daniel A. Walz, Dr. Linda Hazlett, Deanna Dona and all Department heads for all their support and help.

2024 Keynote Speaker

Dr. Gil Mor, MD, PhD

Gil Mor, M.D., Ph.D. is the John M. Malone Jr. MD, Endowed Chair of Women's Health Research and Scientific Director of The C.S. Mott Center for Human Growth and Development at Wayne State University. He is Professor and Vice Chair of Obstetrics and Gynecology department, and the former Chair of the Department of Physiology. Before moving to Wayne State University, he was a Tenured Professor of Obstetrics and Gynecology and Reproductive Science at Yale University School of Medicine. In his research he examines topics related to the immunology of pregnancy and the role of inflammation in cancer formation and progression. He was the Division Director of the Reproductive Science Division at the Department of Obstetrics and Gynecology Yale and directed the Reproductive Immunology Unit and the Translational Research Program "Discovery To Cure". Dr. Mor was the Editor in Chief of the American Journal of Reproductive Immunology since 2009 to 2019, and the journal Placenta (2020-2022). He is the Past-President of the American Society for Reproductive Immunology.

Dr. Mor has been funded by grants from National Institute of Child Health Development (NICHD), National Cancer Institute (NCI) and National Institute of Allergies and Infectious Diseases (NIAID) as well as by several pharmaceutical companies and is widely published in the areas of immunology and reproduction with more than 340 publications and is the editor of five books on "Immunology of pregnancy" and "Apoptosis and Cancer". He is also the Senior Editor of a book series on Reproductive Immunology with Elsevier.

Dr. Mor is recipient of several national and international prizes, including the Pearl River Professor from Jinan University Guangzhou China, the J. Christian Herr Award- and the AJRI Award from the Society for Reproductive Immunology. He is a member of the Academy of Scholars at WSU and recipient of the ASRI Distinguished Service Award.

GSRPD Committee 2023

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Sonia Khalid
Judges
Dept. of Translational Neuroscience
2nd Year PhD Student

ORAL SESSION I

1.Isabella Cubillejo

Biochemistry, Microbiology, and Immunology

Interactions between Vibrio cholerae colonization and the zebrafish gut microbiome

Cholera is a disease characterized by acute severe diarrhea and transmitted via the fecal-oral route. Vibrio cholerae is its etiological agent, and pandemic cholera is caused by the O1 and O139 serogroups, with the O1 serogroup divided into Classical and El Tor biotypes. Since 1961, El Tor emerged as the dominant cause of the ongoing seventh cholera pandemic. In the environment, V. cholerae colonizes numerous aquatic animals, including many fish species. Our lab has established zebrafish as a natural host model for cholera, due to the non-invasive method of infection, fecal-oral route transmission, and similar presentation of diarrheal symptoms as humans. Previous data from our lab shows that Classical strains are cleared from adult fish within 72 hours post-infection (HPI), while El Tor strains can colonize the zebrafish intestinal tract for much longer. The methods of long-term colonization are unknown. Using 16s rRNA sequencing on 96 homogenized fish gut samples, we identified a more diverse gut microbiome maintained in the El Tor-infected group versus the Classical-infected group, as well as a potential dual-species biofilm interaction with Shewanella, a known gut commensal in zebrafish. These may aid in prolonged colonization.

2. **Michael Muczynski**

Biochemistry, Microbiology, and Immunology

Biochemical and structural characterization of second-generation inhibitors targeting the SARS-CoV-2 3CL protease

Public health responses to COVID-19 rely critically on both preventative vaccines and therapeutic antivirals. Targeting the SARS-CoV-2 main protease (3CLpro/Mpro), which is pivotal in viral replication through its role in processing the coronavirus polyprotein, presents a promising avenue for antiviral drug development. Our research focuses on the design of second-generation direct-acting antiviral agents that inhibit this protease. Employing a combination of biochemical assays, X-ray crystallography, and computational screening, we have identified potent drug leads. We report the design of inhibitors with low nanomolar potency against SARS-CoV-2 3CLpro, supported by in vitro biochemical data and high-resolution co-crystal structures of the inhibitor-enzyme complexes. These findings pave the way to position our compounds as strong candidates for further development in the fight against COVID-19.

3. **Jenna Thibodeau**

Cancer Biology

Cystathionine-β-Synthase activity in cytarabine therapeutic response in Myeloid Leukemia associated with Down Syndrome

Acute myeloid leukemia (AML) and myelodysplasia in children with Down syndrome (DS) collectively define myeloid leukemia associated with DS (ML-DS) according to the WHO 2016 classification. Previous clinical data showed ML-DS patients being highly sensitive to cytarabine (AraC)-based chemotherapy resulting in significantly higher overall survival rates compared to non-DS children with AML. However, relapsed/refractory ML-DS patients have extremely poor clinical outcomes, highlighting the need for a better understanding of AraC-resistance mechanism and the identification of vulnerabilities for the development of effective therapies for this group of patients. Our previous studies demonstrated significant overexpression of a chromosome 21-localized gene, cystathionine-β-synthase (CBS), in ML-DS cells compared to non-DS AML cells. A recent study shows that overexpression of CBS in DS consequently results in overproduction of hydrogen sulfide which inhibits mitochondrial complex IV activity resulting in decreased oxidative phosphorylation (OXPHOS). We hypothesize that the hyper AraC sensitivity in ML-DS patients is due to increased CBS activity and decreased OXPHOS. Our preliminary studies revealed loss of CBS activity in AraC-resistant ML-DS cells compared to the AraC-sensitive controls, accompanied by significantly elevated levels of OXPHOS. Inhibition of OXPHOS could partially resensitize the resistant ML-DS cells to AraC. Furthermore, ectopic overexpression of CBS in an AraC-resistant ML-DS cell line resulted in significantly increased levels of hydrogen sulfide, decreased OXPHOS, and increased sensitivity to AraC. These findings give critical insight into the role of CBS in AraC sensitivity/resistance in ML-DS and will guide the development of new OXPHOS targeted therapies for relapsed/refractory ML-DS patients.

4. **Grant LeVasseur**

Psychiatry & Behavioral Neurosciences (DPBN)

Single prolonged stress effects on conditioned fear extinction retention and fear renewal in Sprague Dawley rats; a fear-potentiated startle (FPS) study.

Posttraumatic stress disorder (PTSD) is known to have a lifetime prevalence of ~8% in US adults, that results in significant functional burden to patients and poses financial burden to the US healthcare system. There is a need for reliable pre-clinical models to understand the underlying neurobiology of PTSD. Single prolonged stress (SPS) is a widely used, 3-pronged stress exposure model that results in the development of PTSD-like characteristics in rats such as abnormal fear learning and increased negative feedback of corticosterone release, common in those with PTSD. Although the SPS model has been used extensively in translational studies, the extent to which its

effects span fear learning models and apply to varying subject characteristics has not been fully explored. For example, the vast majority (>90%) of studies using SPS have excluded females, and have almost always measured freezing as a fear outcome measure. This is despite observations that females are up to 3 times as likely to develop clinical PTSD and rodent freezing may not fully capture the female fear response.

In this study, we use fear potentiated startle to measure fear response post-SPS in both male and female rats. Fear potentiated startle is a more translational measure of fear learning that makes use of the acoustic startle reflex, present in all mammals, to study conditioned fear. Additionally, we expanded conditioned fear testing in the SPS rats to include a test of fear renewal in a novel context.

5. **Anna O' Connor**

Public health

Don't Sugar Coat it: Diabetes Prevention Education

Type II diabetes is a condition which affects how the body uses insulin. Insulin is a hormone which regulates the uptake and use of glucose. With type II diabetes the body does not produce the correct amount of insulin causing hyperglycemia. This can lead to issues such as ulcers and nerve damage. Prevalence of Type II diabetes has been linked to socioeconomic factors such as housing and food security. Studies have shown that people living in areas of low poverty are less likely to experience type II diabetes than people living in areas of high poverty. The aim of the program is to provide nutritional education about type II diabetes to African Americans in the Detroit area. The program will take place over a 12-month period. It will begin with obtaining funding and recruiting nutritionists/dieticians and religious organizations with a social media presence. Recruitment of participants will be through doctors' offices. A survey will be used to determine participant eligibility and knowledge. The second phase will focus on promotion through flyers and social media and a QR code for participants to sign up. The last phase will consist of hosting the workshops. Participants will receive knowledge on available resources, healthy recipes and produce to be able to produce the recipes. A 2-month, 4-month and 6-month follow-up questionnaire will be used to assess how effective the workshop was. The program will aim to provide nutritional education to African Americans in the Detroit area through religious organizations.

ORAL SESSION II

1.**Agnes Malysa**

Oncology

Role of novel R1 complex in regulating DNA replication

Understanding how non-small cell lung cancer (NSCLC) forms/resists drug treatment is critical to the discovery of better biomarkers to predict treatment responses. RRM1 (R1) has come to the forefront as a predictive and prognostic biomarker in NSCLC. While R1 is a well-studied NSCLC biomarker, we have found a novel function for R1 where it forms a complex to potentially stabilize replication specific proteins to regulate DNA synthesis/repair. Utilizing published data and our preliminary data, we discovered a novel complex of replication proteins that interact and are likely regulated by R1. We hypothesize that R1 forms a complex with these replication/repair proteins to mediate exit out of mitosis to enhance the appropriate completion of the cell cycle. This study will give more insight into how R1 expression affects NSCLC clinical outcome as well as provide new biomarkers for NSCLC.

2. **Shichao Wu**

Biochemistry and Molecular Biology

A new humanized aortic aneurysm rupture mouse model caused by the FBN1Q2467X nonsense mutation in Marfan Syndrome

Marfan syndrome is caused by mutations in Fibrillin 1 (FBN1). Aneurysm severity and drug responses of Marfan patients vary with FBN1 mutations, suggesting that different mutations may cause aneurysms through overlapping yet different mechanisms. To elucidate the molecular mechanisms of FBN1 mutations in aneurysm formation, we generated an aneurysm mouse model Fbn1Q2469X/+ containing the corresponding FBN1Q2467X nonsense mutation in Marfan patients. Here we show that FBN1Q2467X mutation causes FBN1 deficiency in Fbn1Q2469X/+ mice. Fbn1Q2469X/+ mice appear normal while Fbn1Q2469X/Q2469X mice develop rapid progressive thoracic aortic aneurysms (TAA), leading to rupture within 10-25 days. Histopathological analyses show distinct uneven degeneration of the vessel wall of aneurysms. Disorganized vascular smooth muscle cells (VSMCs), extensive degradation of collagen and elastic fiber fragmentation are observed in aneurysms at the late stage. RNA-seq analyses revealed that inflammation is the most prominent pathogenic process in aneurysms. Unexpectedly, most of the immune cells, oxidative stress, ERK1/2 and TGFβ signal pathways are not detected in the VSMC and endothelium layers but localized in the adventitia close to the aneurysm rupture region. These findings provide the first transcriptome profile in aneurysm progressing to rupture.

Importantly, this study offers a new humanized aneurysm rupture mouse model that recapitulates the pathogenic processes of human aggressive aneurysm progression to rupture. These findings could contribute to the development of new therapeutic targets for treating aortic aneurysms in patients with aneurysms.

3. **Alyssa Zokvic**

Department of Family Medicine and Public Health Sciences

Antihypertensive medication use during radiation therapy treatment for head and neck cancer: an assessment of overall survival.

Radiation therapy (RT) is an effective form of cancer treatment that can impact a patient's quality of life from its resulting side effects. The antihypertensive medications Angiotensin-Converting Enzyme Inhibitors (ACEI) and Angiotensin II Receptor Blockers (ARB) have shown to be effective at both increasing cancer-related survival and decreasing RT-related toxicities. Studies have examined the effects of antihypertensive medications on RT treatment outcomes on multiple cancer sites, but there exist gaps in literature for head and neck cancer (H&N) patients. This project aimed to examine the effects of antihypertensive medications on the overall survival of H&N cancer patients. A survival analysis was conducted using a final dataset containing extracted variables of interest from four health system in-house datasets. Descriptive statistics showing ACEI/ARB medication prevalence were output, followed by the survival analysis to determine if any differences in survival existed for ACEI/ARB users during their RT compared with non-users. A significance level of 0.05 was used. The sample size was 864 patients (51 ACEI/ARB, 813 no ACEI/ARB). Results from the analysis showed a slight increase in survival for ACEI/ARB users where they had a 10% decrease in the risk of death after RT [hazard ratio= 0.90 (0.56- 1.45)], but the results were not statistically significant (Chi-squared test, p=0.66). While not statistically significant, the results from this analysis show a potential impact of ACEI/ARB on survival for H&N cancer patients receiving RT and can act as a foundation for future research to be built upon.

4. **Anna Gretzinger**

Pharmacology

Establishing a molecular tool to study dendritic protein synthesis in vivo

Protein synthesis is critical for learning and memory. Given that neurons exhibit a high degree of polarity and activity-dependent plasticity compartment-specific translation is likely required to maintain synaptic proteins appropriately. Evidence indicates the presence of synapse-associated ribosomes in dendritic spines and local mRNA pools being translated by ribosomes in neurites. In fact, several key proteins involved in maintaining the dendritic spine architecture are reported to

be preferentially translated in the neuropil. Additionally, dysfunctional spine architecture is observed in neurodegenerative disorders such as Alzheimer's Disease (AD), indicating a possible disturbance in dendritic protein homeostasis. Despite the accumulating evidence supporting local translation, its roles in learning and memory remain elusive. To address this question, we generated a viral construct expressing a genetically encodable protein synthesis inhibitor designed to be targeted selectively to postsynaptic regions (postPSI). We validated the efficacy of our construct in a heterologous cell system utilizing a puromycylation assay. We then validated its compartment-specific inhibition of protein synthesis utilizing in vivo puromycylation assay in mice. Using these molecular approaches, we report that inhibition global and dendritic protein synthesis alters fear memory of mice. These data may provide insights into the memory process mechanisms, which are of benefit in understanding the progression of many dementia-associated neurodegenerative disorders.

5. **Katherine Dwyer**

Biological Sciences

Mapping the interactions between transcription and splicing factors in a dynamic protein network

Introns, once dismissed as 'junk DNA,' have emerged as important regulators of eukaryotic gene expression. They are removed from the primary transcript by the process of splicing. Despite their evolutionarily conserved nature, the precise function of introns in eukaryotes remains elusive. It has been established that introns regulate gene expression, contribute to proteomic complexity, and aid in genetic stability and cellular stress response. The focus of my investigation is the role of intron in enhancement of transcription or IME. The presence of an intron in a gene enhances its transcription. The molecular basis underlying the enhancement effect, however, is still not entirely clear. Additional studies revealed that the effect of an intron on transcription is splicing-dependent, thereby leading to our hypothesis that there are direct interactions between splicing factors and the transcription machinery that facilitates this enhancement effect. To investigate the molecular interactions between splicing factors and the transcription factors TFIIH, CPF, CF1 and Rat1, we affinity purified each one of them and investigated their interacting partners. The interactions were detected using mass spectrometry and subsequent normalization of spectral counts. We discovered interactions between splicing components and critical termination factors and the initiation factors, underscoring a potential widespread association of splicing factors with transcription machinery during cotranscriptional splicing. However, to ascertain the direct involvement of these interactions in splicing-mediated enhancement of transcription, further experiments are in progress. Beyond unraveling the mechanism behind 'IME,' these findings also hold promise for optimizing gene expression of heterologous proteins in microbial cell factories.

ORAL SESSION III

1.**Sanjeev Ganesh**

Oncology

Role of ZFHX3 in Endometrial cancer progression

Endometrial cancer (EC) is the most prevalent gynecological cancer and the 4th most common cancer in women worldwide. The incidence and prevalence of EC are rising, unlike other common cancers. Numerous facets connect to this increasing occurrence including lifestyle factors and metabolic disorders. Recently, the focus has shifted towards the study of the molecular mechanisms of tumor initiation and tumor microenvironment. ZFHX3 (ATBF1), is a transcription factor with known functions in embryogenesis and regulation of steroid hormone signaling pathways. Additionally, ZFHX3 has been identified as a tumor suppressor gene in multiple cancer types. ZFHX3 mutations have been observed in normal endometrium and recent reports suggest that ZFHX3 is mutated in about 20% of EC cases. Even though the mutation is quite frequent, studies to fully comprehend the molecular mechanisms behind ZHFX3 inactivation and its subsequent role in initiating EC are few. Our study aims to find the role of ZFHX3 in initiating EC. Methods: We used 12Z cells and knocked down ZFHX3 via siRNA, followed by mRNA-seq, to examine the function of ZFHX3 in the endometrial epithelium. Our preliminary data suggests that ZFHX3 regulates c-MyB, a proto-oncogene, suggesting its role as tumor suppressor gene in EC. We performed transcriptomic analysis on endometrial cells following knockdown of ZFHX3 and identified differential expression of cell cycle and cell adhesion-related genes, suggesting important roles for ZFHX3 in oncogenic processes. Future studies will focus on protein-protein interactions, binding of ZFHX3 throughout the genome and elucidating its role as a tumor suppressor.

2. **Savni Sawant**

Biochemistry Microbiology Immunology

Associations between sperm epigenetic age and semen parameters

The well documented relationship between chronological age and the sperm methylome has allowed the construction of epigenetic clocks that estimate the biological age of sperm based on its methylation, which is termed sperm epigenetic age (SEA). A total of 379 men from the Longitudinal Investigation of Fertility and Environment (LIFE) Study, a non-clinical cohort, and 192 men seeking fertility treatment from the Sperm Environmental Epigenetics and Development Study (SEEDS) were included in the study. Semen analyses were conducted for both cohorts, and SEA was previously generated using a machine learning algorithm and DNA methylation array data. Association analyses were conducted via multivariable linear regression models adjusting for

BMI and smoking status. We found that SEA was not associated with most general semen characteristics in SEEDS and LIFE. However, SEA was significantly associated with increased sperm head length and perimeter, the presence of pyriform and tapered sperm, and lower sperm elongation factor and sperm motility in the LIFE Study ($p<0.05$). Based on our results, SEA is mostly associated with several defects in sperm head morphological factors that are less commonly evaluated during male infertility assessments, potentially contributing to unexplained male infertility. SEA shows promising capacity to be an independent biomarker of sperm quality to assess male fecundity.

3. **Alixandria T. Mascarin**

Psychiatry and Behavioral Neurosciences

Recent cocaine-use pattern and problem severity differ by corticotropin-releasing hormone receptor 1 (CRHR1) genotype

Stress-exposure plays a critical and complex role in substance use disorders and comorbid negative affective states (e.g., depression, anxiety). Corticotropin-releasing hormone (CRH) signaling at receptor type 1 (CRHR1) mediates stress-reactivity and impacts drug-taking behaviors in animal models. *CRHR1* genetic variation may underlie differences in cocaine-use phenotypes, but the role of common *CRHR1* single nucleotide polymorphisms (SNPs) in cocaine-related behaviors remains unclear. The present clinical study assessed relationships between two *CRHR1* intronic SNPs, rs242924 and rs173365, and various aspects of cocaine use among recent cocaine users. As these SNPs were in linkage disequilibrium, results are reported for rs242924. Based on allelic frequencies, participants were grouped into A/A homozygotes or C-allele carriers (A/C or C/C). Compared to *CRHR1* rs242924 C-allele carriers (n=22), A/A homozygotes (n=40) exhibited significantly (p<.05) greater binge cocaine use and cocaine problem severity. A significantly higher proportion of A/A homozygotes reported having sought treatment for cocaine use, and this group scored significantly higher on measures of impulsivity and depressive symptoms than C-allele carriers. *CRHR1* genetic variation (rs242924 A/A) is associated with increased binge cocaine use, problem severity and associated negative affective states. These findings merit further attention to elucidate mechanisms of and treatments for cocaine use disorder involving CRHR1.

4. **Zachary Shaffer**

Physiology

Development of the guinea pig as an alternative animal model for elucidating microbial causes of obstetric disease

Currently, research into understanding and preventing obstetric disease, such as spontaneous preterm birth, is limited by its multi-faceted nature, ethical restrictions precluding experimental human research, and the physiologic and microbiological differences between human gestation and that of existing animal models, especially mice. To remedy this, we are developing the guinea pig, a species which exhibits greater similarity to humans than mice regarding progesterone dynamics, placentation, control of labor, and occurrence of preterm birth, as an alternative animal model. Here, we generate a microbial atlas of guinea pig gestation to further its utility as a model for microbial based obstetrical disease. Vaginal, oral, and fecal samples were collected from guinea pigs during estrus and across gestation. The microbiomes were characterized using metagenomic DNA sequencing. Variation in the vaginal microbiome across reproductive periods was evaluated using generalized linear modeling. Patterns of variation in the vaginal microbiomes of guinea pigs in pregnancy were compared to those of humans. The vaginal, oral, and intestinal microbiomes of guinea pigs were distinct and varied across reproductive periods. The vaginal microbiome changed with mating and the transition from non-pregnant to pregnant states, but overall exhibited a low alpha diversity. The guinea pig vaginal microbiome differs taxonomically from the human vaginal microbiome, yet both microbiomes are generally predominated by a single taxon (Corynebacterium and Lactobacillus spp., respectively). Together, these data characterize the guinea pig gestational microbiome and provide insights into how key reproductive processes alter the microbiome, furthering the utility of this animal model for obstetrical disease research.

5.**Aditi Singh**

CMMG

Single-cell RNAseq analysis of uterine dendritic cells (uDC): Crucial players in maternal-fetal interactions and implantation success.

Maternal-fetal interactions during embryo implantation demand intricate immunologic tolerance. Our group's research highlights uDCs' pivotal role in regulating inflammation for successful implantation and early placentation. Depletion of uDCs in early pregnancy results in impaired implantation, embryonic resorption, and altered decidual angiogenesis, indicating a role in tissue remodeling beyond maternal-fetal tolerance. Our hypothesis proposes the presence of progenitor DCs in the uterus, giving rise to resident and potentially memory DCs through asymmetric division. Using single-cell RNA sequencing, we explored uDC populations throughout the human menstrual cycle and early pregnancy. Uterine tissue samples were collected from females across different menstrual cycle stages-Proliferative (Early, mid, and late); Secretory (Early, mid, and late); Menstrual; and from first trimester human pregnancies (decidua basalis and decidua parietalis). Single-cell RNA sequencing with R revealed cell heterogeneity using UMAP analysis and assessed cluster-specific gene expression profiles through heatmap analysis. UMAP analysis revealed the existence of 7 unique uDC sub-populations throughout the menstrual cycle. Heat map analysis showed each cluster having their unique signature gene expression. Interestingly, based on the signature gene expression, cluster 5 seems to be the progenitor uDCs. We identify multiple uDC populations in the human female endometrium for the first time. The seven distinct transcriptomic programs suggest diverse uterine DC subtypes. Heatmap analysis supports the hypothesis of uDCs undergoing asymmetric division, generating diverse subtypes crucial for dynamic immunological and angiogenic processes during implantation. This research advances our understanding of uDCs, offering potential therapeutic insights for implantation failure conditions.

POSTER SESSION I

1.Aaron Lotvola

Oncology Cancer Biology

c-Myc is downregulated by ABHD5 in Prostate Cancer Cells

Prostate Cancer has a near 100% 5-year outlook survival of men locally diagnosis, however this rate plummets when metastatic or castration resistant (hormone resistant) prostate cancer (mCRPC) takes hold. To improve patient outcome, the identification of key mechanisms of resistance are essential to provide the foundation for the next-generation of therapeutic modalities in mCRPC. Lipid metabolism, one of the hallmarks of cancer, is now known as a mechanism for emerging therapeutic resistance in PCa. Moreover, we have established that the catabolic co-activator its lipase activity, ABHD5 (αβ hydrolase domain containing-5), can suppress cell growth and proliferation by an unknown mediator in mCRPC. We have demonstrated that ABHD5 is a tumor suppressor based upon RNAseq transcriptomic and gene set enrichment analysis (GSEA) which revealed that ABHD5 suppresses the targets of the MYC oncogene, particularly PHGDH and SHMT2, which are critical in serine-biosynthesis with robust oncogenic activities. Experiments have found that ABHD5 activation by transgenic overexpression or pharmacological activation downregulates c-Myc protein expression. Moreover, we have identified candidate areas within the c-Myc oncoprotein which are sensitive and resistant to ABHD5-mediated tumor suppression. If successful in defining an ABHD5/cMYC/PHGDH axis, we will establish a new paradigm within cancer metabolism, which may serve as a novel platform to innovate cancer intervention by directly targeting cMYC-mediated signaling via ABHD5's regulatory cascade.
Thus, we propose a deeper interrogation upon the molecular mechanism which indicate c-Myc as the vital relaying hub responsible for ABHD5-mediated tumor suppression and downregulation of cancer cell anabolism.

2.Anjalie Amarasinghe

Biological Sciences

Investigating the intersection of SIN3 metabolic gene regulation and metabolic stress on Drosophila viability

SIN3 is the major scaffold protein in the SIN3/HDAC (histone deacetylase) multi-protein complex, that is necessary for cell survival and cellular energy metabolism. Chromatin immunoprecipitation experiments indicate that the SIN3 binds to metabolic gene promoters, such as pyruvate kinase (Pyk). Sin3A knockdown flies have a short lifespan compared to that of control. Many investigations indicate that high and low sucrose food cause dietary stress that affect the Drosophila lifespan. This evidence shows that SIN3 is involved in regulating metabolic genes and both SIN3 and dietary stress influence Drosophila lifespan. The effect of metabolic stress on gene expression combined with the role of SIN3 under metabolic stress in regulating transcription is not known. In this current study, we investigate this intersection of SIN3 regulation and metabolic stress and determine the phenotypic effects of altering SIN3 expression and manipulating diet on Drosophila growth and lifespan. First, we checked the genetic interactions between Sin3A and Pyk by monitoring wing phenotypes in flies with double knockdown. The knockdown of Sin3A and Pyk changed the wing phenotype, indicating genetic interaction. To examine the effect of SIN3 and metabolic stress on fly viability, we applied metabolic stress to Sin3A knockdown adult flies. With the loss of SIN3, flies did not survive well under metabolic stress compared to control flies, revealing the combined effect of metabolic stress and SIN3 on Drosophila viability. These results indicate that SIN3 regulation of metabolic genes is altered under metabolic stress.

3.Apoorva Rao

Biochemistry, Microbiology and Immunology

Characterization of Vibrio cholerae colonization factors in zebrafish

Vibrio cholerae is a gram-negative, aquatic bacterium responsible for the deadly diarrheal disease cholera, which affects millions worldwide each year. Over the last 200 years, there have been seven cholera pandemics caused by the O1 serogroup globally, the first six of which were associated with the classical biotype. The most recent and ongoing seventh pandemic cholera outbreaks, however, have been dominated by the El Tor biotype. The zebrafish (Danio rerio), indigenous to cholera endemic regions, serves as an ideal model organism due to its natural susceptibility to V. cholerae infection. However, the specific genetic factors important for Vibrio holerae colonization in zebrafish are unknown.

Utilizing transposon sequencing analysis (Tn-Seq), previous lab studies identified potential genes crucial for V. cholerae colonization in zebrafish intestine, notably associated with transport and transcriptional regulation.

A few selected genes were subjected to a complete gene knockout (KO) in the El Tor C6706 wild type (WT) strain. The KO strains were generated using Splicing by Overlap Extension method, followed by chitin-induced natural transformation. Using zebrafish as a model, parallel infections were conducted between the KO and WT strains to determine if the suspected colonization factor is important for colonization.

We hypothesize that the mutants created will have significant changes in colonizing the zebrafish intestine compared to the wild type. Identifying genes important for fish colonization holds immense potential and will contribute to our broader understanding of bacterial pathogenesis.

4.**Amanda Paskavitz**

CMMG

Sperm methylation variability predicts time-to-pregnancy in couples from the general population

Infertility affects 16% of couples in the U.S., and although historically viewed as a female problem, approximately 50% of infertility cases can be attributed to male factors. Throughout a man's lifetime, sperm DNA acquires specific epigenetic modifications, including methylation patterns that develop as a result of aging, lifestyle, and environmental exposures. Furthermore, interpersonal DNA methylation variability within a cohort has recently been described as a promising fertility biomarker. Sperm DNA methylation data from 379 men from the general population in the Longitudinal Investigation of Fertility and Environment Study were used to calculate a sperm methylation variability score (VarScore) for each participant. Cox proportional hazard models were used to examine the utility of VarScore in predicting couples' time-to-pregnancy (TTP). Crude models and models adjusted by covariates that are known to contribute to male fertility were performed. Our results showed low TTP prediction strength of continuous VarScore (FOR=0.97, p=0.63, 95%CI=0.84-1.11). However, after dividing VarScore into two groups reflecting low and high sperm DNA methylation variability, TTP prediction was greatly improved (FOR=0.61, p=0.07, 95%CI=0.38-1.01). Among all tested models, the model most precisely predictive of TTP included dichotomous VarScore, adjusted for male age, BMI, and smoking status (FOR=0.55, p=0.02, 95%CI=0.32-0.92). In conclusion, our results indicate that this model may be a useful biomarker of male fertility and diagnostic tool to estimate the amount of time it will take a couple to become pregnant.

5.Ashten Stambersky

Ophthalmology, Visual and Anatomical Sciences

Exploring the Role of the Eosinophil during *Pseudomonas aeruginosa*-Induced Keratitis

Bacterial keratitis is an eye infection that potentially causes blindness. *Pseudomonas aeruginosa (P. aeruginosa)* is one of the most prevalent causes of keratitis, especially among contact lens wearers. After breaching a compromised epithelium, the infection can rapidly develop into a corneal ulcer. Innate immune cells are initially recruited to fight the infection as part of a healthy host response, however, their persistence and chronicity cause tissue damage. The eosinophil secretes its granule contents during inflammation, possesses antibacterial properties and promotes tissue repair during infections. Yet its cellular function is unexplored during bacterial keratitis and, as such, is the focus of the current study.

Bacterial keratitis was induced in BALB/c (resistant; cornea heals) and C57BL/6 (B6) (susceptible; cornea perforates) mice by delivering *P. aeruginosa* ATCC strain 19660 (10^6 CFU/5mL aliquot) to the wounded corneal surface. Flow cytometry quantitated the influx of eosinophils into infected corneas. Key mediators reflecting eosinophil function were detected by real-time RT-PCR and Western blot, including granule proteins (MBP, ECP, EPX/EPO, EDN), cytokines (IL-4, IL-5, Eotaxin-1, Eotaxin-2), and cell surface markers (CD62L, CD101).

Eosinophils were significantly higher in BALB/c vs. B6 mice under normal conditions and through 5 days post-infection. In addition, molecules associated with eosinophil activation/function were differentially expressed at both transcript and protein levels over the infection time course.

To date, this is the first report that eosinophils are involved in the host response to bacterial keratitis and reveals different eosinophil subtypes associated with the resistant and susceptible outcomes.

6.Christine Lee

Translational Neuroscience Program

Acute Air Pollution Exposure Effects on Declarative Memory Decline in the Detroit Aging Brain Study: A Preliminary Analysis

Air pollution is a persistent health concern in the United States, and fine particulate matter (PM2.5) exposure is a suggested risk factor for cognitive decline in aging, Alzheimer's disease and related dementia (ADRD). However, the vulnerability of brain structure and function to PM2.5 across the adult lifespan is unclear. To address this gap, we examined PM2.5 exposure in an established community-based sample of older adults (preliminary sample n = 50; baseline age = 23-77 years). Participants underwent cognitive assessment and an MRI at study baseline and again two years later, from which we tested effects in age-sensitive declarative and working memory measures and the associated hippocampus and caudate volumes. Annual average exposure to PM2.5 during the year prior to baseline was estimated from modeling of national trends. Greater annual average PM2.5 exposure in the year prior to baseline predicted greater 2-year decline in immediate logical memory performance, which is a measure of declarative memory (unstandardized b = -0.789, p = 0.038). There was no significant association between annual average exposure and change in working memory maintenance (p > 0.10). Further, annual average exposure was not significantly associated with 2-year change in brain volume (p's > 0.10). Taken together, acute air pollution exposure was associated with accelerated decline in declarative memory ability—a relevant clinical marker for ADRD—however the association with hippocampal volume was small. We will build upon this preliminary study with large-scale longitudinal analysis of the established cohort that further incorporates MRI biomarkers of neurodegeneration besides volume.

7.Clifford C. Abel II

Psychiatry and Behavioral Neurosciences

*Irregular changes in brain network topology during monotonic learning in health and schizophreni*a

Task-based neuroimaging has recapitulated relationships between behavior and brain imaging measures in specific examples such as retrieval success (proficiency), however relationship dynamics over time remain less elucidated. In iterative associative learning tasks, proficiency increases are associated with changes in effective connectivity which are disordered in schizophrenia (SCZ). However, these relationships have not been examined under the simple principle of monotonicity prevalent in human psychology; while proficiency dynamics are weakly monotonic (each iteration is greater or equal to the previous), do connectomic changes reflect such monotonicity? Methods/Results: Following informed consent, fMRI data (Siemens Verio 3T) were collected while participants (n=88, SCZ=49, Ages: 18-45) learned object-location associations over eight epochs of four conditions: Encoding, Post-Encoding Rest, Retrieval, Post-Retrieval Rest. Relative to healthy controls (HC), a larger proportion of SCZ displayed non-monotonic proficiency dynamics over the eight epochs ($p < 0.05$). Searching for the same group-specific violation of monotonicity in the underlying brain activity, the graph theoretic measure Betweenness Centrality (BC), which indexes the hubness of brain regions, was estimated for each participant within every condition of each epoch. No regions displayed monotonic changes in BC within condition across the eight epochs ($p < 0.05$). Conclusion: This failure to recapitulate the performance dynamics (weakly monotonic) in the connectomic dynamics (devoid of monotonicity), is a successful dissociation of behavior from brain imaging measures since consistent behavioral dynamics are generated from highly variable connectomic fluctuations. A proper investigation of these connectomic dynamics must therefore treat regional variability as part of learning.

8.Danielle Lenz

Family Medicine and Public Health Sciences

MI-COEND: *Michigan Community Overdose Education and Naloxone Distribution*

More opioid-overdose deaths occurred in the U.S. in 2022 than any year prior. Urban and rural Michigan counties face unique challenges to combating overdose mortality. Overdose Education and Naloxone Distribution (OEND) programs are utilized as a method to decrease overdose mortality. This poster presents a theoretical OEND program to address challenges faced by urban and rural communities in Michigan via tailored education sessions and naloxone distribution using Public Health Vending Machines (PHVM). The Michigan Community Overdose Education and Naloxone Distribution (MI-COEND) program aims to enhance community knowledge, change perceptions, and reduce opioid overdose fatalities.

Twenty Michigan counties receive MI-COEND programming over 21 months: 14 months for intervention and 7 months for evaluation. MI-COEND employs a mixed-methods evaluation design. Focus group feedback will be used to create and evaluate educational content, while naloxone distribution and county overdose mortality data will be used to assess program impacts on community perceptions, knowledge, and overdose prevalence.

Education sessions and PHVM will improve community attitudes, perceptions, and knowledge about overdose prevention. Naloxone distribution will increase, and overdose mortality will decrease in MI-COEND communities.

MI-COEND recognizes the need for targeted interventions in Michigan's diverse communities to combat the opioid crisis. Empowering communities with knowledge and resources for overdose prevention can reduce stigma and boost individual confidence to intervene in an emergency. Future programming should draw experiential wisdom from communities with lived experience in overdose prevention efforts. MI-COEND serves as one such model for community-engaged health promotion programming.

9.Doris Rusu

Radiation Oncology

Does organ motion during adaptive radiation treatment matter?

The abdomen is the site with the most amount of organ motion in the body. This is crucial in radiation therapy for abdominal cancers since abdominal organs are highly radiation sensitive and organ motion into the radiation beam could cause significant side effects. In adaptive radiation therapy, there is a long latent time from the moment a patient is imaged to the moment they are treated. This latent time is long enough for the abdominal organs to move. The goal of this work is to analyze the impact of this latent period organ motion. Methods: Ten pancreatic cancer patients were treated with magnetic resonance guided adaptive radiation therapy. Their anatomy was imaged prior to treatment, to allow for treatment plan adaptation, as well as at the end of their daily treatments, to visualize the organ motion throughout the latent period. The radiation delivered was analyzed on the pre- and post-treatment images to quantify the difference in amount of radiation delivered due to organ motion. Results: During treatment the abdominal organs tended to move into high radiation areas, therefore receiving higher amounts of radiation than initially planned. 8 out of 10 patients had at least one organ that exceeded organ safety constraints by the end of treatment, despite 10 of out 10 meeting the constraints after adaptation and prior to treatment. Conclusion: Organ motion during treatment is significant, new methods to account for this motion could increase the effectiveness of adaptive radiation treatments.

10.Dylan Ukasik

Translational Neuroscience Program

Exosomes Secreted from Epileptogenic TSC Tubers are Enriched for Proteins Associated with Vesicle-Mediated Transport and Altered Electrophysiology.

Tuberous Sclerosis Complex (TSC) is a genetic disorder caused by genetic mutations in the TSC genes that lead to the formation of cortical tubers in the brain. A subset of tubers can induce seizures, but this mechanism is not fully elucidated. Recent evidence suggests exosomes, a subtype of extracellular vesicle (EV), may play a role. Exosomes function as intercellular communicators through the transportation of molecular cargo including RNA, DNA, and proteins, which can be selectively packaged into the vesicles by the source cell and provoke a functional response in recipient cells. The protein cargo in exosomes of human epileptogenic brain tissue has not been characterized. We used quantitative proteomics to compare EV cargo proteins in epileptogenic and non-epileptogenic TSC tubers. Methods: Exosomes were isolated from surgically resected human cortical tissue, including 4 epileptogenic tubers (ET), 3 non-epileptogenic tubers (NT), and 3 non-tuber controls (NC). Protein cargo was extracted from vesicles and analyzed using quantitative LC-MS/MS proteomics to identify differentially expressed proteins among the experimental groups and identify those potentially involved in altered electrophysiology and seizures. Results: Principal component analysis demonstrates that exosomal protein cargo is distinct in ET compared to NT and NC controls. Statistical analysis identified 140 proteins differentially abundant in epileptogenic exosomes. Pathway analysis, utilizing Enkefalos, revealed enrichment for proteins associated with vesicle-mediated transport, synapse morphology, altered electrophysiology, and seizures, including Syntenin-1 and YKT6. Conclusion: ET secrete exosomes with altered protein cargo that is associated with altered electrophysiology and vesicle-mediated transport and may contribute to seizure induction.

11.Fatimah Albazron

Psychiatry and Behavioral Neurosciences

Radiological and clinical correlates of absent deep and basal veins in Sturge-Weber syndrome

Sturge-Weber syndrome (SWS) is a rare sporadic neurocutaneous disorder often characterized by facial capillary malformations and intracranial abnormalities. It is manifested with focal epilepsy, motor impairments, learning and behavioral difficulties. Common intracranial vascular abnormalities in SWS include leptomeningeal venous malformation (LVM) and enlarged deep medullary veins (EDMVs). Absent deep veins in SWS have been also reported in a few small studies, but their prevalence and clinical impact remain unknown. Methods: In this prospective study, brain MRI with susceptibility-weighted imaging (SWI) was used to detect brain vascular and structural abnormalities in 30 young patients with unilateral SWS and 20 healthy controls (mean age: 12.2 and 13.7 years, respectively). Presence or absence of four major deep cerebral and basal veins were evaluated and correlated with other brain vascular and parenchymal abnormalities and clinical symptoms in the SWS group. Results: While deep cerebral and basal veins were identified by SWI in controls, one or more deep and/or basal cerebral vein was absent in 19 (63%) SWS patients: internal cerebral vein in 15 (50%), septal vein in 14 (47%), thalamostriate vein in 14 (47%), and basal vein of Rosenthal in 10 (33%) patients. Absent deep cerebral veins were associated with more extensive EDMV and brain atrophy ($p<.01$) and also associated with worse motor functions ($p=0.02$). Conclusions: Absent deep and basal veins are common in SWS, appear to be associated with more severe leptomeningeal venous vascular and brain parenchymal abnormalities, and may be relevant for some of the clinical symptoms, such as motor impairment.

12.Jugmohit Toor

Cancer Biology

Targeting mucosal associated invariant T (MAIT) cells via the gut microbiome as a novel immunotherapy for pancreatic cancer liver metastasis

Pancreatic cancer liver metastasis (PCLM) is present in 50% of patients diagnosed with pancreatic ductal adenocarcinoma which leads to abysmal median survival. Here, we sought to identify options for treating PCLM by targeting mucosal associated invariant T (MAIT) cells, an invariant T cell restricted to MHCI related protein (MR1). MAIT cells are classified as “protumor” MAIT17 cells, induced by MR1 mediated activation, and “antitumor” MAIT1 cells. Interestingly, liver MAIT cells can respond to microbial antigens presented on MR1 that traverse from the gut. We hypothesize that the PCLM tumor microenvironment (TME) induces direct MAIT cell activation via MR1 which promotes MAIT17 cells and modulating the gut microbiome may therapeutically alter MAIT cells in the PCLM TME. In mouse models, we found that the PCLM TME is enriched for MR1 which promoted a MAIT17 phenotype.

When comparing WT mice and MR1 KO (lacking MAIT cells), MR1 KO mice had reduced tumor burden. ScRNA-seq and flow cytometry revealed that the lack of MAIT cells promoted anti-tumor immunity.To reduce the presence of microbial antigens that traverse from the gut to promote liver MAIT17 cells, we subjected mice to oral antibiotics which promoted MAIT1 cells in healthy mice. In PCLM, we found that antibiotic treated WT mice had reduced tumor burden via reduction in exhausted T cells. However, MR1 KO mice did not have a reduction in tumor burden. Overall, our findings suggest that MAIT cells can be therapeutically modulated via the gut microbiome to yield anti-tumor immunity in PCLM.

13.Kailee Hartway

Pathology

Interrogating the phenotype of γδ T cells in pancreatic cancer liver metastasis

Pancreatic ductal adenocarcinoma (PDAC) 5-year survival rate is approximately 12%. This is due to 80% of patients presenting at the metastatic stage of disease progression. Approximately 48% of PDAC patients will experience metastasis to the liver after surgery making it the most common site for metastasis. PDAC exhibits a highly immunosuppressive tumor microenvironment and the role of T-lymphocytes in facilitating PDAC immunosuppression is not fully understood. A rare subset of T-cells called γδ T-cells function in both innate and adaptive immunity contributing to immune surveillance and respond to antigens independent of MHC signaling. Previous work suggests γδ T-cells may promote tumor development in primary PDAC, however, the phenotype of γδ T-cells in the setting of liver metastatic PDAC has not been explored. To investigate this, we utilize a robust in-house single cell RNA-sequencing atlas of human PDAC and liver metastatic tumors. We then performed clustering analysis and labeled cell types based on known lineage markers to identify T&NK cells. We subclustered cells expressing T Cell Receptor Delta Constant (TRDC+), a γδ T-cell enriched gene. We found TRDC+ cells significantly enriched in the metastatic setting compared to adjacent normal pancreas and primary PDAC samples. Sub-clustering revealed unique gene expression profiles, related to functional aspects of T cells in different TRDC+ populations. Lastly, we identified high expression of γδ T cells were associated with overall worse survival in late stages of PDAC. Our study suggests γδ T cells are pro-tumorigenic in the liver metastatic PDAC setting.

14.Margaret Sena Akpo

Ophthalmology, Visual and Anatomical Sciences

Investigating the Role of Self Avoidance Cell Adhesion Molecules in Muller Glia Morphology and Tiling

Muller Glia (MG) are the predominant glial cell type in the mammalian retina known to play critical roles in retinal development and homeostasis relying on their complex morphology. MG "tile" during development so that each MG occupies non-overlapping territories. It is hypothesized that this function requires contact and recognition between developing MG cells. We focus on two families of CAMs that are candidates for mediating MG-neuron and MG-MG contact recognition: clustered protocadherin (cPcdhs) and Dscams (from Down syndrome cell adhesion molecule). Roles for either family have not been explored in MG. Here, we assay their expression in MG and assess the morphological perturbations associated with *Pcdhg* disruption.

RNAScope, an in-situ hybridization method, was carried out using mouse retina for identification of CAMs expressed in Muller glia cells. Employing immunohistochemistry, Muller glia in Pcdhg-mutant mouse retinas were labelled and imaged using confocal microscopy. Morphologies were quantified with the aid of the modular analysis toolkit GliaMorph.

Muller glia cells express Dscam and Dscaml 1. They also express both alpha and gamma protocadherin (Pcdha and Pcdhg). Specific isoform expression analysis shows that C3, C4, C5, and A12 isoforms of the Pcdhg cluster are expressed by Muller glia. GliaMorph analysis of the labelled Muller glia cells showed a reduction in morphological complexity of the MG cells in Pcdhg-mutant compared to control mice suggesting a role of these self-avoidance cell adhesion molecules in Muller glia development.

Ongoing research is focused on labelling individual MG cells in mutant mouse retinas for finer analyses of morphology and tiling.

15.Michael Flynn

Pharmacology

Role of the cell-surface serine protease matriptase in corneal epithelial homeostasis and repair

Maintaining a healthy corneal epithelium is vital to normal ocular health. The corneal epithelium has a complex network of cellular mechanisms and dynamic processes to maintain its homeostatic functions. To date, the role of extracellular proteases in ocular research has mostly centered on their harmful effects in corneal wound healing and infection. Based on our preliminary data, we hypothesize that the cell-surface serine protease matriptase, in contrast, promotes corneal epithelium homeostasis via actions involved in maintenance of barrier function and tight junction integrity, corneal differentiation, and corneal wound healing. Methods/Results: We have developed multiple models to study the functional and molecular consequences of matriptase loss-of-function conditions. Using human corneal epithelial cells with RNAi-mediated matriptase silencing and two in vivo mouse models consisting of a chronic loss model with hypomorphic mice that display low global matriptase expression, and an acute model with mice carrying loxP-flanked matriptase alleles and a ubiquitously expressed tamoxifen-inducible Cre-recombinase. Eye-specific gene ablation is achieved with topical eye drops containing tamoxifen metabolite. In vitro, we observe a decrease in barrier function and tight junction integrity, upon RNAi-mediated matriptase silencing. Under injury conditions, we identified the pro-form of hepatocyte growth factor as a candidate substrate for matriptase in corneal migration/wound healing. In vivo, we observe increased inflammation in the peripheral cornea, corneal thickening, and an abnormal surface in matriptase hypomorphic mice. Conclusions: The goal of this project is to gain a mechanistic understanding of matriptase in corneal epithelial homeostasis and injury and identify targetable factors/pathways for therapeutic options.

16.Neha Rajput

Department of Biological Sciences

Mapping the Neural Basis of Individual Differences in Adult Zebrafish Behavior Combining In-Situ Hybridization Chain Reaction with Adult Zebrafish Brain Atlas and BrainGlobe.

Individual differences in behavioral have been observed across wide range of taxa, including humans, rodents, and fish. However, the biological mechanisms that underlie these differences are not fully understood. To explore the neural mechanisms that underpin behavioral differences, we use adult zebrafish as a model. For example, we have identified four distinct behavioral types in adult zebrafish when exploring a novel environment: bold, shy, wall-huggers and active explorers. To gain a better understanding of the neural basis of these differences, we developed tools for whole-brain activity mapping. We are using situ hybridization chain reaction (HCR) to detect the expression of c-fos, an immediate early gene, as a means of labeling active neurons. To visualize brain-wide c-fos expression, we are utilizing a tissue clearing technique and light sheet microscopy to generate high resolution images. For automatic detection of c-fos positive cells, we have utilized CellFinder, a deep learning-based cell identification approach integrated into the BrainGlobe computational environment. Subsequently, the images are registered to our recently developed adult zebrafish brain atlas (AZBA) through advanced normalization techniques (ANTs). We have successfully trained CellFinder to identify c-fos positive cells with an accuracy of 96% and found that c-fos expression peaks at 15-30 minutes following exposure to a novel tank. With this approach, we will identify the neural mechanisms underlying individual differences in behavior.

17.**Radia Islam**

MS in Basic Medical Sciences

The effects of highly recommended geriatric drugs on Alzheimer's β-amyloid aggregation

In the present study, we compared medication profiles of Alzheimer's Disease AD (n=135), mild cognitive declined (MCI; n=120), and non-demented (ND; n=259) subjects with an aim to determine the effects of commonly recommended medications in the geriatric population in Alzheimer's Disease pathology. We selected 18 highly recommended drugs based on the prescription frequency amongst the cohorts to investigate their neurotoxicity and inhibitory effects against β-amyloid peptides aggregation, a central phenomenon which occurs during the onset of AD. Aggregation of Aβ was monitored using Thioflavin T assay. Then, mouse neuronal cells (N2A) were treated with 50μM drugs, and cell death was measured using Lactose Dehydrogenase assay. Our data suggest that Vitamin D3, Omperazole, and Norvasc might be beneficial against amyloid pathology. However, Vitamin D3 and Norvasc also showed toxicity to N2A cells. Aspirin, Colace, Vitamin C, and Lopressor may have influential effect on Aβ aggregation

18.Ravipaul Singh

Biochemistry, Microbiology, & Immunology

Flagellar motility drives hyperinfectivity in Vibrio cholerae during transmission in zebrafish

Vibrio cholerae is the infectious agent of cholera, an acute intestinal infection in humans characterized by voluminous watery diarrhea that occurs through ingestion of contaminated food or water. V. cholerae primarily exists in the aquatic environment, where vertebrate fish are known to be an environmental host and potential V. cholerae reservoir. Both V. cholerae and zebrafish (Danio rerio) originate from the Indian subcontinent suggesting a long-standing environmental relationship. Our laboratory has described the use of zebrafish as an animal model to study V. cholerae pathogenesis. Methods: We assessed the hyperinfectious nature of two V. cholerae strains (O1 El Tor and non-O1/O139) excreted from zebrafish through competitive colonization assays. To assess changes in gene expression, global RNA sequencing of V. cholerae from culture, zebrafish intestine (actively colonizing) and zebrafish-excreted water (transmitting) was done. Highly expressed genes during transmission were knocked out in V. cholerae to show their effect on the hyperinfectivity of transmitting V. cholerae. Results: Both V. cholerae strains excreted by zebrafish showed more than fifty times higher competitive colonization against LB-grown V. cholerae. Zebrafish-excreted V. cholerae maintained their hyperinfectious nature 48 hours post-excretion. Genes associated with motility, chemotaxis and locomotion were highly upregulated during V. cholerae transmission. Mutant, non-motile V. cholerae showed no effect on colonization in zebrafish but caused a significant defect in the hyperinfectivity of zebrafish-excreted V. cholerae. Conclusion: This work reveals some of the genes associated with the transmission and hyperinfectivity of V. cholerae excreted by zebrafish that could potentially contribute to human disease.

19.Rafael Ramos

Biomedical Engineering

*Culturing primary hepatocytes inside Glycosaminoglycan-based capsules: effects of intracapsular collagen on hepatic organization and functio*n

The liver's high oxygen demand, dual blood/bile circulation, and mechanical fragility of hepatocytes have made it difficult to produce fully functional in-vitro constructs. These challenges are exacerbated by the complex hierarchy between the cellular components that make up hepatic tissue. We previously reported a method of encapsulating hepatocytes within glycosaminoglycan (GAG) stabilized chitosan membranes generated by polyanion-polycation electrostatic interactions. These hollow capsules allow for cellular organization within a defined spherical volume whose size and microenvironment can be tailored through the inclusion of extracellular matrix (ECM) components. In this ongoing study, we explore the role of additional intra-capsule ECM components in promoting hepatocyte organization and liver-specific function over medium-term culture.

Primary hepatocytes were isolated from SD rats and encapsulated within GAG-chitosan membranes. Capsules were cultured in suspension on well plates using a rotary shaker platform at ~80 rpm. Culture medium was changed daily and assayed for urea and albumin secretion as indicators of liver-specific function. Hepatocyte organization was studied using light microscopy, histology and scanning electron microscopy.

Preliminary results suggest that encapsulated hepatocytes will form free-floating spheroids if additional ECM components are not incorporated and become aggregates with a diameter of 268.6±40.5µm after 2 weeks of culture. If ECM components are integrated, hepatocytes will first form a monolayer on the internal membrane surface prior to aggregating into similar spheroid structures of 250.4±50.6µm that remain attached to the membrane during the initial 2 weeks of maintenance. Rotary cultured hepatocytes demonstrated higher rates of both urea of albumin synthesis compared to 2D cultures.

20.Rima Rana

Pharmacology

Defining the molecular mechanisms of DSCAM-mediated self-avoidance

DSCAM (Down Syndrome Cell Adhesion Molecule) belongs to the Ig superfamily of cell adhesion molecules (CAMs) and plays a major role in different neurodevelopmental events including neuronal self-avoidance. Self-avoidance refers to the tendency of branches from the same neuron to avoid each other (iso-neuronal self-avoidance) and the ability of neighboring neurons of the same type to contact each other without becoming entangled (homotypic self-avoidance). It is exhibited by both dendrites and axons. In invertebrates like drosophila, extensive alternative splicing of Dscam1 generates more than 38,000 isoforms, providing molecular diversity to individual neurons. This enables neurons to distinguish between 'self' and 'non-self'. There is no such alternative splicing of Dscam in vertebrates, but it can promote self-avoidance by masking excessive adhesion mediated by other cell adhesion molecules. Dscam's C-terminus is found to be important for promoting self-avoidance in some but not in all cell types. The molecular mechanism behind Dscam's self-avoidance is not clear. Our main aim is to define the molecular mechanism of DSCAM's self-avoidance in vertebrates. We hypothesize 1) Homophilic DSCAM interaction is masking adhesion by triggering changes in local CAMs. 2) DSCAM masks diverse CAMs and masking only a subset of CAMs requires DSCAM's C-terminus. We are focusing on cadherin-3 (CDH3) masking to investigate the candidate molecular mechanism of adhesive masking.

We are trying to use a neuron bead assay in which beads coated with CDH3 or CDH3+DSCAM would be added to the primary neuron culture transfected (electroporated) with CDH3. We have used a gene expression data set and RNAscope to identify CAMs expressed in different retinal cell types.

We found out that Chl1 is expressed by Th+ (dopaminergic) amacrine cells, Cdhr1 by bNOS+ (brain or neuronal NOS+) amacrine cells, and Sdk1 by SYT6+ (synaptotagmin 6+) amacrine cells.

We have identified three candidate CAMs to be tested: Chl1, Cdhr1, and Sdk1 to determine the role of DSCAM's C-terminus in the adhesive masking of different families of CAMs. Invitro neuron bead assay would be further used to test the secondary pathway involved in DSCAM-mediated self-avoidance.

21.Sahar Bannoura

Cancer Biology

Regulating the regulator: regulator of chromosome condensation 1 (RCC1) as a novel therapeutic target for pancreatic ductal adenocarcinoma

Pancreatic ductal adenocarcinoma (PDAC) is a lethal disease with limited therapies. Novel mechanisms and targets need to be unveiled to meet the urgent need for new therapies. Regulator of chromosome condensation 1 (RCC1) is the guanine exchange factor for Ran, a ras-like nuclear protein that maintains proper nucleocytoplasmic transport. To sustain proliferation, cancer cells are reliant on high rates of nuclear shuttling through dysregulation of transport machinery. Thus, an opportunity exists to modulate RCC1 for therapy.

Transcriptomic analysis of PDAC tissues (n=5,071) and of TCGA, CPTAC and GTEx PDAC patient data revealed that RCC1 expression is higher in PDAC compared to normal pancreas. Moreover, PDAC patients with high RCC1 were more likely to have a poor prognosis. Silencing of RCC1 using RNAi and CRISPR-Cas9 reduced PDAC cell proliferation in 2D and 3D cultures and arrested tumor growth in vivo. RCC1 silencing reduced colony formation, induced apoptosis and altered cell cycle in human and murine PDAC cells. Ran GTPase subcellular distribution was disrupted upon RCC1 KO, which resulted in proteome wide alterations in cytoplasmic and nuclear proteins. RNA-seq of RCC1 KO cells showed widespread transcriptional alterations. We found that c-Myc is an upstream regulator of RCC1-Ran axis, and RCC1 KO cells show differential sensitivity to c-Myc inhibitors. Finally, RCC1 silencing sensitizes PDAC cells to Gemcitabine. Molecular characterization of conditional Rcc1fl/fl KO mouse model to study the role of RCC1 in PDAC in vivo is ongoing. Our results show that RCC1 is implicated in PDAC and is a potential therapeutic target.

22.Samantha Heldman

Pharmacology

Early Developmental Exposure to Liquid Crystal Monomer Mixtures Impacts Zebrafish Behavior, Cellular Respiration, and Adiposity

Mixtures of liquid crystal monomers (LCMs) are an essential part of liquid crystal displays in televisions, computers, and smartphones. Many LCMs are predicted to be persistent and bio-accumulative and have been reported in household dust and other environmental samples, suggesting potential chronic human exposure. This may prove problematic as our lab has previously shown a small subset of commercially available LCMs, individually and in mixtures, can significantly disrupt the signaling pathways of nuclear receptors involved in key metabolic pathways as well as induce adipogenesis in vitro. Methods and Results: To explore whether LCMs would similarly induce metabolic disruption in vivo, zebrafish were exposed from 1 to 6 days post fertilization (dpf) to 3 lab prepared LCM mixtures at approximately equimolar 100, 10, 1 and 0.1 nM concentrations that cover occupationally and environmentally relevant exposure scenarios. Larvae were evaluated for changes in energy expenditure and locomotor behavior at 6 dpf as well as body morphometrics (adiposity, weight, length, and BMI) at 30 dpf to quantify the acute and sustained metabolic health impacts of exposure. Results found LCM exposure, at several concentrations and mixture compositions, promoted hyperactivity and decreased rates of cellular respiration at 6pf and increased adiposity, length, weight, and BMI at 30 dpf. Conclusion: Given the ubiquitous environmental presence of LCMs and their detection at and well above, concentrations displaying some of these adverse effects, there is a clear and urgent need to further evaluate and characterize impacts of LCM exposure on human health.

23.**Thamarahansi Mugunamalwaththa**

BMI

The biochemical basis of SMYD5 activating HIV latency via assembling a TAR-RNA Transactivation Complex

SMYD5, a SET and MYND domain-containing protein family member, plays a crucial role in HIV transcription and latency. We hypothesize that SMYD5 activates HIV latency via assembling an RNA-based transactivation complex since it binds to the HIV transactivation response (TAR) element and Tat protein at the HIV promoter. However, the molecular nature of the SMYD5-TAR RNA interaction, which is central to understanding the molecular mechanism of SMYD5 in HIV reactivation, is unknown. We found that the MYND domain of SMYD5 exhibits a highly positively charged surface, suggesting its potential involvement in nucleic acid binding. We also found that TAR RNA can adopt two major forms of tertiary structure, but it is still unknown which form binds to SMYD5 and which form will provide a structural scaffold on which a functional transactivation complex is assembled. We plan to investigate further the interaction between SMYD5 and TAR RNA by site-directed mutagenesis and X-ray crystallography and to reveal the mechanism by which this interaction mediates the assembly of the transactivation complex. Unraveling the biochemical mechanisms of SMYD5 in HIV transcription and latency could unleash its potential as a treatment target for HIV.

24.Yogesh Joshi

Anatomy and Cell Biology (OVAS)

Inhibition of innate immune activation improves Drosophila model of Vps13D-associated neurodegeneration

The innate immune system plays a major role in pathogenesis of several neurodegenerative diseases like Ataxia, Parkinson's, Alzheimer's, and others. Especially in Drosophila, activation of the Innate immune system leads to the production of various Anti-microbial Peptides(AMPs) equivalent to cytokines in humans. Vps13-D is an important protein that plays an essential role in maintaining mitochondrial homeostasis via mitophagy, a type of autophagy. Our lab works on the Vps13D mutant model of Drosophila which is found to have dysfunctional mitochondria unable to undergo mitophagy, especially in neurons. Relish, an NFkB factor, and Kenny, equivalent to the human IKKy factor, are the important proteins of interest in studying the Innate immune system in our fly model. Our experiments have shown that overexpressing Kenny in fly neurons or glial cells can activate the AMPs in heads, and knocking down Relish in neurons and glial cells improve the eclosion rate and extend the lifespan. However, more work is being done to discover Kenny's role in regulating autophagy in large and thus innate immune system our mutant models, which could be used to switch the immune system and prevent adverse neurodegenerative diseases.

POSTER SESSION II

25. **Alaleh Zamiri**

Pathology

*SR-3420, a Selective Synthetic Ligand of ABHD5, Serves as a Radiosensitizer by initiating Ferroptotic Cell Death in Radioresistant HPV(-) HNSCC***.**

Most cancer cells undergo a metabolic shift towards aerobic glycolysis, known as the Warburg effect, favoring it over the TCA cycle and oxidative phosphorylation. Earlier research has demonstrated that human papillomavirus (HPV)-negative head and neck squamous cell carcinoma (HNSCC), characterized by radio-resistance and worse prognosis, exhibits a higher dependency on glycolysis compared to HPV (+) HNSCC.

ABHD5 is a crucial regulator of lipid metabolism in various tissues by working as an activator of adipose triglyceride lipase (ATGL, PNPLA2). The ABHD5/ATGL metabolic pathway is often suppressed in cancer cells that favor glycolysis. Here we showed that SR-3420, a highly selective synthetic ligand of ABHD5 and a potent inducer of ATGL-dependent lipolysis, promotes ferritinophagy and ferroptosis, an iron-dependent programmed cell death, in HPV(-) HNSCC cell lines more effectively than in HPV(+) HNSCC or normal keratinocytes. This can be attributed to increased reactive oxygen species (ROS) production during lipolysis leading to lipid peroxidation and elevated iron level, resulting in Ferroptosis. Importantly, the cytotoxic effect of ABHD5 activation can be significantly enhanced by ROS generation following radiotherapy. Taken together, we propose that pharmacologic activation of ABHD5 can serve as a radiosensitizer by initiating ferroptotic cell death, thereby contributing to overcoming therapy resistance in HPV(-) HNSCC.

26. **Alan Luis Carbajo Jr.**

Biochemistry, Microbiology and Immunology

Synthetic biology or computer games; is there a difference?

In the realm of synthetic biology, recent progress in machine learning has opened new avenues of scientific exploration. The last two years have witnessed the emergence of DNA-based language models such as DNABERT, Nucleotide Transformer, Hyenadna, and the latest addition, ENBED. These models introduced Large Language Models (LLMs) into genomics, with current uses including: detecting epigenetic markers, promoter sites, and generating functional annotations. However, amongst the proliferation of protein-based language models built to tackle protein design, the exploration of genome design remains a relatively uncharted territory. Against the backdrop of the Covid-19 pandemic, the need for innovative tools to prepare for emerging viral outbreaks has become increasingly evident. We introduce a LLM built to synthesize viral genomes from a simple English prompt to quickly, and simply build predictive viral models. Our method modifies the work done in ENBED by pretraining a Transformer-based DNA model using Adenovirus assemblies. Adenovirus genomes are relatively short and simple, which make them great candidates for building synthetic viral genomes using LLMs. Currently, we have a proof-of-concept English-to-DNA translation model with the intent of generating full-length viral genomes by inputting the virus name. Using this, we can generate potential mutations that alter pathogenicity. A long-term goal is to use our LLM in development of treatments for viral diseases by predicting pathogenic mutations and emerging viruses. With this tool, we hope to test the viability of LLMs in synthetic viral genome design.

27. **Alessandra Zieleniewski**

Biological Sciences

Utilizing dCas9 as a tool in observing the function of SIN3 in gene repression

SIN3, a corepressor protein, functions as a pivotal component within a multi-subunit complex alongside histone deacetylase 1 (HDAC1), which modulates gene expression. Members of our laboratory previously determined that the complex is commonly associated with soft repression, characterized by the reduction of gene expression without complete silencing. To elucidate the precise role of SIN3 in soft repression, a strategy employing a dCas9:SIN3 fusion to facilitate the repositioning of SIN3 along the genome will be implemented. This study aims to evaluate how the position of SIN3 relative to distinct genomic elements impacts gene expression. Initial experiments will be conducted in S2 cells as a proof of principle of the technique. Subsequent to the successful validation of our methodologies, the experiment will be further studied in *Drosophila melanogaster*. Furthermore, a SIN3 interacting domain (SID) derived from a smaller protein, Pf1, will be fused with dCas9 to mitigate potential challenges due to the bulkiness of SIN3. We hypothesize that close proximity of SIN3 to gene elements will yield greater effects on gene expression compared to positions further from the promoter. Notably, the dCas9-Pf1 construct housing the SID is postulated to elicit synonymous outcomes to dCas9-SIN3 due to the presence of essential binding domains. Evaluation of gene expression will be carried out through reverse transcription - quantitative polymerase chain reaction to discern the effects of the placement of dCas9 constructs in relation to various promoters. At the conclusion of this study, we expect to gain knowledge regarding the explicit role of SIN3 in repression.

28. **Ali Ranjbaran**

Center for Molecular Medicine and Genetics

Single cell profiling of immune cell responses in asthmatic children across psychosocial experiences

Asthma is a chronic inflammatory disease of the respiratory tract which disproportionately affects children. Glucocorticoids, including cortisol, are potent modulators of the immune response that are commonly used for disease management. Psychosocial stress, lack of sleep, and other psychosocial factors can greatly influence levels of endogeneous glucocorticoid cortisol, with effects on immunological health and asthma. We have previously shown that glucocorticoids have distinct effects across different peripheral immune cell types in children with asthma, and that in peripheral blood leukocytes the expression of genes associated with asthma is modulated by psychosocial factors. Here we aim to utilize scRNA-seq from our full cohort of pediatric asthma (n=232) to characterize the response of immune cell subpopulations to proinflammatory stimuli and glucocorticoids, and how this response is modulated by psychosocial experiences. Specifically, we treated PBMCs with LPS (bacterial cell wall component), PHA (T cell mitogen), and in combination with Dexamethasone (glucocorticoid). We have now sequenced 516,221 high-quality cells classified in four major cell types: T cells, B cells, NK cells, and monocytes and identified differentially expressed genes with LPS 7,380, PHA 17,056, and PHA+DEX 9,338. Monocytes had the most changes (LPS 4,937, PHA 5,758, PHA+DEX 2,686). Our preliminary results have confirmed that glucocorticoid significantly modifies gene expression response to immune stimulation as we previously characterized. We are currently characterizing the effect of psychosocial experiences on the different immune cell types and on their ability to respond to immunomodulators.

29. **Aliyah Goldson**

Biological Sciences

Innate metabolic profiles are not correlated with variation in the exploratory behavior of zebrafish (Danio rerio)

Examining how physiological factors impact individual differences in behavior can shed light on the mechanisms driving behavioral variability. A potential contributor to behavioral variation is individual differences in metabolic rate. The pace of life syndrome (POLS) hypothesis proposes a correlation between the physiological traits of an individual, such as metabolic rate, and their behavioral traits (i.e., risk-taking, aggressiveness, or exploration). This study aimed to explore if baseline metabolism affects individual differences in the exploratory behavior of *Danio rerio* (zebrafish). We hypothesized that fish with greater metabolic rates would exhibit more exploratory behaviors in novel environments due to their need to acquire more resources. To test this, we employed the novel tank test (NTT), an assay in which fish were placed in a novel environment and their exploratory behavior was recorded. Two days later, metabolic activity was captured by measuring oxygen consumption of fish over 30 minutes. We found a positive correlation between oxygen consumption and weight, with female fish having higher metabolic profiles than males suggesting our assay captured individual variability in metabolism. However, there were no significant correlations between the metabolic profiles of fish and their behavior in the NTT. Finally, to directly manipulate metabolism, we starved fish for 16 hours prior to the NTT. We found that 16-hour starvation significantly reduced metabolism but had no effect on behavior. This challenges the POLS hypothesis' proposed link between metabolic rate and behavior. The lack of significant correlation suggests metabolism may have less of an influence on behavior than initially thought.

30. **Annie Thy Nguyen**

Translational Neuroscience Program

Gestational benzene exposure leads to sexually dimorphic immunological adaptations along the placenta-brain axis

Maternal immune activation (MIA) during pregnancy is highly associated with adverse offspring outcomes, such as neurodevelopmental delays and infectious susceptibility. In the modern era, air pollutants, such as benzene, have become one of the most prominent MIA triggers. The placenta-brain axis provides a unique window into how gestational programing facilitates neuroimmune development and predicts offspring disease risk. Microglia, the primary immune cell of the brain, are especially unique targets of study due to their generation solely in fetal life and shared ontology with placental macrophages. However, the mechanisms of how the placenta modulates MIA and how the fetal neuroimmune system responds to placental signals are poorly understood.

To study this, pregnant C57BL/6J mice were exposed to benzene (5 ppm) for 24 hours/day from embryonic day (E) 0.5-12.5. E12.5 litters were sacrificed for bulk RNA-seq, qPCR, and flow cytometry. Placenta transcriptomics showed intrinsic sex differences in regulation of neurodevelopment. After benzene exposure, enrichment analysis showed placenta biological pathways were predominately immunological in males and metabolic in females. qPCR confirmed regulation of interferon-stimulated genes, IFI44 and IRF8, was sexually dimorphic in placenta and fetal brain. MHCII+ placenta macrophages were significantly decreased in males versus females in flow cytometry. Our results suggest benzene-induced MIA causes dysregulation of the developing neuroimmune system in a sex-specific manner. Particularly, the interferon pathway may be a key mechanistic target to understanding sex-specific adaptations and postnatal disease susceptibility.

31. **Bethany Archer**

Family Medicine and Public Health Sciences

Improving Maternal and Infant Health in Detroit, Michigan

The African-American community in Detroit, Michigan, has severe health inequalities for mothers and infants, demonstrated by a maternal death rate higher than the national average. The preterm birth rate surpasses the national average, which is attributed to factors such as genetic predisposition, racial discrimination, chronic stress, and socioeconomic conditions. A targeted educational campaign with prenatal workshops, resources, and brochures addresses maternal and infant health disparities in Detroit's African-American community. The program consists of educating pregnant mothers on preterm birth and associated risk factors through prenatal classes. The implementation team will analyze data derived from survey campaigns and local health statistics. Every six months, vital statistics will be documented to identify population trends. The program will monitor trends in participation in the prenatal educational classes to assess the effectiveness of the educational brochure. After the prenatal course, Qualtrics survey results will be analyzed to determine what was learned and what could be improved. The program's goal is to reduce preterm births by 2% over the next three years. Maternal and infant health disparities within the African American population stem from social determinants of health, i.e., socioeconomic status, racial discrimination, social stress, and healthcare accessibility. A targeted educational campaign will address the maternal and infant health issues resulting in preterm birth, thus increasing healthy literacy and the utilization of local healthcare resources.

32. **DruAnne Maxwell**

Physiology

Mixtures of Per- and Polyfluorinated Substances (PFAS) alter sperm methylome in adult male mice.

Male fertility has been declining worldwide, with the greatest decline in countries with high levels of endocrine disrupting chemicals (EDCs). Based on ability to disrupt normal hormone signaling, per- and polyfluorinated Substances (PFAS) have been classified as EDCs. PFAS exposure has been linked to adverse male reproductive health; however, the mechanisms, including epigenetic modifications in sperm, remain unknown. Thus, the aim of this study was to assess the effect of PFAS mixtures on the sperm methylome. C57BL/6 wild-type adult male mice were exposed to a mixture of five PFAS substances (PFOS, PFOA, PFNA, PFHxS, Genx at 20 µg/L each) for 18-weeks or vivarium water as a control. Epididymal sperm was collected, and genome-wide methylation was assessed using reduced representation bisulfite sequencing and Illumina mouse methylation array. PFAS mixtures resulted in 2,861 (RRBS) and 83 (Illumina) DMRs ($q<0.05$, $\geq$ 5% methylation change). Enrichment analyses revealed PFAS-induced sperm DMRs associated with genes important for behavior and developmental pathways in RRBS, while Illumina DMRs were related to genes in pathways involved in lipid metabolism and cell signaling. 12 overlapping DMRs between methods displayed the same direction of methylation change but had modest correlation in methylation values ($r = 0.48$). To our knowledge, this is the first study to examine PFAS exposure on genome-wide methylation of sperm in adult male mice. Our results demonstrate that exposure to a mixture of legacy and newly emerging PFAS chemicals in adult mice results in aberrant sperm methylation and highlight spermatogenesis as a sensitive window of development.

33. **Eid Alshammari**

Biochemistry, Microbiology, and Immunology

Structural basis and mechanism of regulation of USP10

Ubiquitin-specific protease 10 (USP10) is a cysteine deubiquitinase that is involved in a variety of biological mechanisms like DNA damage repair and promoting lung cancer growth by augmenting the stability and half-life of oncogenic proteins through deubiquitination. Studying the structure and mechanisms of regulation of USP10 can expand our understanding about its functions under normal and pathological conditions. An AlphaFold (AF) structure of USP10 predicted by artificial intelligence was used to conduct structural and comparative analyses with crystal structures of other selected USPs. The sequence alignment revealed that the catalytic triad and adjacent residues in the ubiquitin-binding pocket of USP10 are evolutionarily conserved and may play a role in the enzyme-ligand binding and could be exploited to target USP10's deubiquitinase activity. A group of small-molecule compounds were screened and selected using the colony formation assay and docking analysis. GL-462 compound was able to target and inhibit USP10 in a fluorogenic ubiquitin-rhodamine assay. USP10 also has a long-disordered N-terminal region with three stable motifs that physically interact with the catalytic domain and may be involved in an autoinhibitory mechanism. USP10 regulates oncogenic proteins that promote tumorigenesis of lung cancer, thereby targeting USP10 is of therapeutic significance but requires deep understanding of its structure and mechanisms of inhibition.

34. **Emma Fidler**

Biological Sciences

Comprehensive analysis of role of an intron in transcription and post-transcriptional dynamics

A splicing-competent intron has been found to affect gene expression at almost every step between transcription and translation. These studies, however, were performed with different genes and different introns. We therefore investigated the comprehensive role of introns of two yeast genes, *ASC1* and *APE2*, on cellular fitness and multiple steps of gene expression. Intronless versions of both genes grew slower by 30-60% than their intron-containing counterparts, and their growth was compromised on ethanol and glycerol medium. Furthermore, there was enhanced R-loop signal in the coding region of both *ASC1* and *APE2* in the absence of intron. Steady state RNA level of *ASC1* and *APE2* decreased by about 30-folds and 5-folds respectively in the absence of intron. Nascent transcription analysis using TRO approach revealed a drop in transcription of both *ASC1* and *APE2* by 4-10 folds and 2-5 folds respectively in the intronless state. mRNA half-life of both genes decreased by about 2-3 folds in the absence of intron. FISH approach however could not detect any impact of intron on nucleocytoplasmic transport of mRNA. Measurement of protein level by Western blot found absolutely no detectable signal for either protein in the absence of intron. These results suggest that introns of *ASC1* and *APE2* affect the expression of their genes at the level of transcription, mRNA stability and translation but not at the level of nucleocytoplasmic transport. Furthermore, both *ASC1* and *APE2* introns affect the fitness of cells measured in terms of growth rate and ability to grow on different carbon sources.

35. **Bedri Ranxhi**

Pharmacology

Investigating the Therapeutic Efficacy of The Akt Modulator A-443654 in a Drosophila Model of Parkinson's Disease

Parkinson's disease (PD), a neurodegenerative disorder affecting over 10 million globally, presents complex symptoms impacting motor and cognitive functions. Despite multifaceted research, PD's origins remain elusive, likely influenced by genetic, environmental, and age-related factors. A commonality in PD is α-synucleinopathy, marked by toxic α-synuclein protein accumulation, particularly in dopamine-producing neurons of the substantia nigra, causing degeneration. The Akt modulator A-443654 emerges as a potential therapeutic agent, showing promise in reducing α-synuclein mRNA and protein production in studies. Our investigation, utilizing Drosophila melanogaster as a model organism, focuses on two experimental models involving α-synuclein overexpression and rotenone-induced toxicity. Flies exhibited diminished lifespan and motility, mirroring PD symptoms. Remarkably, A-443654 administration significantly extended lifespan in both models without affecting climbing ability. These findings underscore A-443654's potential for PD treatment, providing crucial insights for future exploration in mouse models and paving the way for promising therapeutic interventions in PD.

36. **Isaac Baiden**

Physiology

Loop Diuretic Resistance in a Mouse Model of Cardiorenal Syndrome

Cardiorenal syndrome (CRS) is a disease condition that encompasses concurrent damage to the heart and kidneys. Patients with uncompensated heart failure (HF) develop edema, renal injury and are treated with loop diuretics. However, over 50% of HF patients are resistant to loop diuretics. The molecular mechanisms underlying the development of diuretic resistance remain unclear. Aim: We explored whether C57Bl6J mice would develop kidney damage and loop diuretic resistance after MI-induced HF.

HF was induced through ligation of the left anterior descending coronary artery (LAD) and classified as MI group and compared to a sham surgery group (without ligation) as controls. Both groups were assessed for cardiac function through echocardiography and renal function by measuring GFR. MI mice had a 50% reduction in ejection fraction (EF) 4 weeks post-surgery compared to sham ($p<0.05$). Six months after surgery, MI mice showed decreased GFR compared to Sham ($p<0.05$). A saturating dose of the NKCC2 inhibitor, bumetanide (20 mg/Kg), induced diuresis and natriuresis in sham mice (ΔUNa: 117.2 ± 11.02µmols/4h) but had little effect in MI mice which exhibited an attenuated response ($p<0.05$), indicative of loop diuretic resistance. However when challenged with hydrochlorothiazide (100mg/kg), the diuretic response was enhanced in MI mice (ΔUNa: 129.54 ± 11.59µmols/4h, $p<0.05$).

Our data suggest that C57Bl6J mice develop CRS and loop diuretic resistance which may be secondary to enhanced DCT NaCl transport. This model could be useful to study the molecular mechanisms causing decreased renal function and loop diuretic resistance after MI-induced HF.

37. **Iyman Hamad**

Master of Public Health

When black women speak, why don't doctors listen?

Black women in the United States face significant healthcare disparities despite the nation's consistent advancements. Acknowledging the substantial impact of healthcare disparities on vulnerable populations' well-being, plans are in motion to expand Black Maternal Week into a month-long campaign, aiming to confront these inequalities. This initiative intends to deliver workshops, educational sessions, and community events tailored to vulnerable populations. A 10-question guide empowering women with essential knowledge about their health and pregnancy with collaboration with professionals and doctors would also be shared with these communities.

Furthermore, the intervention would focus on feedback collection and evaluations to ensure the efficacy of the implemented strategies, aiming for tangible improvements in maternal health outcomes. By utilizing data-driven approaches, this effort strives not only to reduce pregnancy complications but also to foster a more equitable society that is both accessible and affordable.

The envisioned impact extends beyond immediate health outcomes. Observing long-term trends, such as increased access to doula services and a decline in Black maternal mortality rates, will serve as benchmarks for success. Additionally, the initiative's annual summit seeks to continually enhance community awareness and education on Black maternal health, empowering women to advocate for themselves effectively.

Through this multifaceted approach driven by data and evaluation, the intervention aims to diminish healthcare disparities and pave the way for a society where Black women receive equitable healthcare and experience improved maternal outcomes.

38. **Jasnoor Kaur and Tyiesha Head**

Family Medicine and Public Health Sciences

End the silent suffering of mothers

Peripartum depression is an episode of major depression temporarily associated with childbirth, which can occur during pregnancy or shortly after childbirth. The prevalence of African American women reporting peripartum depressive symptoms was 43.9%, compared to 31.3% among White women. African American women experience higher risks of poor peripartum outcomes. The burden of stress can lead to a higher risk of poor birth conditions. Suicide attempts and rates are on the rise within African American women, who are already at higher odds of peripartum depression which is very concerning. We have developed a health promotion program to provide African American mothers with prenatal and postnatal psychoeducational sessions using cognitive behavioral therapy and interpersonal therapy. This will help them deal with peripartum depression and prevent suicide. It will increase African American mothers' knowledge and awareness of the symptomology of peripartum depression, reduce symptoms of peripartum depression in African American mothers, and increase access to auxiliary community-based services. Participation will be based on provider referral of interested patients. We will evaluate our health promotion program using pre- and post-program self-report questionaries, interviewing the providers who referred patients to gain insight on improving participation (to make any necessary adjustments), and process-based evaluations from random selected participants to receive unbiased objective feedback on the program. This health promotion program aims to ensure African American mothers have access to and seek peripartum care, prenatal and postnatal, in hopes of decreasing the symptoms of peripartum depression and providing a safe space for those.

39. **Jillian M. Eichstaedt**

Translational Neuroscience Program

Evidence of dACC glutamate modulation during top-down inhibitory control predicting weight loss ability in individuals with obesity using ^{1}H fMRS

Poor top-down inhibitory control and its association to weight loss maintenance is poorly understood. The dorsal anterior cingulate cortex (dACC) is central to inhibitory control that is driven by the interplay of glutamatergic/GABAergic neurotransmission. ^{1}H fMRS can assess changes in glutamate driven by task condition, illuminating neurobiological mechanisms. Here, we present preliminary evidence of dACC glutamate modulation being impacted by emotionally valanced food cues during inhibitory control and its association with weight loss ability in individuals with obesity. ^{1}H fMRS from the dACC was collected in 13 individuals with obesity/overweightness immediately post-6-month clinical weight loss program (WLP). A visually guided motor tapping task requiring participants to respond to stimuli under two modes, "Non-Selective" (motor control response to 100% of trials) and "Selective" (withholding `prepotent` responses on 20% of trials - involving both motor control and inhibition), and under two stimuli types (Squares and emotionally valanced Food/Non-Food cues). Glutamate modulation (expressed relative to the total signal) was tested across main task conditions (Fixation-Crosshair, Squares and Food/Non-Food) using a repeated measures GEE approach (SAS GENMOD). The task condition term was not significant (χ^2=3.99, p=0.136), however, post-hoc analyses demonstrated significantly increased glutamate during Squares (z=-2.25, p=0.025), but not during Food/Non-Food (z=-1.55, p=0.122), compared to the Fixation-Crosshair condition. A trending correlation was observed between decreasing dACC glutamate modulation (Selective mode, Food/Non-Food) and less weight loss during the WLP [R^2=0.274, F(1,11)=4.15, p=0.066]. Results provide initial support that emotionally balanced food cues may impact top-down inhibitory control ability and predict one's long-term inability to lose weight.

40. **Kyle Siegel**

Pharmacology

In vitro endocrine and cardiometabolic toxicity of artificial turf materials

Artificial turf, a chemically complex consumer product used for recreational and residential purposes, can prospectively harbor mixtures of chemicals that act as endocrine disruptors. To determine potential endocrine disruptive effects of turf, we used a luminescent reporter bioassay in human cell lines to test for turf-mediated activity on androgen receptor (AR), estrogen receptor α (ERα), glucocorticoid receptor (GR), thyroid receptor β (TRβ), peroxisome proliferator activated receptor γ (PPARγ), and aryl hydrocarbon receptor (AhR). Immortalized human cell lines were transiently transfected with plasmids encoding the receptor, a receptor-specific luminescent reporter, and constitutively expressed reporter to normalize by cell number. Transfected cells were exposed to chemical for 24 hours and lysed prior to luminescence quantification. From 18 surveyed extracts, 15, 11, 13, and 6 extracts activated AR, ERα, GR, and TRβ, respectively. 15, 4, 6, and 13 extracts altered canonical agonist-mediated activity for AR, ERα, GR, and TRβ, respectively. 12 extracts activated PPARγ. To test for adipogenic effects, confluent human mesenchymal stem cells (hMSCs) were differentiated down the adipocyte lineage concurrent with turf exposure. 13 turf extracts modestly increased DNA content in hMSCs. A different set of 11 extracts minutely to modestly increased lipid accumulation. 17 extracts significantly activated AhR; two of these induced cardiotoxicity in rat cardiomyoblasts following 24 hours of exposure and viability measurements by MTT assay. Artificial turf can thus produce endocrine disruptive effects that warrant further study.

41. **Li Tao**

Physiology

A modified method to extract DNA from FFPE samples

Formalin-fixed paraffin-embedded (FFPE) samples have proven to be a feasible source for genomic (gDNA) extraction, sequencing, and genotyping. However, the current protocols for extracting gDNA from FFPE tissues require relatively large sample amounts, limiting the usage of FFPE samples with small quantity. We aim in this study to improve the yield of DNA extraction from FFPE samples. Specifically, we optimized the deparaffinization, protein digestion, and gDNA lysis steps and tested in extracting DNA from FFPE liver samples with different sample quantity. Our findings indicated that with standard commercial kits, an extended heating step combined with a manual removal of paraffin significantly increased the DNA yield by 67% while also improving the DNA quality. Our improved technique provides an improved strategy for isolating gDNA from FFPE samples, increasing the chance of sample usage when the quantity of biospecimen sample is limited.

42. **Maryam Safdar**

Physiology

Genetic and pharmacological exercise mimetics rescue endurance and climbing speed in Drosophila Clk^{out} mutants with circadian rhythm disruption.

Circadian rhythm disturbances are associated with various negative health outcomes, including an increasing incidence of chronic diseases with high societal costs. While exercise can protect against the negative effects of rhythm disruption, it is not available to all those impacted by sleep disruptions, in part because sleep disruption itself reduces exercise capacity. Thus, there is a need for therapeutics that bring the benefits of exercise to this population. Here, we investigate the relationship between exercise and circadian disturbances using a well-established *Drosophila* model of circadian rhythm loss, the Clk^{out} mutant. We find that the Clk^{out} mutant flies display a reduced exercise capacity, measured as post-training endurance, flight performance, and climbing speed, and that these phenotypes are not rescued by chronic exercise training. However, exogenous administration (and genetic overexpression) of molecules known to mediate the effects of chronic exercise is able to effectively rescue mutant exercise performance, including upregulation of other known exercise-mediating transcripts, without restoring the circadian rhythms of mutants. This work points the way toward the discovery of novel therapeutics that can restore exercise capacity in patients with rhythm disruption.

43. **Mizumi Setia**

Ophthalmology, Visual and Anatomical Sciences

The prevalence of senescent cells in the epithelium and stroma of Herpes Simplex Virus (HSV-1) infected corneas

While viral infection-induced senescence is established for RNA viruses like COVID-19, Vesicular Stomatitis Virus, and Dengue virus, the impact of corneal HSV-1 infection on cellular senescence and its contribution to pathogenesis is unclear.

HSV-1 McKrae-infected mice were euthanized at different days post-infection (p.i.). Corneal epithelium (CE) and corneal stroma (CS) were separated using EDTA or Dispase. Flow cytometry based EdU (5-ethynyl-2'-deoxyuridine) staining assessed CE proliferation, and senescence in CE and CS was determined via senescence-associated (SA) β- galactosidase (β-gal) staining with Flow Cytometry and Histochemistry. RT-qPCR measured SA-gene expression in CE.

Corneal HSV-1 infection led to a decline in CD326+CD45-ve epithelial cells at 3-, 6-, and 8-day p.i. However, the numbers of epithelial cells increased significantly at 16-day p.i. EdU staining revealed a higher frequency of EdU+ve CD326+CD45-ve epithelial cells at 4-, and 10-day p.i. compared to uninfected CE. Median fluorescence intensity (MFI) of SA- β-gal increased progressively in epithelial cells at 4- and 10-day p.i., indicating hyper-proliferation associated senescence in infected CE. Furthermore, the β-gal staining in whole mounts of CS showed greater number of senescent cells at 10-day p.i. compared to 4-day p.i. and uninfected CS, suggesting the presence of senescent cells in HSV-1 infected CS. Additionally, we observed a significantly higher mRNA expression of SerpinB2, one of the components of SASP (Senescence associated secretory phenotype) in CE at 5- and 9-day p.i. compared to uninfected CE.

Our preliminary findings suggest the prevalence of senescent cells in CE and CS following corneal HSV-1 infection.

44. **Rayane Dennaoui**

Cancer Biology/Oncology

Cooperative functions of cytokine signaling through JAK1 and JAK2 in orchestrating postnatal mammary gland development

Janus kinases (JAKs) and Signal Transducers and Activators of Transcription (STATs) are in 'the lines of fire' of several hormones and cytokines that mediate essential functions in the mammary gland during gestation. Previous studies have shown that JAK1 and JAK2 have non-redundant functions in the activation of STAT5 and STAT3 transcription factors, respectively, during distinct stages of the gestational cycle of the mammary gland. We found that female mice with a mammary epithelial-specific deletion of both JAK1 and JAK2 exhibited a severe block of the development of mammary ducts. This suggests that cooperative functions of cytokines through JAK1 and JAK2 are obligatory for the earliest stages of mammary epithelial development that precede the subsequent action of steroid hormones that control epithelial growth and differentiation at puberty. We also determined high activation of STAT3 in newborn mammary ducts and compensatory activation of STAT5 in JAK1 knockouts. We developed a novel STAT3/5a/5b conditional triple knockout (cKO) mouse model to determine whether these STAT proteins are the essential mediators for proliferation and lineage specification of ductal progenitors. The histological examination of STAT3/5 cKO mammary glands revealed normal ductal morphogenesis but impaired alveologenesis and lactation. We uncovered that STAT1 was highly activated in STAT3/5 cKO mammary epithelial cells. Experiments using STAT1/3/5a/5b cKO mice are underway to investigate whether mammary gland development biological significance of STAT1 upregulation in epithelial cells that are deficient in STAT3 and STAT5. Our study will decipher previously unknown mechanisms downstream of cooperative functions of JAK1 and JAK2 in early mammogenesis.

45. **Ryan Katz**

Ophthalmology, Visual and Anatomical Sciences

Evidence for photoreceptor oxidative stress detected by OCT biomarkers in patients at the earliest stage of diabetic retinopathy

It is unclear if oxidative stress in the outer retina occurs early in patients at the beginning of non-proliferative diabetic retinopathy (DR), the hypothesis examined herein.

Twelve patients with type 2 diabetes, little to mild non-proliferative DR and no macular edema underwent standard ophthalmic clinical evaluation and OCT. From each OCT, we examined the foveola, fovea, parafovea, perifovea, and peripheral retina and measured two oxidative stress-linked biomarkers: i) the mitochondrial configuration within photoreceptors measured from the profile shape aspect ratio (MCP/AR) of the hyperreflective band posterior to the external limiting membrane (ELM), and ii) the external limiting membrane to retinal pigment epithelium thickness (ELM-RPE). To model the impact of retinal acidification on the OCT biomarkers, 129S6/ev mice were given a single IP injection of acetazolamide (ACZ, carbonic anhydrase inhibitor) or vehicle.

MCP/AR and ELM-RPE thickness were both lower-than-normal in all macular regions in the T2D group. In a companion experimental study involving an ACZ challenge, we tested whether this biomarker pattern is consistent with an oxidative stress / acidification signaling pathway. Indeed, in response to ACZ, non-diabetic mice also showed subnormal MCP/AR and ELM-RPE thickness.

An OCT energy-linked biomarker pattern was identified in patients with type 2 diabetes that appears in-line with an oxidative stress / acidification signaling pathway. We predict that administration of anti-oxidants in future studies will correct these OCT biomarker lesions and confirm the presence of oxidative stress.

46. **Sarah Eringaard**

Family Medicine and Public Health Sciences

Coughing Up the Facts: Asthma in Detroit Covered

This research highlights the prevalence rate of asthma in the city of Detroit. The city of Detroit has a rich industrial history which has had lasting health effects on the residents of Detroit. This research focuses on the environmental, economic, and social factors that contribute to the disease. A health promotion program has been curated to help diminish the prevalence of asthma. The program includes components such as doctor collaboration, virtual connection, giving appropriate incentives for asthmatic individuals, and providing them with resources and education related to asthma. The health promotion program is targeted at Detroit residents, specifically those between the ages of 5 and 45 who come from low socioeconomic backgrounds. This program is administered in three stages and will last for a year to track patients through all seasons and identify asthma triggers. An educational component called the asthma management modules will be provided through patient portals to spread more awareness of asthma. Additionally, we will provide high-efficiency particulate air (HEPA) filters and central furnace filters and inform participants of free home assessments provided by the City of Detroit that may help identify asthma triggers to address indoor environmental concerns. The main goal of this program is to provide people with the knowledge and tools they need to properly manage their asthma at home.

47. **Shreya Nirmalan**

Molecular Medicine and Genetics

Microbiome and host genetic effects in Inflammatory Bowel Disease

Dysbiosis of the gut microbiome and host genetics contribute to inflammatory bowel disease (IBD) risk, with a key role for non-coding genetic variants. Both host genetic variants and the gut microbiome regulate host gene expression in the colon; however, it is still unknown whether interactions between host genetics and the microbiome (GxM) regulate host gene expression in the gut in IBD. Here, we used data from the Human Microbiome Project to perform interaction eQTL mapping to identify GxM in IBD. Our sample consisted of host genotype, and paired host gene expression and mucosal gut microbiome (16S rRNA) data from rectum biopsies for 64 patients with IBD and 22 controls. We identified 3307 genes with eQTLs (eGenes, FDR = 10%) . We integrated the microbiome data with the eQTLs to identify GxM. We tested for interaction with the relative abundance of each microbe and found 65 interactions for 39 genes and 36 microbial taxa (FDR = 10%). We also tested for interaction with the presence/absence of a microbe and found 19 additional GxM (12 genes and 10 taxa; FDR = 10%). The expression of 14 genes with GxM are associated with IBD risk in PhenomeXcan. Our results show the first evidence of genetic effects on gene expression that are modulated by the microbiome composition in IBD, and provide insight into how IBD risk could be decreased by targeting specific microbial taxa depending on host genotype.

48. **Sonia Khalid**

Psychiatry & Behavioral Neurosciences

Chronic intermittent gestational morphine use impairs mouse maternal behavior development

Maternal behavior is modulated by the endogenous opioid system, which is also a target for drugs of abuse, like morphine. Clinical studies suggest that chronic morphine leads to opioid receptor sensitization and reduced responses to infant cues (Wallin et al. 2021; Miranda-Paiva et al. 2001). Preclinical rodent studies imply that chronic morphine in late gestation led to prolonged latency of last pup retrieval, decreased preference for pup odors, reduced licking/nesting behavior, and increased non-maternal activities, such as self-grooming and digging (Wallin, et al. 2021; Slamberová & Szilágyi, 2001). The purpose of this study is to evaluate if intermittent, voluntary morphine exposure started prior to pregnancy and continued throughout gestation - mimicking human drug-taking - differentially alters maternal behavior. Female mice (9-10 weeks old) began morphine drinking (0.2 mg/ml) two weeks prior to breeding and continued consumption until pups were weaned. Dams were longitudinally assessed for anxiety and maternal behaviors, including pup retrieval, nesting/grooming, and olfactory discrimination. Pup retrieval time was decreased when measured at mid (4) compared to early (1-2) postnatal days (PD) in control dams, reflective of maternal learning, which was absent in morphine dams. On the other hand, morphine dams displayed reduced licking and nesting behavior during pup retrieval, spent less time seeking pup olfaction cues, and showed greater anxiety-like behavior compared to control dams. These data suggest a robust negative impact of intermittent, chronic morphine intake on maternal behavior development that may involve mood dysregulation.

49. **Susheel Pangeni**

Physics and Astronomy

Myo16a is a slow ATPase motor

Myosin 16 (Myo16) is a single-head molecular motor with one IQ motif and N-terminal ankyrin repeats (ANK). The ankyrin repeats enable it to bind with protein phosphatase 1 (PP1) catalytic subunits 1alpha and 1gamma. Recent studies suggested that the primary role of Myo16 lies in the development and functioning of the nervous system, mainly guiding specific cell types during migration. It plays a vital role in coordinating essential cellular processes within neural tissues. Myosin 16 exists in two isoforms that has shorter tail isoform, Myo16a, and a longer tail isoform, Myo16b. To understand Myo 16a kinetics, we used stopped-flow techniques. In our study, we used Myo16a-dANK. The maximum ATPase rate and Km of actin were measured as 0.58 /s and 4.1 uM, indicating that Myo16a is a slow motor and weakly binding to actin filament. The mantATP binding to myosin with (k2) and without (k2') actin filament were measured at similar rates as 97.98 $\pm$101.94 /s and 81.14$\pm$97.44 s/, respectively. The binding of myosin to actin was studied using pyrene fluorescence. The rate (k6) was found to be 69.36 $\pm$ 21.24 /s. Finally, we studied the myosin dissociation (k7) from the actomyosin complex using pyrene fluorescence, and the rate was observed to be 70.13 $\pm$15.95 /s.

50. **Taylor Vensko**

Biochemistry, Microbiology, and Immunology

The way out: do Rabs 3A, 11A, and 27A regulate HCMV virion egress?

Human cytomegalovirus (HCMV) reprograms most cellular processes to enable virion assembly and egress. These tightly regulated processes use virally modified cellular trafficking pathways to assemble virion subunits and transport virion-containing vesicles through the cytoplasm to the plasma membrane for regulated egress. To identify the major pathway(s) used to transport virion-containing vesicles during egress, we are focused on Rab GTPases, critical cellular regulators of pathway-specific vesicle trafficking, which guide vesicles to microtubules. Our previous systems-level analysis suggests that during HCMV infection, enhanced trafficking occurs along the plasma membrane-proximal Rab 3A/27A secretory pathway(s), and reduced exocytic trafficking along the Rab 11A recycling pathway. Therefore, we hypothesize that Rabs 3A and 27A regulate delivery of virion-containing vesicles to the plasma membrane. To test this hypothesis while limiting off-target effects due to modulating critical host proteins for prolonged periods, we developed a system for rapidly regulating stability of Rab proteins expressed by recombinant HCMV strains. These viruses transduce dominant negative (DN) Rab 3A, 11A, or 27A fused to a FKBP-12 protein destabilization domain. In this work we: (i) assess Rab 3A and 27A localization throughout HCMV infection, (ii) profile proteomic datasets for Rab proteins and their operational partners to define their spatial/temporal interactomes, (iii) assess the predicted structures of virus-transduced Rab proteins, (iv) validate experimental methods for measuring virion release within a 2-8 hour period, and (v) measure the impact of DN Rabs 3A, 11A, and 27A on HCMV virion egress.

51. **Ummay Tamima Tasnim**

Biochemistry Microbiology and Immunology

Vibrio cholera biofilm and Cholera transmission

Cholera is a severe human disease that affects millions of people each year. Currently, we are in the seventh cholera pandemic, caused by the *Vibrio cholerae* El Tor biotype, which is more persistent during infection and in the environment as compared to the Classical biotype. Research indicates important contributions of *V. cholerae* biofilms in cholera transmission. Previous studies showed that *Vibrio* polysaccharide protein R (VpsR) and VpsT regulate *V. cholerae* biofilm extracellular matrix proteins (*rbmA*, *rbmC* and bap1). Hence biofilm specific genes have been found to play critical role in the intestinal colonization during infection. A protocol has been established in our lab to use zebrafish as an animal model that offers several advantages over using mice model. Therefore, we hypothesize that *Vibrio cholerae* El tor strain N16961 (wild type=WT) that forms biofilm may colonize adult zebrafish guts more efficiently in comparison with the biofilm knockout (KO) strain ΔVpsR N16961. We also predict the biofilm mutant will have defects in hyperinfectivity and transmission after 24 hours infection. The major goal of this study is to determine if biofilm-specific genes are important for colonization and hyper-infectivity of *Vibrio cholerae* during zebrafish natural host infection. We performed a competitive index assay between the WT and a ΔVpsR strain of *Vibrio cholerae* to assess gene defects during colonization and transmission. The competitive index study between the WT and ΔVpsR strains showed a significant ($p<.0001$) defect in cholera transmission, which indicates the importance of biofilm genes in cholera transmission in the aquatic environment.

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