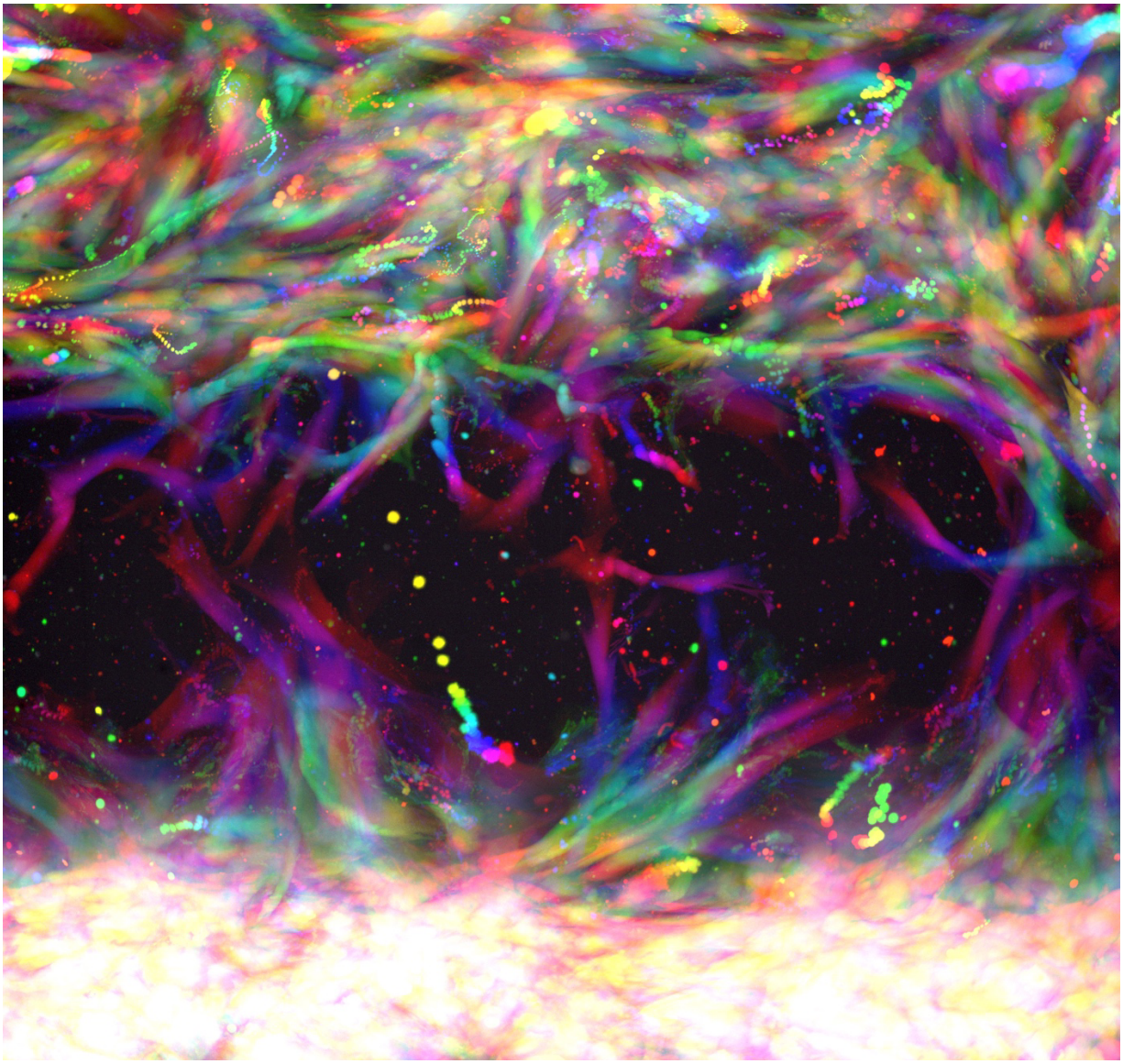
UNIVERSITY of MARYLAND BALTIMORE

47th Annual

Graduate Research Conference



Credit: Beth Pattie

Monday, April 28th, 2025

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47th Annual
Graduate Research Conference

Monday, April 28th, 2025
SMC Campus Center
Baltimore, MD

Organized by:

The School of Graduate Studies
The Graduate Student Association

Chair: Lakota Watson
PhD Candidate, Program in Neuroscience

Cover Art: ***Light Paint Microscopy***

This image depicts the migration patterns of fibroblasts over 24 hours via live cell microscopy. Each time point was assigned a unique color along the visible spectrum and then projected into a single image, creating a similar effect to long exposure techniques used in light painting photography.

Credit: Beth Pattie
PhD Candidate, Program in Neuroscience

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Foreword

Welcome to the 47th Annual Graduate Research Conference (GRC) at the University of Maryland, Baltimore (UMB)! The Graduate Student Association (GSA) is proud to host this unique opportunity for doctoral and master's students to present their hard work to the broader campus community.

The interdisciplinary nature of UMB allows us to showcase an exciting variety of topics under one roof, including basic, social, clinical, and translational sciences. This year, over 120 graduate students will present their research, hailing from over 30 unique programs and departments across UMB and the University of Maryland, College Park. After the scientific sessions, we will end the day by recognizing outstanding student presenters and celebrating the doctoral candidates who recently passed their qualifying exams.

The GSA graciously acknowledges those who helped make the GRC possible. Special recognition is given to Dr. Golembewski for her invaluable guidance and dedication to graduate student affairs. We also thank President Jarrell and Dean Wong for their staunch support of interdisciplinary research here at UMB. We are immensely grateful to the faculty judges for donating their time, expertise, and critiques. We extend special thanks to our amazing sponsors and supporting organizations for making this event possible. Finally, we thank the members of GSA and the GRC planning committee for their service throughout the year. It is our pleasure to host the 47th annual Graduate Research Conference, and we hope you enjoy the day's program!

GSA Executive Board

Jonathan Lawton - President
Divya Hosangadi - Vice President
Bernadette Hritzo - Treasurer
Lakota Watson - Secretary
Elizabeth Pattie - Public Relations Officer
Aman Shrestha - Graduate Council Representative

President's Message

Dear Graduate Students,

Congratulations on your 2025 Graduate Research Conference. This year marks the 47th year that the University of Maryland, Baltimore (UMB) has hosted this conference. It serves as a testament that we are committed to our mission to the human condition and to serve the public good. If this year has taught us anything, it's the importance of understanding that we are interconnected. The biggest breakthroughs in human health and well-being often happen at the intersection of scholars, schools, and disciplines.

True creativity and innovation occur when we see each other as sources of good ideas, when we're eager to talk with one another, to work with one another, to redesign the way we think about problems and solutions. When we collaborate and share, we see possibilities open up before us where we thought we had reached a dead end. We dream up new applications for our work, ways to broaden its reach or amplify its impact.

I wish you the best of luck at your Conference – and hope that you take a spirit of collaboration with you now and in the future.

Sincerely,

Bruce Jarrell, MD, FACS
President

Schedule of Events

8:00 – 9:00am	**Breakfast & Registration**	Second Floor
9:00am	**Opening Remarks**	Room 349
9:00 – 10:30am	**Poster Presentations*** **Session A** **Session B** **Session C**	Room 349
10:00 – 11:30am	**Oral Presentations** **Session D** **Session E** **Session F** **Session G**	Elm Ballroom Room 223 Room 203 Room 115
11:30 – 1:00pm	**Lunch**	Second floor
1:00 – 2:30pm	**Poster Presentations*** **Session H** **Session I** **Session J**	Room 349
2:00 – 3:30pm	**Oral Presentations** **Session K** **Session L** **Session M** **Session N**	Elm Ballroom Room 223 Room 203 Room 115
3:30 – 4:00pm	**Break**	
4:00 – 5:00pm	**GRC Awards** **Advancement to Candidacy Ceremony**	Elm Ballroom
5:00 – 6:30pm	**Reception**	Second Floor

*Poster setup will commence one hour prior to each session

Session Assignments

Poster Session A – 9:00-10:30am – Room 349

#1 Erica Leyder
#2 Vanshika Patel
#3 Alexander Laurenson
#4 Jeremie Piña
#5 Donald Amenah
#6 Racheal Ayankunbi
#7 Jillian Bishop
#7 Ivione Davis
#7 Julie Johnstone
#8 Christie Dionisos
#9 Daniela Franco
#10 Zahra Gohari
#11 Eunji Lee
#12 Destiny Black

Poster Session B – 9:00-10:30am – Room 349

#13 Douglas Gyamfi
#14 Anne Hagan
#15 Jinger Wang
#15 Trinity Little
#16 Melissa McClean
#17 Shabnam Lateef
#18 Ozi Iyalomhe
#19 Alissa Saverino
#20 Rebecca Cherian
#21 Paul Paronich
#22 Erin Walton
#23 Lynn Huang
#24 Jiwon Park

Poster Session C – 9:00-10:30am – Room 349

#25 Safiullah Rifai
#26 Yasaman Abbasi
#27 Daisy Rowser-Grier
#28 Simon Doss-Gollin
#29 Kieran Johnson
#30 Destinee Duffy
#30 Julian McKenzie
#30 Kathryn Gogolen
#31 Julia Rutherford
#32 Soyeon Shim
#33 Agbo-oma Uwakweh
#34 JaNya Brown
#35 Laura Carreto-Binaghi
#36 Kurt Espinosa

Oral Session D – 10:00-11:30am – Elm Ballroom

#37 Kelly Griffiths
#38 Ryan Mayers
#39 Tehmeena Akhter
#40 Jaylyn King
#41 Cosette Schneider
#42 Susweta Roy

Oral Session E– 10:00-11:30am – Room 223

#43 Lindsey Mathis
#44 Anne Brong
#45 Sushrut Pathy
#46 Aman Shrestha
#47 Kylie Tomlin
#48 Abigail Vigderman

Oral Session F – 10:00-11:30am – Room 203

#49 Roshini Patel
#50 Anjana Santosh Kumar
#51 David Annis
#52 Gautam Kumar
#53 Joshua Lucker
#54 Sasha Cardozo

Oral Session G – 10:00-11:30am – Room 115

#55 Aishwarya Venkataraman
#56 Phylicia Cooper
#57 Allison Deitz
#58 Sorah Levy
#59 Ian Mills
#60 Philippa Murray

Poster Session H – 1:00-2:30pm – Room 349

#61 Moses Akwobugi
#62 Ben Friedman
#63 Yu-Hua Fu
#64 Grace Charles Mazinga
#65 Heba Alqarni
#66 Ardith Allison
#67 Ashley Benton
#68 Tharyn Giovanni
#69 Lydia Fassett
#70 Darrel Freeman
#71 Sara Geriesh

Poster Session I – 1:00-2:30pm – Room 349

#72 Katherine Dudek
#73 Chioma Ezeajughi
#74 Suzanna Fitzpatrick
#75 Ye Jun Kim
#76 Hyung Seok John Kim
#77 Crystal Trent Paultre
#78 Viktoria Van Nederveen
#79 Ian O'Keefe
#80 Ria Parikh
#81 Alexa Stern

Poster Session J – 1:00-2:30pm – Room 349

#82 Nader Almutairi
#83 Laportia Sherrill
#84 Stephen Eaton
#85 Mohand Altemani
#86 Grace Garrett
#87 Mikah Green
#88 Emma Gudmundsson
#89 Mary Hackbarth
#90 Josline Ali-Napo Dibonge
#91 Hilary Phillips

Oral Session K – 2:00-3:30pm – Elm Ballroom

#92 Emmanuel Asiedu
#93 Salma Bargal
#94 Andrea Cottingham
#95 Shruti Dharmaraj
#96 Mingzhe Shen
#97 Erika Ventura Castellon

Oral Session L – 2:00-3:30pm – Room 223

#98 Ruth Akinlosotu
#99 Shahd Alajaji
#100 Lori Anderson
#101 Abagail Postle
#102 Kaylie Pinto
#103 Ningjin Wu

Oral Session M – 2:00-3:30pm – Room 203

#104 Payel Das
#105 Rutu Valapil
#106 Amna Zaib
#107 Brock Brethour
#108 Kenneth Dietze
#109 Sophie Elvig

Oral Session N – 2:00-3:30pm – Room 115

#110 Rex Gonzales
#111 Dominic Isaacs
#112 Julia Ju
#113 Christina Kratzmeier
#114 Emma Salazar
#115 Pranjali Kanvinde

Student Award Winners

The GSA would like to congratulate the recipients of select awards during the 2024-2025 academic year. The Professional Development Award allows students to participate in enrichment opportunities such as workshops or certificate programs. The Research Award provides supplemental funding for research supplies and logistics. The Travel Award and Global Travel Award support students so they may attend seminars and conferences in their fields.

Dr. Patricia Sokolove Outstanding Mentor Award

Dr. Susan dosReis

GSA Professional Development Award

Brianna D'Ambrosio
Erica Leyder
Erin Walton

GSA Research Award

Molly Pruitt
Kylie Tomlin

Center for Global Engagement Travel Award

Alex Laurenson
Jennifer Mariano
Ryan Mayers
Kayleigh Majercak
Meng-Hsuan Yu
Sarah Margerison
John Rizk

Student Award Winners

GSA Travel Award

Nesreen Alissa
Theeb Alquria
Hugo Bibollet
Annie Brong
Haixi Cui
Yali Deng
Tara Dillman
Suzanna Fitzpatrick
Yu-Hua Fu
Tharyn Giovanni
Da'Kuawn Johnson
Haesung Kim
Shabnam Lateef
Sorah Levy
Rebecca Lorsung
Ryan Mayers
Kevin Nguyen
Mitasha Palha
Noah Pollack
Abagail Postle
Molly Pruitt
Julia Rutherford
Jannat Saini
Cosette Schneider
Sorina Tomoiaga
Abigail Vigderman

Abstracts

1. Eosinophils Ameliorate Chronic Lung Allograft Dysfunction Through Alteration of the Cytokine Microenvironment of the Allograft

Erica Leyder

Poster Session A (Room 349)

Leyder, E.C., Mei, Z., Taheri, M., Jacobsen, E.A., Krupnick, A.S.

Long-term survival of the lung remains substantially worse than that of all other solid transplantable organs. The main barrier to survival of the lung allograft is the development of a fibrotic form of chronic rejection, known as chronic lung allograft dysfunction (CLAD), with over 50% of grafts being claimed by CLAD within 5-7 years post-engraftment. Human observational studies have identified high numbers of eosinophils in chronically rejected lungs, and based on their known cytotoxic function, this association has led to the presumption that eosinophils may contribute to CLAD pathogenesis. To study this, we transplanted B10 minor antigen mismatched lungs into B6 recipients or mice rendered deficient in eosinophils through the deletion of GATA1. Unexpectedly, we noted that markers of CLAD histology; airway obliteration (17.3±2.3), peri-airway fibrosis (1.8±0.7), and lung parenchymal fibrosis (9.8±4), were substantially lower in the presence of eosinophils. Such data suggested that eosinophils ameliorate, rather than potentiate CLAD. Gene expression analysis revealed upregulation of pathways associated with Th17 polarization (IL-17a, IL-17Rα, RORγT, IL-6) in the absence of eosinophils. Further cytokine analysis demonstrated that eosinophils are the dominant source of IFNγ in the chronically rejected lung allograft. Mechanistically, Th17 has previously been linked to chronic rejection in multiple transplant models. Due to the antagonistic nature of Th1 and Th17, along with our current data, eosinophil-production of IFNγ may mediate Th1 rather than Th17 polarization to ameliorate CLAD. Our murine data suggests that augmenting or targeting eosinophils may be one method for improving clinical outcomes of chronic lung rejection.

2. Regulation of Retinoic Acid Signaling and ERK 1/2 Pathway in Asthma

Vanshika Patel

Poster Session A (Room 349)

Patel, V., Yu, J., Weldemariam, M., Shapiro, P., Deshpande, D., Kane, M.

Current therapies for asthma fail to effectively address airway remodeling, a major hallmark in asthma patients that leads to long-term structural damage, highlighting the need for developing effective therapies. One promising target is the activator protein-1 (AP-1) transcription factor complex, which is elevated in asthma. In addition, AP-1 is activated when ERK 1/2 (extracellular signal-regulated kinases 1 and 2) signaling is dysregulated. Simultaneously, retinoic acid, an active metabolite of vitamin A, inhibits AP-1. Therefore, this study investigates the effects of

selectively inhibiting ERK 1/2 and activating retinoic acid receptors (RARs) on AP-1 activity. We used interleukin 13 (IL-13) to induce an asthmatic phenotype in A549 alveolar lung cells and BEAS-2B bronchial epithelial cells, followed by treatment with ERK 1/2 modulator (SF-3-030) and RAR agonists (ATRA or CD1530), both individually and in combination. LC-MS/MS-based proteomic profiling showed significant differentially expressed proteins, or DEPs in IL-13-treated cells, consistent with asthma. Combination therapy resulted in more pronounced protein changes than individual treatments. Pathway analysis revealed modulation of key asthma-related pathways involved in inflammation, proliferation, and airway remodeling. Collagen staining assay demonstrated decreased collagen deposition, while western blot analysis confirmed the downregulation of TGFBI and EGFR and modulation of AP-1-related immediate early genes (IEGs). These findings suggest that dual targeting of RAR and ERK 1/2 pathways may provide a novel therapeutic strategy for mitigating asthma-related airway remodeling.

3. A novel computational approach to Plasmodium falciparum vaccine design to address HLA restriction and parasite diversity

Alexander Laurenson

Poster Session A (Room 349)

Laurenson, A.J., Laurens, M.B.

Developing a highly effective malaria vaccine remains challenging due to Plasmodium falciparum's antigenic diversity and human HLA polymorphisms, which limit immune recognition. Existing vaccines, such as RTS,S and R21/Matrix-M, provide only partial, strain-specific protection with waning immunity. To address these challenges, we developed a computational tool that integrates P. falciparum sequence diversity, predicted T cell epitope-HLA binding affinities, and HLA allele frequencies from sub-Saharan Africa to identify conserved, immunogenic epitopes with broad population coverage. We analyzed 42 P. falciparum proteins, generating consensus sequences using data from 18 African countries and incorporating HLA allele frequencies from 24 sub-Saharan populations. CD8+ and CD4+ T cell epitopes were predicted using NetMHCpan-4.0 and NetMHCIIpan-4.1. A Mixed-Integer Linear Programming approach optimized epitope selection based on conservation (>95%), binding affinity (median rank <10%), and broad HLA coverage, minimizing redundancy to reduce immune escape risks. Our tool identified 65,996 MHC I and 1,992 MHC II conserved epitopes spanning liver, blood, and sexual stage proteins. Key MHC I epitopes from LSA1, PL, LISP1, SLARP/SAP1, and TLP achieved 100% HLA-A, HLA-B, and HLA-C coverage, while MHC II epitopes from PALM, AMA1, RON2, and PfRh5 provided 98.5%–100% coverage. This strategy improves malaria vaccine design by integrating epitope promiscuity and multistage antigen selection for broad, durable protection. Our computational framework is adaptable for vaccine development against other genetically diverse pathogens, accelerating epitope selection for emerging diseases. Experimental validation and vaccine formulation optimization are needed to enhance immunogenicity and durability.

4. Single Cell Spatial Transcriptomics Reveals ECM Aberrations in Cleft Palate

Jeremie Piña

Poster Session A (Room 349)

Piña J., Raju R., Myo A., Stipano E., Wang Z., Ono M., Chattaraj P., Furukawa M., D'Souza R.

BACKGROUND: Despite advances in understanding the morphological disruptions that lead to defects in palate formation, the precise perturbations within the signaling microenvironment of palatal clefts remain poorly understood. To explore in greater depth the genomic basis of palatal clefts, we designed and implemented the first single cell spatial RNA-sequencing study in a cleft palate model, utilizing the Pax9-/- murine model that exhibits a consistent cleft palate defect. METHODS: A novel platform for true single-cell resolution spatially resolved transcriptomics (Visium HD, 10x Genomics, Inc.) was employed. Time-bred wild-type (WT) and Pax9-/- murine embryos were dissected at (E)12.5 and 13.5 and processed for H&E, Visium HD, and RNAscope validation. Custom bins of 2x2 μm spatial gene expression data based on the identified cell nuclei were created to facilitate whole transcriptome single-cell analysis. Segmented single cells were identified via performed principal component analysis (PCA), uniform manifold approximation and projection (UMAP), and unsupervised clustering, allowing for the identification of differentially expressed cell-type-specific markers. Differentially expressed genes were subsequently used for over-representation analysis to identify enriched biological functions via functional enrichment and trajectory analyses. RESULTS: Key signaling disruptions noted in the Pax9-/- cleft palate included: negative regulation of cell growth, negative regulation of Wnt signaling, chondrocyte development, negative regulation of muscle cell development, and intrinsic apoptotic response to DNA damage. Spatial mapping of key genes associated with Wnt signaling regulation (Sfrp2) and collagen fibril organization (Col1a1) allowed for quantitative spatial comparison of expression patterns between WT and Pax9-/- palatal shelves. CONCLUSIONS: These results showcase the use of spatial transcriptomics at a single cell resolution in a well-established cleft palate model. As a key step toward laying the framework for identifying key molecular targets these data can be used for translational studies aimed at developing effective therapies for human palatal clefts.

5. Barriers and Facilitators to Perinatal Care Access and Utilization among African American Multiparous Women in the United States: A Scoping Review

Donald Amenah

Poster Session A (Room 349)

Amenah, D. B., Bobi, UA. W., Fu, Y., Robinson, K. N.

Background: African American (AA) multiparous women experience disparities in accessing timely and adequate perinatal care, leading to adverse maternal and infant health outcomes. However, little is known about the multilevel factors hindering or facilitating their perinatal care access and utilization. Objectives: To identify and synthesize empirical literature on the barriers and facilitators to perinatal care access and utilization among AA multiparous women through an integrated lens of the Social-Ecological Model and the Three Delays Model. Methods: We conducted a scoping review following the Joanna Briggs Institute's methodology and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews. We searched Medline via Ovid, Embase, Scopus, APA PsycINFO, CINAHL, and ProQuest Dissertation and Theses Global from inception to March

2025. Results: Our preliminary results indicate that AA multiparous women's access to and utilization of perinatal care are influenced by a complex interplay of barriers and facilitators at individual, interpersonal, community, and societal levels. Key individual and interpersonal barriers included prior traumatic births, unintended pregnancies, financial hardship, childcare demands, low autonomy, limited health literacy, provider mistreatment, and discrimination. Community and societal barriers involved inadequate insurance, long wait times, transportation challenges, and racism. Conversely, common facilitators included higher education status, increased health literacy, culturally sensitive care, and positive prior care experience. Conclusion: Our findings underscore the urgent need for multi-level interventions to address the barriers AA multiparous women experience in perinatal care while strengthening the facilitators, ultimately leading to better maternal and infant health outcomes.

6. Optimizing Dual-sgRNA CRISPR/Cas9 Lentivectors for SIX1 Knockout in Erythropoietic Cells

Racheal Ayankunbi

Poster Session A (Room 349)

Ayankunbi, R.A., Kim, M.J., Civin, C.

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)-Cas9 is an RNA-guided genome editing tool that enables targeted DNA cleavage using a single guide RNA (sgRNA) and the Cas9 endonuclease. A key advancement involves using two sgRNAs to excise DNA segments between cut sites, generating more reliable knockouts. This project aims to develop and optimize the CRISPR/Cas9 knockout lentivector system containing two sgRNA cassettes. Typical knockout vectors using one sgRNA produce shorter (<20 bp) indels. We hypothesize that a dual-sgRNA vector will generate larger indels at a specific genomic locus, more effectively disrupting protein production. The Civin lab showed that SIX1 overexpression in TF1 and CD34+ hematopoietic stem-progenitor cells (HSPCs) enhances erythroid differentiation and GATA1 expression while suppressing GATA2 and CD34. In contrast, CRISPR/Cas9-mediated SIX1 knockout impairs erythropoietin-stimulated erythropoiesis, revealing cooperation between the PAX-SIX-EYA-DACH and GATA networks. We constructed lentivectors to selectively knockout SIX1 in TF1 and HEK293T cells. The knockout efficiency of sgRNAs targeting SIX1 were validated by ICE analysis and Western blot. In HEK293T cells, the designed vector generated large indels (~142 bp) with ~40% knockout efficiency. We are now testing this dual-sgRNA vector in TF1 cells, expecting similarly large (>120 bp) indels. We will compare knockout efficiency between HEK293T and TF1 cells. These studies aim to clarify how SIX isoforms and its interacting molecules (e.g., GATA1) influence human hematopoiesis, with implications for ex vivo erythropoiesis in transfusion and transplantation.

7. Identifying Risk Factors in Child Abuse Related Homicides: a forensic autopsy case study in the State of Maryland, 2016-2023

Jillian Bishop

Poster Session A (Room 349)

Bishop, J., Mufareh, E., Davis, I., Johnstone, J., Ling L.

This study focuses on identifying risk factors of child abuse homicides in the State of Maryland, using data from the Office of Chief Medical

Examiners. During 2016 to 2023, there was a total of 61 child abuse related homicides in Maryland ages from newborn to 5 years old. There was no significance between the sex of the victims. Of the 61 cases, 14 had previous CPS involvement, 20% (N=12) were between the age of newborn and 4 months and 30% were children of 2 years of age. African Americans made up most of the cases with 65% (N=40). More than 44% of the incidents occurred in Baltimore city (N=27). There was a significance in the perpetrator (p=0.0043), with 44% perpetrators being the father and 25% being the mother. The victim's home was the most common location of the incident (77%). Of the 61 cases, 61% of the victims were the youngest child, a major relevance, whereas the only child was at 36%. This correlates to the significance in the number of siblings each victim had (p=0.02), 39% one sibling and 28% being only child. The most common cause of death was multiple injuries mainly due to blunt force trauma (41%) followed by intoxication (28%), asphyxia, sharp force injuries, thermal injuries, and complications of prematurity (16%), gunshot wounds (12%), and neglect (3%). Through this research, we hope more research can be done to reduce the risk factors pf child abuse related homicide in order to provide prevention measurements.

8. Effects of developmental THC exposure on the neonatal amygdala and social play behavior in rodents

Christie Dionisos

Poster Session A (Room 349)

Dionisos, C.V., VanRyzin, J.R., McCarthy, M.M.

Cannabis is the most commonly used drug of abuse during pregnancy in the United States (US), with self-reported use reaching 28% among young, urban, and socioeconomically disadvantaged individuals. Persistence as an illegal substance at the federal level has greatly restricted research on the effects of cannabis use, specifically prenatal Tetrahydrocannabinol (THC) exposure. We will use an early postnatal rodent injection model to mimic fetal neurodevelopment in the third trimester to investigate the long-term sociobehavioral deficits from developmental THC exposure with a focus on the amygdala due to its role in mediating sex differences in adolescent social play. Males have higher endocannabinoid levels than females, resulting in fewer newborn cells in the developing amygdala and more robust social play to establish proper socio-sexual adult behaviors. Thus, a disruption by THC, an exogenous cannabinoid, could adversely affect these behaviors. We hypothesize that intra-amygdala injection of THC during the critical period for sexual differentiation is necessary and sufficient to masculinize social play behavior. Here, we seek to exclusively target the amygdala through intra-amygdala injection to more directly determine the "where" and "when" of THC's effects on the masculinization of social play. We hope to establish the sufficiency of the amygdala in masculinizing newborn cell number and social play, as well as the necessity of the amygdala by administering THC but blocking cannabinoid receptors in the amygdala specifically. These findings on adverse outcomes of developmental THC exposure will address a critical issue impacting pregnant women.

9. IMPACT OF SOCIAL STRESS ON MICROGLIA-NEURON INTERACTIONS IN THE NUCLEUS ACCUMBENS

Daniela Franco

Poster Session A (Room 349)

Franco, D., Siemsen, B. M., Kumar, G., Key, S. L., Fox, M. E., Lobo, M.K.

Chronic stress is a risk factor for neuropsychiatric disorders, and it has been shown to alter neuron and myeloid cell structure and function in brain reward areas. The nucleus accumbens (NAc), a hub for integrating reward and motivation, exhibits molecular and cellular alterations that are found in postmortem tissue of patients with major depressive disorder and drive motivational deficits in rodents. Preclinical work from our lab has shown that exposure to chronic social defeat stress (CSDS), a validated animal paradigm of social stress, yields dendritic atrophy in NAc dopamine receptor-1 expressing medium spiny neuron (D1-MSNs) in mice that display negative affective behavior. Since microglia plays a mediating role in regulating neuronal dendritic adaptations after social stress, we subsequently characterized microglia and D1-MSN interactions in the NAc after 10 days of CSDS. We observed a cell-subtype specific reduction in microglia-D1-MSN contact in the NAc, a negative correlation between microglia-D1-MSN contact and CSDS-induced decreases in social interaction, and reduced microglia complexity in the D1-MSN microenvironment of mice with low social interaction. In contrast, preliminary work shows that mice that underwent Chronic Witness Defeat Stress (CWDS), a validated paradigm of vicarious social stress, show an increase in microglia-D1-MSN contact in the NAc. Thus, social stress, direct and indirect, may alter microglia-D1-MSN contacts in opposing ways. Ongoing work seeks to characterize the molecular mechanisms mediating neuron-microglia interactions during stress. Identifying microglia mechanisms contributing to altered cellular morphology and negative affective behaviors can provide therapeutic targets for stress-related disorders and improve current treatments.

10. Role of BRCA1 Mutations in Modulating ZNFX1 and Immune Responses in BRCA-Deficient Cancers

Zahra Gohari

Poster Session A (Room 349)

Gohari, Z., Stojonovic, L., Rassool, F. V.

Women with harmful BRCA mutations are at a higher risk of developing ovarian and triple-negative breast cancer due to compromised DNA repair capability, leading to genomic instability. This instability can activate the STING (Stimulator of Interferon Genes) pathway, which is crucial for the immune response, through the presence of cytosolic dsDNA. Our research identified a novel gene ZNFX1, a zinc finger protein, as a vital sensor of this cytosolic DNA and a regulator of mitochondrial dysfunction and STING-dependent immune signaling. We discovered that BRCA mutations enhance ZNFX1 expression in genetically altered mouse cell lines mimicking human ovarian tumors. This upregulation correlates with increased mitochondrial dysfunction and more intense immune signaling through the STING pathway. Our initial results from TNBC and ovarian cancer cell lines with CRISPR-induced BRCA1 knockouts confirm these findings, demonstrating elevated immune responses and suggesting potential sensitivity to PARP inhibitors (PARPis) and DNA methyltransferase inhibitors (DNMTis). Future studies will explore the impact of ZNFX1 knockout on immune responses and treatment efficacy in BRCA-deficient cancers, aiming to translate these findings into in vivo models to assess drug

efficacy. These investigations will further define the therapeutic potential of targeting ZNFX1 and its pathways as a strategy to enhance treatment outcomes in breast and ovarian cancers. This research provides insight into the molecular mechanisms connecting BRCA mutations with immune responses, highlighting ZNFX1's role in this process and its therapeutic promise for improving outcomes in breast and ovarian cancers.

11. Parental adaptability: A concept analysis

Eunji Lee

Poster Session A (Room 349)

Lee, E., Mooney-Doyle, K.

Parents of children with complex chronic conditions must continuously adapt to evolving caregiving demands. Parental adaptability is a dynamic, real-time, and multidimensional process distinct from resilience or coping, yet it remains underexplored. This study systematically analyzes parental adaptability, examining its attributes, antecedents, and consequences within the caregiving context of children with complex chronic conditions. Using Rodgers' evolutionary method and Bronfenbrenner's ecological model, a systematic review of 23 articles published between 1983 and 2024 was conducted. The analysis identified three key attributes categorized at different levels: (1) responsiveness (parent-level), reflecting parents' ability to recognize and respond to their child's dynamic healthcare needs; (2) balancing (family-level), integrating caregiving responsibilities with family roles; and (3) care management (system-level), involving proactive engagement with healthcare systems. Antecedents and consequences were classified across four levels: child, parent, family, and system, highlighting the multilevel factors influencing parental adaptability. Recognized as a critical construct for managing complex chronic care, parental adaptability provides a framework for designing interventions and policies that support caregivers in navigating caregiving challenges. Enhancing adaptability not only empowers caregivers but also contributes to broader family well-being. Future research should further refine the concept, considering diverse cultural and contextual influences to enhance its applicability and impact.

12. KCNMA1 Effect on Sleep-Wake Cycle

Destiny Black

Poster Session A (Room 349)

Black, D., Viechweg, Shaun, Mong, J.

KCNMA1 encodes the α-subunit of the large-conductance calcium- and voltage-activated potassium (BK) channel, which plays a critical role in regulating neuronal excitability and neurotransmission. Emerging evidence suggests that mutations in KCNMA1—collectively referred to as KCNMA1 channelopathy—are associated with a range of neurological phenotypes, including epilepsy, dyskinesia, and neurodevelopmental disorders. However, the impact of KCNMA1 dysfunction on sleep-wake behavior remains underexplored. In this study, we investigated the effects of both gain-of-function (GOF) and loss-of-function (LOF) KCNMA1 mutations on sleep architecture using mouse models. Continuous electroencephalogram (EEG) and electromyogram (EMG) recordings can reveal significant alterations in sleep-wake cycles, including disrupted circadian rhythmicity, decreased non-rapid eye movement (NREM) sleep stability, and increased sleep

fragmentation, particularly in LOF models. Our research may provide novel insights into how KCNMA1 channelopathy may contribute to sleep disturbances observed in affected individuals and highlight the BK channel as a potential therapeutic target for sleep-related symptoms in this disorder.

13. Staff Level Predictors of Function Focused Care within Long-Term Care Settings

Douglas Gyamfi

Poster Session B (Room 349)

Gyamfi, D., Doran, K., Resnick, B., Ebangwese, A., Anyoha, A., Anderson, L., Zhu, S.

Introduction: Sedentary behavior in older adults is associated with cognitive decline, falls, disability, and mortality. With over 84% of assisted living residents classified as sedentary, interventions like Function Focused Care (FFC), which promotes residents' physical activity by engaging them in routine tasks, are crucial. However, implementation barriers include low staff self-efficacy for providing FFC and limited control over work tasks. This study investigated factors influencing Long-Term Care (LTC) staff's promotion of FFC. We hypothesized that staff with lower sedentary behavior, higher self-efficacy, and greater control over work tasks would demonstrate increased FFC engagement. Methods: This was a secondary data analysis using baseline data from a worksite wellness study in six LTC facilities in Maryland. Fifty-six participants provided data for this analysis. Staff data collected included: demographics, direct observation of FFC engagement, self-efficacy for engaging residents in FFC, decision authority via the Job Strain Model tool and sedentary time via MotionWatch 8. Generalized linear mixed models with Poisson distribution was used to test our hypothesis. Results: Participants were predominantly female (92.6%) and Black or African American (84.0%), with a mean age of 47.5 years (SD=12.53). Two factors significantly predicted Function-Focused Care engagement: higher sedentary time was associated with lower FFC engagement [IRR: 1.003 (1.002, 1.004), p<.001], while greater decision authority also correlated with reduced FFC engagement [IRR: 0.90 (0.83, 0.98), p=.02]. Conclusion: This finding suggests that staff who are more physically active may be more inclined to provide FFC. Thus, physical activity interventions are essential for staff when implementing FFC.

14. Development and Psychometric Testing of the Social Isolation Visual Analogue Scale Among Older Adults in Low-Income Senior Housing

Anne Hagan

Poster Session B (Room 349)

Hagan, A., Resnick, B., Holmes, S., Klinedinst, J., Brandt, N.

Background and Purpose: Social Isolation, an epidemic among older adults, impacts more than seven million older adults, with one in four experiencing it. Social isolation is defined as an abject lack of social support or connection. It has been conceptualized as a distressing situation of "solitary confinement or torture." Contributing factors include age, low income, disability, and changes in living environments, making it a distressing and pervasive issue. This study aimed to test the reliability and validity of the Social Isolation Visual Analogue Scale. Methods: This was a descriptive study using a repeated measure design. Residents from four low-income senior housing communities were

interviewed about social isolation, depression, and social network at baseline and two weeks later. Results: The mean age of the participants was 78.8 (SD=8.1); the majority were female (86%) and Black (60%). There was evidence of test-retest reliability with a significant correlation between baseline and two-week follow-up of the Social Isolation Visual Analogue Scale (r=.74, p<.05). There was a significant relationship between evidence of social isolation and depression (F= 10.7, p< .001; R2 .26, and p < .001), and social isolation and social networks (F= 13.6, p<.001; R2 = .10, p= .002). These variables explained 72% of the variance in social isolation and social networks. Conclusions: This study's findings provided some preliminary evidence of the reliability and validity of the Social Isolation Visual Analogue Scale.

15. Sudden Death due to Pulmonary Embolism: a forensic autopsy population stodgy, 2020-2023

Jinger Wang

Poster Session B (Room 349)

Wang, J., Little, T., Wishop, S., Dean, S., Li, L.

This study retrospectively examines PE-related sudden deaths from 2020 to 2023 using data from the Office of the Chief Medical Examiner (OCME) of Maryland. Researchers assessed epidemiological, pathological, and medical history to identify trends and potential risk factors.A total of 122 cases were analyzed. 77.05% (N=94) cases were classified as natural, 16.39% (N=20) were accident, and undetermined and homicide all account for 3.28% (N=4). Most decedents were middle-aged (N=75, 61.50%). There was a difference in race with African American being the most predominate at 65% (N=80) followed by White at 26% (N=32). Of the 122 cases, witnessed collapsed (N=56) takes up 45.90% and unwitnessed collapsed (N=66) takes up 54.10%. Obesity (N=28), history of hypertensive cardiovascular disease (N=31), and history of feeling pain (N=21) were common medical conditions amongst the deceased. Recent surgery (N=15) and fracture (N=10) take up 12.30% and 8.20% separately. Seasonal analysis indicated a peak in autumn (27.90%) and winter (27.00%). Autopsy analysis revealed that 45.90% of decedents had underlying cardiac disease, with 30.36% exhibiting cardiomegaly and 26.79% having hypertensive cardiovascular disease. Saddle pulmonary thromboembolism was identified in 20.50% of cases. Additionally, 40.16% of cases showed deep vein thrombosis in the lower extremities. Toxicology report was positive in 59 cases, with common substances including diphenhydramine (N=8), fentanyl (N=9), and lidocaine (N=7). The analysis provides data insight of the risk factors, forensic diagnostic, and prevention strategies as it relates to PE. More research and data collections are needed to address the risks of PE and develop PE prevention programs.

16. Balancing Infection Risks and Residents Social Activity Preferences: Nursing Home Staff Risk Perceptions

Melissa McClean

Poster Session B (Room 349)

McClean, M., Akter. N., Kowalchik, K. H., Mogle, J., Kitt-Lewis, E. A., Paudel, A., Roman Jones, J., Carpenter, J. G., & Behrens, L. L.

Background and Objectives: Social activities are recognized as vital for older adults' quality of life. The COVID-19 pandemic presented challenges for nursing home (NH) staff as they

attempted to balance infection risks with residents' preferences for social activities. The purpose of this study was to gain an understanding of NH staff's experiences and actions accommodating resident preferences for social activities during pandemic restrictions. Research Design and Methods: This study used a convergent mixed methods approach to provide an in-depth description of NH staff's (N=24) risk propensity and decision-making. Quantitative data included self-reported demographics and risk perceptions using the Risk Propensity Scale. Qualitative data included semi-structured individual interviews. Data were integrated to explain the link between individual risk perceptions and infection control practices related to social activities. Results: Participants were purposively sampled to reflect a range of direct care NH staff roles including certified nursing assistants (29%), activities staff (25%), social workers (25%), and licensed nurses (21%). Participants were on average 39 years of age, mostly white (79%), and female (88%). Most identified as risk-avoiders (58%). Guided content analysis of interviews revealed two main themes that describe staff's behaviors while balancing infection control and residents' social activity preferences: factors of decision-making (family influence, organizational, staff and resident characteristics) and staff influencing preference-based care (cognitive skills and technical skills). Discussion and Implications: Risk perceptions and resultant decision-making vary among direct care NH staff. Mixed interpretation offers insight on staff's attempt to balance infection risks with residents' preferences to engage in social activities.

17. Changes in Stability After a Walking Trip in People with Chronic Stroke: A Pilot Study

Shabnam Lateef

Poster Session B (Room 349)

Lateef, S., Gray, V.L.

Background: People with chronic stroke are 2.5 times more likely to experience a fall compared to age-matched older adults, even after the completion of rehabilitation. People with stroke are more likely to fall when the position and velocity of the Center-of-Mass [CoM] fall outside the Base-of-Support [BoS], defined by the anterior-posterior and lateral margins of the feet. After a trip while walking, people with stroke are less likely to recover balance because a smaller recovery step length fails to slow the CoM velocity resulting in a greaterer CoM velocity, placing the CoM outside the anterior BoS. However, previous work has not compared changes in stability between people with stroke and healthy age- and sex-matched controls. Methods: Preliminary data includes two community-dwelling people with chronic stroke and one age- and sex-matched healthy control. Participants walking at their self-selected speed on a treadmill were asked to recover their balance and continue walking after a trip. Outcomes: Changes in CoM position and velocity with respect to the BoS were compared before the trip, during the trip, and immediately after the trip (during balance recovery), in two people with stroke and one control. Results: The two people with stroke successfully prevented a fall while demonstrating increased variability in CoM position and velocity with respect to their BoS before, during, and after the walking trip task compared to the control. Conclusion: People with chronic stroke can recover their balance by adjusting CoM position and velocity and changing their BoS, albeit with more variability.

18. Geographic Disparities in Older Adults' Access to Resources in Rural and Urban Maryland: A GPS-Health Analysis

Ozi Iyalomhe

Poster Session B (Room 349)

Iyalomhe, O. E., Huang, S. J., McCoy R. G.

Background: Older adults in rural areas experience worse health outcomes than their urban counterparts due to geographic isolation and limited access to care. Traditional social determinants of health (SDOH) indices lack the geographic resolution to capture these differences, limiting the ability to improve resource access for rural older adults. Objective: To quantify rural-urban differences in health-promoting resources for older adults across Maryland and inform place-based interventions. Methods: Using the Geographic Patterns of Social Determinants of Health (GPS-Health) dataset, we analyzed 2.1 million residential addresses classified by Rural-Urban Commuting Area codes: urban(1–3), large rural(4–6), small rural(7–9), and isolated rural(10). We calculated great-arc distances to hospitals, Federally Qualified Health Centers (FQHCs), Supplemental Nutrition Assistance Program (SNAP) retailers, civic centers, major roads, environmental hazards, gun violence, and eviction zones. Each model adjusted for property-level housing values and census tract-level race, income, and disability. Results: Older adults made up a greater share of the population in isolated rural areas (27.71%) compared to urban areas (17.05%; $p<0.001$). Compared to urban addresses, isolated rural addresses were significantly farther from hospitals [+4.22 miles (95% CI: 3.32, 5.13)], SNAP retailers [+1.14 (0.82, 1.46)], civic centers [+1.08 (0.66, 1.49)], and major roads [+7.32 (7.25, 7.39)], but closer to FQHCs [–1.76 (–2.65, –0.87)]. In contrast, large and small rural addresses were <0.7 miles farther from resources than urban. Conclusion: Older adults in isolated rural areas face substantial geographic barriers to accessing health-promoting resources. Addressing these disparities requires moving beyond a rural-urban binary and implementing policies tailored to specific community needs.

19. IP6: From Seeds, to Science, to Clinical Applications

Alissa Saverino

Poster Session B (Room 349)

Saverino, A.M., Vucenik, I.

Inositol hexaphosphate (IP6), also known as phytic acid, has gained attention as a bioactive molecule with promising therapeutic potential across various cancer types and clinical conditions. Preclinical and clinical observations indicate that IP6, alone or in combination with inositol, selectively targets cancer cells and enhances chemotherapy efficacy. Moreover, growing evidence suggests that IP6 plays a protective role in cardiovascular health, neurodegenerative disorders, and metabolic diseases. Although clinical trials remain sparse, extensive in vitro, in vivo, and epidemiological studies highlight the broad health-promoting properties of IP6. Notably, the benefits of IP6 have also been observed through dietary intake, as phytate-rich diets are associated with reduced risks of cancers, vascular calcifications, metabolic conditions, and an array of other chronic disorders. As research progresses, further clinical investigations are crucial to fully elucidate IP6's therapeutic applications and role in disease prevention.

20. Impending Healthcare Crisis for Clinical Laboratory Diagnosis due to MLT/MLS Workforce Decline in the United States

Rebecca Cherian

Poster Session B (Room 349)

Mazinga, G.C., Cherian, R.V.

Healthcare systems in the United States have been on the brink of crisis for decades. Properly trained Clinical Laboratory Scientists (CLS) and Medical Laboratory Scientists have been declining nationally. These professionals play a critical role in diagnosing diseases, monitoring treatment effectiveness, and guiding patient care decisions through accurate and timely laboratory testing. However, a combination of factors, aging workforce, reduced educational program availability, low enrollment rates, and lenient standards outlined in current regulations has led to the severe shortage of qualified laboratory personnel. A decline in available programs coupled with the rising demand for these types of professionals has created a gap in the workforce and inadvertently increased the risk of misdiagnosis. Additionally, lenient CLIA '88 regulations have allowed individuals who lack specialized training to fill laboratory positions, further endangering the quality of diagnostic services. The consequence of this shortage includes diagnostic errors, prolonged hospital stays, higher healthcare costs, and eroded patient trust in the system. Addressing these issues requires a multitude of combined efforts to repair: enhancing recruitment through targeted outreach, expanding educational curricula to incorporate new technologies collaborations, and fostering a culture of professional development. Furthermore, policy advocacy and collaboration between educational institutions, clinical settings, and technology providers are vital for revitalizing the MLS/MLT workforce. If this problem is left to fester, the decline in the laboratory workforce will have serious consequences for the quality of care provided to patients in the United States healthcare system.

21. Investigating how the Novel non-coding RNA Ganon-1 Interacts with mTOR to Mediate Neuronal Outgrowth In-Vitro

Paul Paronich

Poster Session B (Room 349)

Paronich, P. J., Crutcher, G., Robertson, C., and Poulopoulos, A.

Neurons in the developing brain exhibit much greater potential for regeneration than in the adult central nervous system (CNS). During development, neurons extend axons and dendrites to form intricate networks of connections, which are essential for establishing cognition and behavior. Axon growth is largely regulated by growth cones - specialized molecular structures capable of responding to environmental cues to direct the trajectory of growth. Establishing a mechanistic understanding of the biological pathways responsible for how the window of axon growth closes after development will move us closer to developing regenerative interventions aimed at treating adult CNS injury. Further investigation into the growth cone intracellular environment revealed dense accumulation of the growth-regulating protein complex mTOR, along with mRNAs sharing mTOR-dependent motifs. Recently, while performing transcriptomic analysis, my lab discovered a novel non-coding RNA, we termed Ganon-1, to be expressed in cortical neurons during development and subcellularly enriched in growth cones. 5'/3' rapid amplification of cDNA ends (RACE)

experiments with Ganon-1 revealed the presence of a 5' terminal oligo-pyrimidine (TOP) motif, typically linked with mTOR-dependent mRNAs. To test whether this motif was functional, mTOR was isolated via co-immunoprecipitation - the resulting protein fractions were found to be enriched with Ganon-1, suggesting a possible regulatory relationship. Additionally, Ganon-1 overexpression yielded increased neurite outgrowth in primary cortical neurons. To further characterize the role of Ganon-1, I'm using a CRISPR/Cas9 system to conduct cre-mediated knock-outs in primary cortical neurons and neuro-2a cells to measure putative effects of Ganon-1 deletion on neurite outgrowth and mTOR localization.

22. Environmental and Individual Factors and Repeat Violent Injury: A Parametric Survival Analysis

Erin Walton

Poster Session B (Room 349)

Harfouche, M., Kaushik, K., Wooster, E., Gertner, M., Unick, G.J.

Survivors of firearm violence face a heightened risk of subsequent violent injuries and premature death, particularly in socioeconomically disadvantaged neighborhoods with high alcohol outlet density (AOD). This study applied a mixed-effects parametric survival analysis to examine the interplay between individual and community-level factors in predicting repeat firearm violence. Data from the Maryland State Trauma Registry (2000-2020) included 9,615 shootings across 8,915 individuals in Baltimore City. Findings reveal that young Black men are at the highest risk of repeat firearm injuries, with men 21 times more likely than women to experience a subsequent injury. Neighborhood AOD, specifically the presence of taverns with Class BD7 licensees (LBD-7), significantly increased the hazard of repeat firearm injuries. Each LBD-7 tavern in a zip code corresponded to a 6% increase in the risk of repeat injury. These findings emphasize the need for multi-level interventions that include addressing structural drivers of violence.

23. Hospital-level e!ects on cardiovascular monitoring among cancer patients treated with cardio-toxic therapies

Lynn Huang

Poster Session B (Room 349)

Huang, P.L., Mysore, M.M., Barr, B., Onukwugha, E.

OBJECTIVES: Despite guideline recommendations, cardiac surveillance rates remain suboptimal for cancer patients exposed to potentially cardiotoxic treatments (PCT). The role of hospital-level factors in explaining suboptimal monitoring rates is understudied. We quantified the relationship between hospital-level factors and cardiac monitoring following the PCT initiation. METHODS: This study used SEER-Medicare patient-level data linked with hospital-level data. We included patients aged 66+ years who received PCT, including anthracycline, anti-HER2 agents, and immune checkpoint inhibitors (ICIs), between 1/1/2014 and 12/31/2018. Patients without a cancer diagnosis in the prior 24 months and hospitals with fewer than two eligible patients were excluded. The study outcome was 12-month cardiac monitoring rate following PCT, defined as the number of unique cardiac evaluation visits. Adequate monitoring was defined as 4+ visits. A multilevel regression model with random intercept was used to

estimate incidence rate ratios. RESULTS: A total of 2,134 patients were identified. The mean age was 74 years (SD=6). Overall, 10% of patients received adequate monitoring within one year. Among those treated with anti-HER2 therapy, anthracyclines, and ICIs, the proportions receiving adequate monitoring were 34%, 7%, and 4%, respectively. Hospital-level factors significantly associated with higher cardiac monitoring rates included for-profit/private hospitals, total beds, ICU beds, surgical ICU beds, total discharges, and the number of providers (e.g., physicians, registered nurses). CONCLUSIONS: Only 1 in 10 patients exposed to PCT received adequate cardiac monitoring. Hospital characteristics were associated with the cardiac monitoring rate. Given cancer treatment-induced cardiotoxicity can be mitigated, collaborative institutional efforts are needed to improve cardiac monitoring.

24. Factors Influencing Wearable Device Usage: The Role of Cancer History and Psychosocial Variables Using the HINTS 6 Dataset

Jiwon Park

Poster Session B (Room 349)

Park, J., Nahm, E.-S., Zhu, S.

Background: Wearable devices are increasingly used for health monitoring, but adoption varies by demographic, health-related, and psychosocial factors. Understanding these predictors can inform strategies to support self-management and long-term health promotion. Purpose: This study examines factors influencing wearable device usage, including cancer history and interactions with health-related and psychosocial variables. Methods: This secondary analysis used 2024 HINTS data (N = 5,877), classifying adults as having a cancer history (15.3%) or not (84.7%). Wearable device use in the past year was the outcome. Two survey-weighted logistic regressions were conducted: a base model and an IPTW-adjusted model. Results: In the base model, cancer history was not significantly associated with wearable use. After IPTW adjustment, the association became marginally significant (OR = 1.42, 95% CI [1.00, 2.03], p = .053). Older age (OR = 0.97, p < .001) and male gender (OR = 0.67, p = .005) were linked to lower use, while higher education (OR = 2.85, p < .001) and being in a committed relationship (OR = 1.70, p < .001) were associated with increased use. Among participants with a cancer history, severe isolation reduced usage (OR = 96.62, p < .001), while moderate meaning and purpose in life increased it (OR = 7.24, p = .020). Conclusion: Wearable device use is influenced by demographic and psychosocial factors, with cancer history interacting with isolation and meaning and purpose in life. Tailored strategies should consider both psychosocial context and personal health history to promote meaningful engagement with wearable health technologies.

25. Identification of Prostate Cancer Recurrence Signatures Using Unsupervised Machine Learning

Safiullah Rifai

Poster Session C (Room 349)

Rifai, S., Rifai, A., Meher, Z., Khan, M.A., Wang, L., Guang W., Hussain, A.

Androgen-targeted therapy is the standard treatment for prostate cancer, yet approximately 30% of patients experience biochemical recurrence—a rise in prostate-specific antigen (PSA) levels that signals potential cancer persistence. The time to

biochemical recurrence serves as an important clinical indicator of disease aggressiveness, with earlier recurrence linked to worse patient outcomes. Understanding the factors driving early recurrence is therefore critical. Our study examined transcriptomic data from 74 patients in the TCGA Prostate Adenocarcinoma dataset who experienced biochemical recurrence after radical prostatectomy for localized disease. We stratified patients into quartiles based on time to recurrence and analyzed their gene expression profiles using K-means clustering and Principal Component Analysis. K-means clustering revealed distinct gene expression patterns associated with earlier biochemical recurrence. Over-representation analysis across multiple Gene Ontology collections highlighted immune cell signatures as major contributors to these patterns. Principal Component Analysis identified epithelial splicing regulatory protein 1 (ESRP1) – a regulator of epithelial-mesenchymal transition – as significantly associated with early recurrence in a subset of patients. Future directions include deconvolution of the bulk RNA sequencing data to better characterize immune signatures across recurrence quartiles, and extension of our analysis to include methylation and protein expression data.

26. Spatial Lipidomic Analysis of Gingiva in mice with periodontitis

Yasaman Abbasi

Poster Session C (Room 349)

Abbasi, Y., Bergamin de Castro, T., Yang, H., Scott, A. J., Chung, MK.

Periodontitis, a chronic inflammatory disease affecting over 47% of U.S. adults, results from an immune response to microbial biofilms, causing destruction of tooth-supporting tissues and increasing systemic disease risks. Despite available therapies, periodontitis often resists conventional treatment. Lipids significantly impact cellular signaling, inflammation regulation, and gingival tissue integrity. Disrupted lipid metabolism can exacerbate chronic inflammation; however, the exact functions and spatial distribution of lipids in periodontitis remain poorly understood. Lipidomics, a specialized metabolomics approach, enables comprehensive profiling, providing valuable insights into lipid involvement in periodontal inflammation and disease progression. This study aims to spatially map lipid profiles in gingival tissues using mass spectrometry imaging (MSI) in a mouse periodontitis model, exploring lipid roles in inflammation, tissue destruction, and disease advancement. Ligatures were placed around the second maxillary left molar of three female WT mice, using the right side as control. After seven days, palatal gingival tissues were harvested, snap-frozen in gelatin, and cryosectioned. Spatial lipidomic analysis was performed in negative ion mode using Matrix-Assisted Laser Desorption Ionization MSI (MALDI-MSI). Hematoxylin and Eosin (H&E) stained images were used for histological overlay. The top 100 peaks with highest intensities were putatively identified using Alex123, and pair-wise statistical comparisons were conducted. Preliminary results revealed distinct differences in lipid intensity differences between periodontitis and control groups in epithelial and connective tissues, notably ions m/z 713.361, 890.639, 891.642, and 906.635. These findings highlight altered lipid profiles due to periodontitis, suggesting potential targets for further investigation.

27. Responsible Use of AI/ML in Decision-Making: Employee Selection as a Case Example

Daisy Rowser-Grier

Poster Session C (Room 349)

Rowser-Grier D., Dinkel O., Byun C., Marcrum E., Epistola J.

This presentation uses employee selection as a case example to examine broader issues of legal risk, fairness, and validity in the application of artificial intelligence (AI) and machine learning (ML) in high-stakes decision-making. As AI/ML becomes increasingly integrated into organizational processes, its influence on strategic choices and industry practices continues to grow. However, when implementation neglects critical contextual and legal considerations, organizations may face significant reputational and legal consequences. To fully leverage the strengths of AI/ML, decision-makers must understand the regulatory and strategic context required to develop valid and compliant algorithms. Drawing on lessons from selection and employment law, this presentation offers guiding principles and best practices for responsible AI/ML use in applied decision-making.

28. Altered Mechanisms of Cell Entry in Clinical Isolates of the Seasonal Coronavirus OC43

Simon Doss-Gollin

Poster Session C (Room 349)

Doss-Gollin, S., Frieman, M., Deming, M.

OC43 is a seasonal human coronavirus in the betacoronavirus genus which causes a mild upper respiratory infection, and which can serve as a model for development of broad-spectrum pan-betacoronavirus therapies for future pandemic preparedness. While the laboratory VR-1558 strain of OC43 has been studied extensively, this strain has undergone significant adaptation for growth in cell culture and no longer infects primary human lung epithelial cells. In contrast, circulating clinical isolates can infect primary cells but are unable to infect and grow on standard cell culture lines. We hypothesize that structural differences in the receptor-binding site between VR-1558 and circulating clinical isolates have resulted in alterations to the binding profile of the viral Spike proteins which mediate the different permissiveness of these cell lines. Using Alphafold to predict the three-dimensional structure of Spike from a clinical isolate of OC43, we have identified differences at a region previously identified as the binding site for its 9-O-acetylated sialic acid receptor. To test whether 9-O-acetylated sialic acids are used by circulating clinical isolates, we will manipulate expression levels of enzymes involved in their production including SIAE and CasD1. Furthermore, by harnessing carbohydrate microarray technology, we will identify differences in the carbohydrate binding profiles between the Spike proteins of these two OC43 strains. Additional screening using a lentiviral overexpression library may further identify key proteins mediating differential cell permissiveness to OC43 strains. These approaches will offer insights into how this seasonal coronavirus enters cells, providing essential tools for understanding betacoronavirus pathogenesis and evaluating potential interventions.

29. Pseudomonas aeruginosa Heme Sensing and Utilization Inhibitors Targeting HasAp and HemO

Kieran Johnson

Poster Session C (Room 349)

Johnson K., Frank A., Centola G., Witt W., Hwang L., Barbier M., Wilks A., MacKerell A., Fengtian X.

Pseudomonas aeruginosa is a gram-negative, opportunistic pathogen that primarily infects immunocompromised patients in the hospital. P. aeruginosa has been known to colonize a number of different areas of the body, including burn wounds, urinary tract, lung, and blood based infections. P. aeruginosa is also able to form biofilms and a number of strains are multidrug resistant, making the treatment of P. aeruginosa infections very difficult. Because of the current challenges in treating P. aeruginosa infections novel treatment methods are required. Past methods to starve P. aeruginosa of its iron sources during infection showcased its ability to up-regulate various systems to uptake iron. Due to this, our lab is pursuing heme mimicry as a means to disrupt the heme acquisition and sensing systems of P. aeruginosa without iron starving the bacteria. Our lab utilizes Salophen based small molecule scaffolds with a gallium metal center in order to mimic heme and target the extracellular homophor HasAp, which along with the outer-membrane receptor HasR, internalizes heme into the bacteria during infection. Our goal is to synthesize a potent inhibitor of the P. aeruginoas Has system, effectively dysregulating heme uptake as well as heme sensing.

30. Sudden Death Due to Drowning in Maryland: A retrospective forensic autopsy study 2021-2023

Destinee Duffy

Poster Session C (Room 349)

Duffy, D., Gogolen, K., McKenzie, J., Pratt, J.

In the State of Maryland, sudden deaths due to drowning continue to be a public safety issue, affecting every county and reaching every demographic. Drowning was reported as the fifth leading cause of death in Maryland between 2010 and 2019 and is the third leading cause of injury-related death worldwide. This research paper comprehensively analyzes drowning related deaths between 2021 and 2023, investigating common trends and patterns, and highlighting potential risk factors such as drug and alcohol use, and past medical history. Collecting data obtained from Maryland's Office of the Chief Medical Examiner's database, this research qualitatively analyzes cases of drowning investigations throughout the State of Maryland. Drowning related fatalities continue to be a public health and safety issue. There are many contributing factors to drowning related deaths. Certain circumstances impair people's ability to swim, such as drug and alcohol use, and medical issues. Further research is needed to mitigate the death rate of drowning related fatalities.

31. Tristetraprolin induces an antitumorigenic phenotype in triple negative breast cancer via a novel non-canonical mechanism

Julia Rutherford

Poster Session C (Room 349)

Rutherford, J.L., Stemberger, M.B., Mahmud, R., Ross, C.R., White, E.J.F., Wilson, G.M.

The ultimate cause of death for most triple negative breast cancer (TNBC) patients is metastatic disease, which has a five-year survival rate of 12.8%. This low survival rate is partly due to the lack of targeted treatments for metastatic TNBC. As such, further research is

needed to identify novel molecular mechanisms that can be targeted to suppress TNBC malignancy. Tristetraprolin (TTP) is an RNA-binding protein that binds to AU-rich elements (AREs) in the 3' UTRs of select mRNAs, including many that encode proteins involved in cancer-related processes, and targets these mRNAs for degradation. Loss of TTP in tumors correlates with increased disease severity and decreased survival, suggesting a role as a tumor suppressor in breast cancer. While previous research has shown that TTP can suppress proliferation in breast cancer, the mechanism remains weakly defined. We analyzed TTP-induced changes in gene expression patterns among TNBC cell lines using RNA-sequencing and observed that TTP significantly suppresses pathways that contribute to the development of neoplasia. Our subsequent functional analyses revealed that TTP potently suppressed tumor phenotypes in these cell models. Furthermore, in vivo studies reveal that TTP significantly attenuates tumor growth. Actinomycin D time course assays surprisingly revealed that TTP had no effect on the decay kinetics of several known TTP targets, suggesting that TTP's antitumorigenic properties observed in TNBC cells are independent of its RNA-destabilizing function. Collectively, these findings reveal that expression of TTP can potently suppress several oncogenic phenotypes in TNBC cells via a mechanism independent of its canonical RNA-binding/destabilizing functions.

32. A Structural Equation Modeling Approach to Predicting Nurses' Intentions to Report Colleagues' Substance Use Problems Based on the Theory of Planned Behavior

Soyeon Shim

Poster Session C (Room 349)

Shim, S., Trinkoff, A. M.

BACKGROUND: Easy access to medication and exposure to psychological trauma are major risk factors for substance use issues among nurses. While early identification is crucial for harm reduction and treatment, barriers and hesitancy exist in reporting colleagues' substance use issues in the workplace. The Theory of Planned Behavior provides a well-established framework for understanding behavioral intentions. However, there is limited theory-based research on nurses' intentions to report colleagues' substance use issues. This study aims to explore nurses' intentions to report suspected substance use using the Theory of Planned Behavior. METHODS: This study analyzed secondary data from the Nurses Worklife and Wellness study, which included 1,170 registered nurses from nine states. Structural equation modeling was used to apply the Theory of Planned Behavior, assessing the effects of attitudes, subjective norms, and perceived behavioral control on reporting intention. Sociability, workplace bullying, awareness of substance uses issues, and job satisfaction were also considered as covariates. RESULTS: After the model modification, the fit indices improved, with RMSEA of 0.060, CFI of 0.952, and TLI of 0.949, indicating acceptable model fit. The final model showed that subjective norms were the strongest predictor of intention to report ($\beta = 0.519$, $p < 0.00$), aligning with the original model's findings. CONCLUSION: The Theory of Planned Behavior offers empirical insights that can guide policy interventions to foster a supportive reporting culture in healthcare settings. Addressing subjective norms could strengthen reporting systems for substance use impairment among nurses.

33. Developing an Analytical Method for Oligonucleotide Incorporation Using Ion-

Pair Reverse-Phase Liquid Chromatography Mass Spectrometry (IP-RPLC-MS)

Agbo-oma Uwakweh

Poster Session C (Room 349)

Uwakweh, A. A., Parakra, R. D., Obi, J. O., Deredge, D.J.,

Detection and analysis of nucleotide incorporation by DNA/RNA polymerase is integral to antiviral research. Traditional methods like radio-labeling, and electrophoresis-based assays have limitations like safety concerns, gel-migration issues or detection limits. Mass Spectrometry based enzymatic assays are increasingly considered as an alternative due to their specificity and high-throughput capability. Our research explores the ability to detect nucleotide incorporation by an RNA Dependent RNA Polymerase (RdRp) from Dengue Virus Non-Structural 5 Protein (NS5), a target in antiviral drug development research. We optimized our Ion-Pairing Reverse Phase Liquid Chromatography-Mass Spectrometry (IP-RPLC-MS) assay using a primed-template (ptRNA)18/30 substrate from the 3' end of the genomic RNA. Column temperature and elution gradient conditions were optimized to increase separation between the 18/30 ptRNA. The best condition was a 10-minute separation between the 18 and 30 length oligonucleotides (18-nt, 30-nt) at a column temperature of 75˚C and gradient of 40-55%B in 30 min. Peaks corresponding to the 18-nt (18 min) and 30-nt (28 min) species were identified by mass deconvolution. Nucleotide incorporation was performed by incubating the RdRp enzyme at 30˚C with the ptRNA and individual nucleotides in reaction buffer. The reaction was quenched, and RNA products purified for analysis by IP-RPLC-MS. After 4 hours, peaks corresponding to the nucleotides 19-nt, 20-nt, and 21-nt were observed between the 18-28-minute window. At 17 hours, each of the incorporated products (19-nt to 30-nt) were observed by UV and identified by mass deconvolution. Future directions include applying this technique to detect the inhibition of Nucleotide and Non-Nucleotide Inhibitors.

34. Development of a CRISPR-Based Genome Restoration Strategy to Correct Pathogenic Variants in Exon 12 of the CFTR Gene

JaNya Brown

Poster Session C (Room 349)

Brown, J. B., Adedeji, O. B., Richardson, C. D., Poulopoulos, A.

Cystic Fibrosis (CF) is an autosomal recessive genetic condition caused by pathogenic sequence variation in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene, which contains 27 exons. Exon 12 has been identified by the CF Foundation as a critical region, harboring approximately 7% of all pathogenic variants that significantly impair CFTR protein development and function. While there are currently FDA-approved medications for CF in the United States, patients with exon 12 variants are often left with symptomatic treatments rather than therapies that target channel function. The Poulopoulos Lab, which specializes in advanced CRISPR-based therapeutic strategies, is developing a novel approach involving Cas9-RC (Richardson et al, CRISPR J, 2023) and CFTR exon restoration. This method aims to substitute the pathogenic sequences in exon hotspots with a non-pathogenic sequence, restoring proper channel function. Unlike genome-modifying agents, such as base editors and prime editors, this approach has the potential to benefit multiple

pathogenic variants simultaneously, significantly increasing therapeutic coverage among CF patients. Preliminary experiments are currently being conducted in vitro using human embryonic kidney (HEK) cells to check the efficiency of guide RNA targeting and removal of the exon, as well as quantifying the efficiency of homologous recombination knock-in of the restored exon using sequence tags. Further studies will be performed on immortalized human bronchial epithelial (HBE) cells genetically engineered to model various exon 12 CFTR pathogenic variants. These cells assess the restoration of CFTR mRNA expression and protein function following exon replacement, demonstrating the therapeutic potential of Cas9-RC genome restoration.

35. Predominance of S. Typhi-specific CD4+ over CD8+ T Cell Responses in Individuals without Prior Exposure

Laura Carreto-Binaghi

Poster Session C (Room 349)

Carreto-Binaghi, L.E., Booth, J.S., Wahid, R., Salerno-Goncalves, R., Toapanta, F.R., and Sztein, M.B.

CD4+ and CD8+ T cell responses (T-CMI) against Salmonella enterica serovar Typhi (S. Typhi), the causative agent of typhoid fever, have been reported in healthy individuals, likely representing cross-reactivity to other Enterobacteriaceae in the microbiota. It remains unclear whether cross-reactive responses are more pronounced in different T cell subsets and whether distinct Salmonella species elicit comparable responses. We used mass cytometry to assess frequencies of T cell subsets (Teffector/memory -TEM-, TCD45+effector/memory -TEMRA-, Tcentral/memory -TCM-, Tnaïve, Tstem-cell-memory -TSCM-, Tfollicular/helper -cTFH-, and mucosal-associated-invariant-T-cells -MAIT-) and cytokine production (IFNγ, TNFα, and IL2) following in vitro stimulation. Peripheral blood mononuclear cells from 15 healthy participants with no history of typhoid fever were co-cultured with target cells infected with S. Typhi (ST) or S. Typhimurium (STm). Non-infected B-LCL (NI) were used as controls. Increased percentages of CD4+ TEMRA and TCM and decreased percentages of CD4+ TNaïve and TSCM cells were observed in ST-infected-target-cultures compared to NI. Higher percentages of CD4+ cTFH cells were present in ST- compared to STm-infected-target-cultures. Salmonella-specific IFNγ production from CD4+ TEM and cTFH cells and TNFα production from CD4+ TEM, TSCM, cTFH, and CD8+ MAIT cells were higher in ST- compared to STm-infected-target-cultures. Moreover, higher percentages of IL2-producing CD4+ cTFH and TSCM cells were found in ST-infected-target-cultures compared to NI. Overall, CD4+ TCM, TEMRA, TNaïve, TSCM, and cTFH cell subsets are main contributors to baseline responses and should be considered when evaluating T-CMI to vaccination and natural infection. Further studies are needed to elucidate the underlying mechanisms driving these responses.

36. Specificity of thymine DNA glycosylase for G:T mismatches arising from 5-methylcytosine deamination

Kurt Espinosa

Poster Session C (Room 349)

Espinosa, K.B., Dow, B.J., and Drohat, A.D.

DNA methylation is an epigenetic mechanism that controls transcription. Once modified, 5-methylcytosine (mC) can spontaneously deaminate to thymine (T), yielding a G:T

mismatch. The formation of these mismatches primarily occurs at CpG sites, which is a significant source of mutations and is implicated in nearly one-third of cancers. Base excision repair (BER) is a DNA repair pathway that can correct G:T mismatches from mC deamination. Thymine DNA glycosylase (TDG) initiates this pathway by excising T from G:T mismatches. TDG activity must be highly regulated to avoid excision from proper A:T base pairs and from polymerase misincorporation. Uncontrolled activity of TDG may lead to DNA single or double strand breaks, but its specificity is not fully understood. The current paradigm suggests that TDG achieves G:T mismatch recognition through opposing G interactions that is not compatible with opposing adenine (A). We are exploring another possibility that TDG recognizes G:T mismatches due to its lower stability relative to A:T base pairs. Base flipping of T into the active site is required for TDG excision, and the unstable G:T mismatch may facilitate that conformational change. We are approaching this possibility by conducting a structure-activity relationship study to determine whether base pair stability contributes to TDG specificity. The thermodynamic stability of purine analogs paired with T (x:T) was assessed by calorimetry, and the activity of TDG on x:T was determined through single turnover kinetics. This work can provide a framework in exploring the specificity of other BER glycosylases that require base flipping for excision.

37. Obscurin as a chemosensitizer in breast cancer cells

Kelly Griffiths

Oral Session D (Elm Ballroom)

Griffiths, K., Eason, M., Kontrogianni-Konstantopoulos, A.

Triple-negative breast cancer (TNBC) is highly aggressive and exceedingly difficult to treat. The standard of care for most TNBC patients is non-targeted systemic chemotherapy, such as the anthracycline doxorubicin, the efficacy of which is limited due to a very small therapeutic window. Doxorubicin is particularly cardiotoxic, often leading to dilated cardiomyopathy and eventual heart failure. Despite this severe side effect profile, it remains one of the most effective drugs on the market and a mainstay of treatment for TNBC. Thus, there is an urgent and unmet clinical need for a therapeutic regimen with improved efficacy and reduced toxicity. Interestingly, our lab has shown that breast cancer cells harbor a survival advantage following treatment with sublethal doses of doxorubicin, likely due to the onset of therapy-induced cellular senescence, with upregulation of the PI3K/AKT/NF-KB pathway being a major underlying mechanism. Obscurin, a large cytoskeletal protein richly expressed in normal breast epithelium but lost in advanced breast cancer cells, is a known to bind with nanomolar affinity to the P85 regulatory subunit of PI3K and regulate its activity. Interestingly, obscurin expression correlates with response to anthracyclines as well as overall survival in invasive breast cancer patients. The pleckstrin homology domain of obscurin (obscurin-PH) operates as the functional unit in epithelial tissue, ectopic delivery of which prevents invasion, migration, and metastasis, and synergizes with doxorubicin allowing for the use of lower doses. Therefore, we hypothesize that obscurin-PH is a potent chemo sensitizer that functions via inhibition of the PI3K/AKT pathway in TNBC.

38. Mitochondrial Deficits in HAP1 TPCN1 Knockout Cells are Unlikely Due to

Alzheimer's Disease-Linked TPCN1 Gene Ablation

Ryan Mayers

Oral Session D (Elm Ballroom)

Mayers, R.P. and Polster, B.M.

We identified large decreases in both Tpcn1 mRNA and its encoded Two-Pore Channel 1 (TPC1) protein in pro-inflammatory microglia, coinciding with mitochondrial bioenergetic impairment. Mitochondrial dysfunction is thought to contribute to chronic pro-inflammatory responses involved in Alzheimer's Disease and Lewy Body Disease, conditions for which TPCN1 variants are risk factors, so we employed a near-haploid human TPCN1 knockout (KO) cell line to test if TPC1 is required for mitochondrial homeostasis. These cells exhibit impaired oxygen consumption and severe reductions in mitochondrial electron transport chain (ETC) Complexes I, III, and IV. However, re-expression of TCPN1 failed to rescue ETC subunit levels. Whole-genome sequencing revealed that TPCN1 KO cells have many unexpected rare single nucleotide variants in protein-encoding genes. One – MTFMT p.R332X – occurs in patients with Leigh Syndrome, a neurometabolic disorder associated with severe deficits in mitochondrial ETC Complex I and IV subunits. Efforts to independently CRISPR-correct both the introduced TPCN1 variant and the unintended MTFMT gene variant are underway to determine if either mediates the HAP1 TPCN1 KO cell line's mitochondrial phenotypes. MTFMT p.R332X was not a predicted off-target consequence of the process used to introduce TPCN1 KO, and we also identified 673 variants unique to wild-type parental cells. These variants likely represent de novo mutations undetectable by routine quality control screening for CRISPR-edited cell lines. While haploid cell lines facilitate gene editing, our findings indicate that the high cell culture de novo mutation rate necessitates higher standards of rigor than typically employed for genetic studies.

39. Hemizygous variants in the CCDC120 protein cause a distinct neurodevelopmental disorder in humans

Tehmeena Akhter

Oral Session D (Elm Ballroom)

Akhter, T., Ahmed, M. Z., Wegner, D., Barakat, S. T., Fernández-Jaen, A., Rahikkala, E., Shillington, E., Rabin, R., Friedman, R. J., Bierhals, T., Mahida, S., Laracy, K., Urpa, L., Riazuddin, Sh., Riazuddin, S.

Coiled coil domain containing protein-120 (CCDC120) plays an important role in cytoskeletal rearrangement and neurite outgrowth. In this study, we report a frameshift and thirteen hemizygous missense variants of CCDC120 in individuals exhibiting the characteristics of neurodevelopmental disorder (NDD), including mild to severe intellectual disability, facial and skeletal dysmorphism, microcephaly, epilepsy, motor delay, and other behavioral phenotypes. We employed a multidisciplinary approach combining cellular and animal models to understand the molecular mechanisms underlying CCDC120-related neurodevelopmental phenotypes. In-silico analysis and 3D protein modeling simulation predicted alteration of CCDC120 protein folding for missense variants, which was consistent with the observed changes in heterologous cells. Overexpression of CCDC120 NDD-associated variants in heterologous cells revealed significantly reduced mRNA and protein steady-state levels (HEK293 cells), as

well as compromised protein localization within the growth cone and neurite shaft (Neuro2a cells), suggesting a damaging and pathogenic nature of these variants for normal protein expression and function. Also, we are in the preliminary stage of generating a knockout human neuronal cell line using the CRISPR/Cas9 genome editing approach to study the impact of this genetic variation on neurogenesis. Additionally, knocking down ccdc120 in zebrafish using a morpholino-mediated approach resulted in severe developmental and behavioral deficits comparable to those in human subjects, which were rescued by co-injection of human CCDC120WT mRNA but not by transcripts encoding NDD variants, emphasizing their loss-of-function impact. Taken together, our in vitro and in vivo studies revealed CCDC120 as a significant player in neurodevelopment and suggest that its variants contribute to NDD phenotypes.

40. Instead of IDK, how's IDO: Understanding the Role of Tryptophan Metabolism as an Age-Specific Mechanism for Pertussis Outcomes

Jaylyn King

Oral Session D (Elm Ballroom)

King, J.I. , Rajbanshi, N. , Scanlon, K. M.

Pertussis, caused by Bordetella pertussis (Bp), is a respiratory infection that displays age-dependent severity. Infants demonstrate the highest rates of pertussis-related hospitalization and mortality, but the mechanisms promoting severe disease in infancy are poorly understood. Products of tryptophan (TRP) metabolism by the enzyme indolamine-2,3-deoxygenase (IDO) into the kynurenine pathway (KP) have been shown to inhibit immune activation. Due to dietary differences, infants have significantly higher plasma TRP levels compared with older children. Therefore, we hypothesize i) during Bp infection, TRP metabolism by IDO promotes immune tolerance; and ii) elevated TRP levels and IDO induction in infants amplifies this mechanism promoting age-dependent outcomes. Our work, using a non-targeted approach, identified significantly higher Bp-induced IDO in infant mice compared with adults and age-dependent differential expression of downstream KP enzymes. In addition, the presence of IDO inhibited the expression of several cytokines associated with correlates of protection to Bp. Specifically, IFN-γ, IL-17, and pan IFN-α displayed significantly greater expression in infant and adult IDO knockout (KO) mice compared to wildtype mice. IDO KO infants also displayed elevated basal levels of IFN-γ, indicating this pathway serves to alter immune functions in early life, even in the absence of infection. Additionally, IDO controls age-dependent induction of the immunosuppressive cytokine IL-10. Overall, we conclude TRP metabolism by IDO is a key mechanism for promoting immune tolerance, and this function is exacerbated in early life. Further investigation into this pathway and its implications during Bp infection may lead to the identification of novel targets for therapeutic development.

41. Adenoviral Vector Encoding Neuraminidase from Avian H5N1 Influenza A Virus Elicits Broadly Cross-Reactive Cellular and Humoral Immune Responses Following Prime Immunization

Cosette Schneider

Oral Session D (Elm Ballroom)

Schneider, C.G., Hayes, J., McIntire, K., Souquette, A., Rodriguez, A., Germain, J., Ward, A.B., Han, J., Coughlan, L.

Seasonal and emerging zoonotic influenza A viruses (IAV) have the potential to cause significant global morbidity and mortality. The emergence in late 2023, and ongoing spread of highly pathogenic avian influenza (HPAI) H5N1 in the United States has led to the mass culling of poultry and infections in dairy cattle with spillover into humans. This unprecedented outbreak indicates a significant increase in the public health risk posed by zoonotic influenza viruses, necessitating the development of universal influenza virus vaccines capable of eliciting durable, broadly cross-reactive immune responses, with an emphasis on immunity to emerging avian strains and subtypes. To elicit heterosubtypic and/or pan-group immunity, efforts should prioritize the identification and targeting of conserved antigens or epitopes, in combination with the investigation of diverse vaccine platforms. Here, we evaluated the potential of a non-replicating adenoviral (Ad) vector encoding influenza neuraminidase (NA) from the avian H5N1 A/Vietnam/1203/2004 strain (Ad-N1) to elicit broadly cross-reactive immune responses to antigenically diverse seasonal and avian N1s. Ad-N1 elicited cellular and humoral immunity in mice after one dose, with significantly greater magnitude and breadth across diverse N1 strains as compared to matched inactivated vaccines, or adjuvanted recombinant NA controls. Future work will assess the in vivo efficacy of this vaccine candidate, allowing us to dissect out the functional roles of cellular and humoral immunity against NA. Together, this study improves our understanding of Ad vectors and NA-based immunity, and how these will contribute to the design of broadly protective universal influenza virus vaccines for pandemic preparedness.

42. Exploring structural variants and adaptation in the Andean highland and coastal populations using long-read sequencing

Susweta Roy

Oral Session D (Elm Ballroom)

Roy, S., Borda, V., Yan, S.M., Gouveia, M.H., Cifuentes, K., Juscamaita, R., Sanchez, C., Caceres, O., Padilla, C., Guio, H., Tarazona-Santos, E., Rotimi, C.N., McCoy, R., Santolalla, M., O'Connor, T.D.

The migration of humans from the coastal lowlands of South America to the high-altitude Andes began 10,000–12,000 years ago. These early settlers faced extreme environments, including hypoxia and cold temperatures, requiring both physiological and genetic adaptations. While physiological traits are well studied, the genetic basis—especially involving structural variants (SVs ≥ 30 bp)—remains less understood. To investigate the role of SVs in high-altitude adaptation, we generated high-coverage PacBio HiFi long-read sequencing data for two Peruvian individuals with >99% Indigenous American ancestry. These were combined with 34 publicly available long-read datasets to build a structural variant panel of 200,341 SVs. Using PARAGRAPH, we genotyped these SVs in short-read data from the Peruvian Genome Project, Human Genome Diversity Project, and 1000 Genomes Project, spanning three highland and two lowland populations, resulting in 110,588 genotyped SVs. Population branch statistics (PBS), using the Yoruba population as an outgroup, revealed two novel SVs highly differentiated between highland and lowland groups (PBS > 99th

percentile). One is a 132 bp deletion in the first intron of LINC01725 (allele frequency: 0.7 highland vs. 0.2 lowland); the other is a 344 bp deletion in TSGA10 (0.86 vs. 0.4). Both genes are linked to traits such as reticulocyte count and hemoglobin levels—key in adapting to hypoxic conditions. These findings suggest SVs contribute to Andean adaptation and highlight their broader role in evolutionary genetics. Our approach offers a path to uncovering variants shaped by natural selection during human migration into extreme environments.

43. Associations Between Peak Expiratory Flow and Functional Goal Achievement After Rehabilitation: A Nationally Representative Cohort Study of Older Adults

Lindsey Mathis

Oral Session E (Room 203)

Mathis, L., Sun, N., Ho, S., White, L., Addison, O., Savin, D., Falvey, J.

Rationale: Physical rehabilitation prevents disability in older adults recovering from major injuries and illnesses. However, individuals with impaired lung function often struggle to engage in rehabilitation, potentially hindering recovery. Current research focuses on individuals with known lung diseases or in pulmonary rehabilitation programs, limiting understanding of functional recovery among older adults with sub-clinical lung impairments. Objectives: This study utilizes nationally representative pulmonary function metrics, specifically peak expiratory flow (PEF), to examine relationships between lung function and achievement of functional goals after rehabilitation among community-dwelling older adults. Materials/methods: A cohort of 927 community-dwelling rehabilitation users (weighted n=5,225,263) from the National Health and Aging Trends Study (NHATS) who reported completing an episode of rehabilitation within the previous year. Logistic regression adjusted for age, gender, and chronic conditions. Results: Of the weighted sample, 7% had severely impaired PEF (weighted n = 369,437) and were more likely to be male and identify as Black. The adjusted odds of met goals were 47% lower for the severely impaired groups compared to normal (aOR= 0.5, 95% CI 0.3- 1.0), and 36% lower for the moderately impaired groups (aOR= 0.6, 95% CI 0.4- 0.9). Conclusions: Among 5 million older adults in the US using rehabilitation annually, approximately 29% have impaired lung function and are less likely to achieve their rehabilitation goals. These findings suggest that PEF measures may predict rehabilitation success beyond standard geriatric screening, highlighting needs for pulmonary assessments even in individuals without primary lung diagnoses.

44. Constitutive deletion of the obscurin Ig58/59 domains elicits chamber- and sex-specific cardiac remodeling

Anne Brong

Oral Session E (Room 203)

Brong, A., Grogan, A., Joca, H., Boyman, L., Kaplan, A., Ward, C., Greiser, M., Kontrogianni-Konstantopoulos, A.

Obscurin is a giant cytoskeletal protein that supports muscle development, tethers intracellular compartments to the sarcolemma, and regulates contraction. In the ObscnΔIg58/59 mouse model, expressing obscurin lacking Immunoglobulin (Ig) domains 58 and 59, males exhibit atrial fibrillation accompanied by atrial and ventricular dilation. Following extensive characterization of

ObscnΔIg58/59 ventricles, we hypothesized that Ig58/59 deletion elicits unique structural and functional consequences in the atria. Indeed, ObscnΔIg58/59 atria, but not ventricles, exhibited misalignment of Z-disks in electron micrographs. Spontaneous and stimulated Ca2+ cycling behavior were differentially disrupted in atrial cardiomyocytes from 6- and 12-month ObscnΔIg58/59 males. Furthermore, ΔIg58/59 atrial cells showed an age-dependent deterioration of the transverse-axial tubule network. Our work in males indicates that the atria are principally and particularly affected by Ig58/59 elimination and that our model mirrors essential aspects of atrial cardiomyopathy. Critically, ObscnΔIg58/59 females are phenotypically normal. We sequentially postulated that ovarian estrogens and dietary phytoestrogens insulate ΔIg58/59 females against cardiac pathologies. To this end, we surgically excised the ovaries (OVX) of young ObscnΔIg58/59 females and switched them to a soy-free (phytoestrogen-free) chow. Depletion of endogenous and exogenous estrogens induced age-specific remodeling of the left ventricle in ΔIg58/59 females yet failed to provoke progressive arrhythmias. We are currently interrogating whether extragonadal estrogens and/or the relative absence of androgens insulate soy-free, OVX ObscnΔIg58/59 females. Collectively, our work suggests that the contribution of obscurin and its Ig58/59 domains to cardiomyocyte performance is differentiated across cardiac chambers and, further, that ovarian sex hormones alone cannot explain cardioprotection in ObscnΔIg58/59 females.

45. Validating D-Galactose Injection as a Model for Inducing Aging in Musculoskeletal Tissues

Sushrut Pathy

Oral Session E (Room 203)

Pathy, S.M., Bopp, T.S., Ward, C.W., Stains, J.P.

Efficient maintenance of musculoskeletal health is a dynamic balance between anabolism and catabolism. This balance becomes difficult to maintain with aging as metabolic and inflammatory disorders accumulate, shifting the scale towards catabolism and resulting in osteosarcopenia. We aim to validate an inducible aging model in mice to better investigate the responses to major bone fracture in aging, co-morbidity afflicted, and transgenic mice. Our model of interest induces aging by injecting mice with solutions of D-galactose (D-gal). Chronic and excessive administration of D-gal results in non-enzymatic bonding with protein residues, making an advanced glycation end product (AGEs). These AGEs are thought to promote disease and disorder by (i) covalently crosslinking long lived cellular machinery resulting in functional impairment, by (ii) interacting with the receptor for advanced glycation end product (RAGE) to launch an inflammatory signaling cascade, and by (iii) generating reactive oxygen species, which promotes oxidative stress and mitochondrial dysfunction. Previous work has shown that D-gal treatment in rodents has promoted aging-like dysfunctions in various organ systems. Unfortunately, much of this work is done in skeletally immature mice treated with D-gal, which may show effects of hindered development, rather than aging. Our group recently tested this model in musculoskeletally mature mice. D-gal treated mice began to mimic aged mice in performance on rotarod, DEXA femur BMD, and bone microCT parameters after 12 weeks of treatment. These data suggest a D-galactose dependent musculoskeletal decline in mature mice, which may simulate aging.

46. Systematic Review and Meta-Analysis of Prevalence of Domestic Elder Abuse in South Asia

Aman Shrestha

Oral Session E (Room 203)

Shrestha, A., Ghimire, S., Sapkota, K.P., Karmacharya, I., Ghosh, I., Danquah, A., Shelawala, N., Gorman, E.

Background: Elder abuse is a critical public health and human rights issue, particularly in South Asia, where patriarchal norms, family-centered caregiving, and inadequate institutional support exacerbate the issue. Despite global focus, regional data on elder abuse in South Asian countries are limited. This systematic review and meta-analysis estimated the prevalence of community-based elder abuse and its subtypes among older adults (≥60 years) in South Asia and explored the gender differences in abuse experiences. Methods: A comprehensive search of six databases and gray literature identified 33 relevant studies from Bangladesh, India, Nepal, Pakistan, and Sri Lanka. Data were extracted using Covidence, and study quality was assessed with the modified Newcastle-Ottawa Scale. Meta-analyses were conducted using random-effects models, with heterogeneity evaluated via the I^2 statistic. Results: Most studies were from India (n=21) and Nepal (n=7), with an overall elder abuse prevalence of 31.8%, ranging from 25.8% in India to 49.9% in Nepal. Women experienced higher abuse rates (33.0%) than men (24.3%). Caregiver neglect and psychological abuse (around 20% each) were the most common, disproportionately affecting women. Physical abuse (3.9%), financial exploitation (8.0%), and sexual abuse (0.7%) were less frequent, with women experiencing higher abuse in all categories except sexual abuse. Conclusions: This study underscores the significant prevalence of elder abuse in South Asia, with women being disproportionately affected, emphasizing the urgency for culturally appropriate interventions. Targeted policies and community-driven initiatives are essential to combat elder abuse, enhance eldercare, and safeguard vulnerable populations in the region.

47. Motor Skill Learning in Amnestic Mild Cognitive Impairment

Kylie Tomlin

Oral Session E (Room 203)

Tomlin, K.B., Westlake, K. P.

Global population aging has led to an increased prevalence of neurocognitive disorders, including mild cognitive impairment (MCI). Although individuals with MCI are significantly more likely than their age-matched, cognitively intact peers to utilize healthcare services, there is limited understanding of how age-related cognitive decline influences motor training and rehabilitation. Specifically, it is unclear whether motor learning is impaired in older adults with amnestic MCI (aMCI). The aim of this ongoing original research study is to compare acquisition, retention, and transfer of a visuomotor task in older adults with aMCI and non-cognitively impaired (NCI) matched controls, using behavioral and neurophysiological approaches. Participants (n= 8 aMCI, n = 10 NCI; target n= 30 [15 MCI, 15 NCI]) trained a rotated-cursor tracing task on a movement tracking device (KinereachTM) over 3 visits. Online acquisition, 24-hour offline consolidation, 1-week delayed retention, and intermanual transfer were assessed using normalized change in movement time and accuracy. Task-based cognitive workload was index by EEG ERP responses to task-irrelevant

auditory stimuli. Data on participants' sleep quality, interest, and effort was collected through self-report. Findings from the completed study will elucidate whether older adults with aMCI demonstrate motor learning impairments at the behavioral or neural level. Results will inform clinical decision making in physical and occupational therapies by clarifying whether standard training approaches are appropriate in aMCI or if population-specific motor training approaches are indicated. Future research should explore motor training approaches to optimize learning outcomes for functional motor tasks in larger samples.

48. Early ensheathing pericyte dysfunction in a mouse model of CADASIL

Abigail Vigderman

Oral Session E (Room 203)

Vigderman, AS, Hariharan, A, Weir, N, Xiang, L, Longden, TA

Small vessel disease (SVD) of the brain underlies 25% of stroke cases and is the most common cause of vascular cognitive impairment. The most common monogenic form of SVD is CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy), caused by mutations of the NOTCH3 protein which is widely expressed in mural cells (vascular smooth muscle cells [SMCs] and pericytes), although little is known regarding pericyte pathology in this disease. Pericytes proximal to the penetrating arteriole (PA), known as ensheathing pericytes, contract and relax to rapidly regulate capillary diameter and thus blood flow in the downstream capillary tree. We conducted two-photon laser scanning microscopy (2PLSM) of blood flow and pericyte contractile responses with CADASIL Notch3R169C transgenic and control mice. Our data indicate that ensheathing pericyte responses to capillary electrical signals are impaired prior to other known CBF deficits, thus raising the tantalizing possibility that ensheathing pericytes could be a target for early clinical intervention in CADASIL. We also show that thin-strand pericyte KATP and endothelial KIR-mediated electrical signals to PA SMCs are intact at this early time point before their breakdown later in CADASIL pathology. Taken together, this work provides a new candidate mechanism by which CBF is diminished early in CADASIL pathogenesis for potential therapeutic intervention.

49. Impact of Drug Incorporation into Micelle on Reduced Griseofulvin across a Hollow Fiber Membrane (HFM)

Roshni Patel

Oral Session F (Room 223)

Patel, R.P; Polli J.E

The objectives were to assess the impact of drug micellization into surfactants on drug permeation across an HFM and identify a preferred permeation model from three models: permeation from only free drug, from both free drug and micelle-bound drug, and permeation with enhancement from micelle shuttling. Drug permeation studies using Hollow fiber membrane were conducted under unsaturated drug conditions using griseofulvin with and without surfactants SLS, PS80, and POE for 300 min. The donor contained drug solution with or without surfactant in 900 ml. Flow rates for donor and receiver solutions (37°C) were 2 ml/min. The donor solution was pumped into the HFM module, with the outflow recycled back to donor chamber for recirculation.

Simultaneously, a continuous receiver solution flow surrounded the hollow fibers, matching the donor's surfactant type and concentration but without drug. Drug solubility and micelle sizing studies were also performed. From solubility studies, griseofulvin was extensively incorporated into micelles, although permeation decrease was not as large as reduction in drug free fraction due to micellization. For 2% surfactant and 6 μg/ml griseofulvin donor, permeation decreased ~10-fold with SLS, ~3-fold with PS80, and ~3-fold with POE compared to no surfactant; meanwhile, free griseofulvin concentration in solubility studies was reduced ~160-fold, ~10-fold, and ~15-fold, respectively. The model incorporating permeation from both free drug and micelle-bound drug accommodated flux was the preferred model, with drug-containing micelle PDM = 5-15$\times 10^{-6}$ cm/sec. The micelle shuttling model also accommodated flux and provided literature-comparable ABL thicknesses, but was less preferred.

50. Single-nuclei RNA sequencing provides insights into the molecular signatures of the Huntington's disease mutation in the mouse striatum the therapeutic potential of an HTT-lowering antisense oligonucleotide.

Anjana Santosh Kumar

Oral Session F (Room 223)

Kumar, A. S., Ament, S. A., Herb, B. R., Giglio, M. G

Huntington's disease (HD) is a progressive neurodegenerative disorder caused by a trinucleotide CAG repeat expansion in the HTT gene, with early pathological changes observed in striatal medium spiny neurons (MSNs). To investigate early, cell-type-specific transcriptional alterations and the therapeutic potential of HTT-lowering strategies, we performed single-nucleus RNA sequencing (snRNA-seq) on the striata of HttQ111/+ mice and wild-type littermate controls. Mice were treated with saline, control antisense oligonucleotide (ASO), or an HTT-targeting ASO designed to reduce HTT protein levels via RNase H-mediated degradation. Pseudobulk differential expression analysis revealed substantial transcriptional dysregulation in the Genotype contrast (674 DEGs), with strong enrichment of canonical HD gene sets in GSEA. In contrast, HTT-lowering ASO treatment resulted in only 12 significant DEGs and no enrichment of HD-related pathways, indicating limited molecular rescue. The ASO_Toxicity contrast identified 15 DEGs and showed modest enrichment of neurodevelopmental gene sets, suggesting minor, non-toxic transcriptional shifts. No overlapping DEGs were found between Genotype and HTT-lowering ASO at standard thresholds. Broader comparisons revealed genes with large logFC differences, though they lacked statistical significance, potentially reflecting subtle or heterogeneous ASO effects. These findings highlight robust HD signatures in the HttQ111/+ model and suggest that optimized HTT-lowering strategies may be needed to achieve consistent transcriptomic reversal.

51. The Impact of Melanoma Cell Adhesion Molecule (MCAM) on Non-Adherent Non-Tumorigenic and Tumorigenic Mammary Basal-like Epithelial Cells in the Metastatic Cascade

David Annis

Oral Session F (Room 223)

Annis, D. A., Thompson, K.N., Mull, M.L., Ju, J.A., Gilchrist, D.E., Vitolo, M.I., Martin, S.S.

Melanoma cell adhesion molecule (MCAM) is a protein located on the cell surface that was first discovered in advanced primary tumors and metastatic lesions. Overexpression of MCAM is associated with triple-negative breast cancer, among many other cancer types, and decreased patient survival. Additionally, breast cancer cell lines overexpressing MCAM show an increase in migration, invasion, tumorigenesis, and induction of vimentin and slug indicative of EMT. Early work has shown MCAM expression can alter the actomyosin cytoskeleton, however, the impact of MCAM on the microtubule network and non-adherent cells has not been well studied. Given that microtubules are a very common target of multiple cancer therapies, we set out to explore changes to microtubule modifications and intermediate filament impacts due to MCAM expression alterations. This study will utilize the triple negative breast epithelial cell lines of MCF10A to overexpression MCAM, and tumor derived (TD) MDA-MB-231 and MDA-MB-436 cell lines with CRISPR MCAM. To achieve the goal of this study we will be focused on microtubule-based phenotypes of microtentacles(McTNs) alterations and homotypic cell clustering, using Tether Chip Technology, and further explore the impact of MCAM expression changes on spheroid invasion and cellular migration. We've shown overexpression of MCAM results in increases to McTN protrusions, homotypic cell clustering, migration, and spheroid invasion. Moreover, the knockout of MCAM in our tumor derived MDA-MB-231 and MDA-MB-436TD decreases McTN protrusions and homotypic cell clustering. However, there were no observable alterations to microtubule modification, meanwhile vimentin saw an increase in protein levels when MCAM expression was increased.

52. Profiling sex-specific behavioral patterns and nucleus accumbens neuronal subtype transcriptome networks in chronic social stress

Gautam Kumar

Oral Session F (Room 223)

Kumar, G., Franco, D., Fox, M., Basu, M., Olusakin, J., Campbell, R., Ament, S., Lobo, M.K.

Sex-specific neurobiological effects of chronic stress contribute to the higher depression rates observed among females. The nucleus accumbens (NAc), a hub in the reward circuitry, is altered in MDD subjects and mouse models. The nature of chronic stress-induced alterations on the two subtypes of medium spiny neurons (MSNs) found in the NAc and their role in producing sex-specific behavioral outcomes remains poorly understood. Using D1- and A2A-Cre-RiboTag (RT) female mice, we performed the chronic witness defeat stress paradigm (CWDS) followed by the 3-chamber social interaction test (3ChSI) to identify a susceptible and resilient group based on social preference and sequenced their ribosome-associated mRNA. Weighted gene co-expression network analysis (WGCNA) using the output data with a publicly available dataset from socially stressed male mice identified subtype-specific modules differentially regulated across sex and stress groups involving mitochondrial biogenesis and synaptic and morphological adaptations. Recordings of 3ChSI were processed to obtain spatiotemporal data of mouse activity for a more granular characterization of the social behavior. Factor analysis using behavioral variables created from this data identified latent factors driving behavior during 3ChSI including exploratory behavior, social preference and surveillance behavior. By deconstructing the

MSN subtype gene expression and social interaction behavioral profiles in stress groups using dimension reduction techniques, we home to enhance knowledge of the sex-specific alterations induced by chronic social stress and the impacted social behavior components. These studies can contribute to the development of targeted forms of treatment that address specific behavioral issues across vulnerable populations and address mental health disparities.

53. The Effects of Beryllium on the Plasma Membrane, and the Evolution of the Beryllium Force Field in CHARMM

Joshua Lucker

Oral Session F (Room 223)

Lucker, J. A., Meuse, C., Sukharev, S. I., Klauda, J. B.

Beryllium (Be2+), an alkaline earth metal widely utilized across various industries (e.g. aerospace, military, nuclear, and sports equipment manufacturing), is known to compete with calcium ions (Ca2+) in plasma membranes. This competition impacts the recognition of phosphatidylserine (PS) by scavenger cell receptors, hindering the clearance of apoptotic cells by macrophages. Accumulation of these cells may contribute to the development of berylliosis, a chronic condition marked by persistent granulomatous inflammation in the lungs. The precise mechanisms underlying berylliosis remain unclear, particularly regarding the competitive interactions between beryllium and calcium with the charged lipid components in cell membranes. This study aims to compare computationally derived FTIR spectra with experimentally measured FTIR spectra using PS liposomes, shedding light on ion binding configurations to lipid headgroups along with evaluating the effectiveness of the current Be2+ force field in CHARMM. Molecular dynamics simulations were performed for 100 nanoseconds involving 100 PS molecules for both Ca2+ and Be2+. The different ion configurations were identified and analyzed using K-means clustering. For each cluster, model compounds representing lipid headgroup components were constructed, and vibrational spectra were computed via quantum mechanics (QM). The resulting computational FTIR spectra were then compared with experimental data to assess their correlation and determine whether the simulated binding states of PS liposomes accurately reflect that observed in experiments. This iterative approach, involving configurational refinements, simulations, and QM calculations, aims to pinpoint predominant binding configurations and make necessary force field adjustments. This presentation will discuss recent developments of this project and explore its future directions.

54. When the Toxin Calms the Storm: B. pertussis Peptidoglycan Puts the Brakes on TREM-1 to Evade Amplification of Host Immune Responses

Sasha Cardozo

Oral Session F (Room 223)

Cardozo, S., Rickert, David., Skerry, C.

Whooping cough (pertussis) is a highly contagious pulmonary disease caused by the bacterium Bordetella pertussis, characterized by severe spasmodic coughing and long-term pulmonary damage. Despite widespread antibiotic and vaccine use, pertussis continues to infect over 24.1 million people annually. Tracheal cytotoxin (TCT), a disaccharide

peptidoglycan released by B. pertussis during infection, impairs mucociliary clearance. We hypothesized that TCT release promotes pertussis pathogenesis. Surprisingly, we found that adult mice infected with TCT-overproducing strains exhibited significantly reduced pulmonary inflammation at seven days post-infection compared to those infected with TCT-deficient or wild-type strains, suggesting that TCT dampens pertussis immunopathology. To explore this mechanism, we performed bulk and single-cell RNA sequencing to identify receptors that recognize peptidoglycan and regulate innate immune responses. We observed elevated transcripts of pro-inflammatory receptor, TREM-1, in the lungs of infected adult mice. In vitro, TREM-1 was also upregulated on B. pertussis-stimulated bone marrow-derived neutrophils and J774 macrophages. TREM-1 signaling is activated by host protein-peptidoglycan complexes. Strikingly, our reporter cell assays revealed that TCT reduced TREM-1 activation. We hypothesized that if TCT dampened immunopathology by suppressing TREM-1 activation, depletion of TREM-1 should reduce inflammation. TREM-1 depletion significantly reduced lung pathology and downregulated CCL2 and IL-6 transcripts in infected adult mice. In infant mice, loss of TREM-1 markedly improved survival compared to wild-type controls. Collectively, these findings establish TREM-1 as a correlate of disease severity and identify peptidoglycan release as a means of immune evasion, highlighting the potential for targeting TREM-1 to reduce pertussis immunopathology and offering new therapeutic insight.

55. Characterization of the cellular immune response in temporomandibular disorder

Aishwarya Venkataraman

Oral Session G (Room 115)

Venkataraman, A., Mocci, E., Ament, S., Colloca, L., Lvovs, D.

Background: The etiological heterogeneity of temporomandibular disorder (TMD) is reflected by the several biological processes (BPs) involved, positioning it as a complex, multi-system disorder. Aims: 1. Characterize immune signatures in TMD; 2. Test their associations with clinical features like impact pain, pain catastrophizing, anxiety. Methods: We performed non-negative matrix factorization (NMF) using CoGAPS to identify patterns associated with BPs by analyzing transcriptomic data from blood samples of a multi-ethnic cohort of 173 individuals with TMD. We employed a digital cytometry tool (CIBERSORTx) to estimate immune cell type proportions from the transcriptomic data. We examined correlations between CoGAPS-derived patterns and immune cell type fractions, demographic variables, and clinical phenotypes. The patterns were further assessed for enrichment in immune and inflammatory BPs. Finally, we selected the genes with the highest amplitudes for each pattern and tested them for differential expression by high and low impact pain, and by different levels of pain catastrophizing and anxiety. Results: The 18 patterns derived from CoGAPS showed significant correlations with immune cell types, demographic variables, clinical features. Gene set enrichment analysis revealed enriched immune and inflammatory pathways in 4 of 18 patterns. One of these 4 patterns was not only enriched in BPs related to cytokines, but was also associated with 25 genes (including cytokines CXCL9, CXCL10, CXCL11) demonstrating significantly higher expression in individuals with high impact pain than those with low impact pain. Conclusion: Our study

provided insight into the inflammatory context of TMD that affects clinical features of pain, while elucidating key underlying BPs.

56. Characterizing the Synaptic Effects of Ketamine Metabolites (R)- and (S)-Norketamine

Phylicia Cooper

Oral Session G (Room 115)

Cooper, P.R., Brown K.A., Gould T.D.

One-third of patients with Major Depressive Disorder do not respond to at least two trials of antidepressant treatments. (R,S)-ketamine was primarily used as an anesthetic and has been found to also be a rapid-acting antidepressant for treatment resistant depression (TRD). Due to action at the NMDA receptor, ketamine can induce dissociation which can lead to misuse. Recent work has found that a metabolite of ketamine, (R,S)-norketamine [(R,S)-NK], alone is sufficient to promote antidepressant-like behaviors in mice. However, there is little known about what (R,S)-NK does synaptically as compared to (R,S)-ketamine. Our preliminary data has found that 45 uM of both enantiomers of norketamine potentiate glutamatergic transmission at the Schaffer Collateral-CA1 synapse. A concentration-effect curve experiment also found that 30 uM and 100 uM of (S)-NK significantly potentiate glutamatergic transmission at this synapse. Current experiments include performing a concentration-effect curve for (R)-NK at this synapse in the hippocampus. Future experiments aim to follow up with in vitro and in vivo experiments to investigate if there is a relationship between projections from the Anterior Cingulate Cortex (a brain region involved in rumination and suicidal ideation) to the hippocampus (involved in emotional regulation).

57. Exploratory Structural Equation Model of Objectification and Fragmentation in Sex Trafficking

Allison Deitz

Oral Session G (Room 115)

Deitz, A. H. H.

Domestic sex trafficking, or the sexual exploitation of U.S. citizens within the U.S., is a persistent problem that remains underexplored. Empirical anti-sex trafficking research is fragmented in its use of theory, which hinders the advancement of policy and practice. As a guiding tool for research, theory can reflect and reinforce the status quo, but it can also disrupt it. The assumptions we carry with us into any clinical or research scenario affect our construct operationalizations and causal attributions. The research question concerned the overall correspondence between the theoretical cycle and the means of control (MOCs) endorsed by survivors of domestic sex trafficking, or SDSTs, in the Counter Trafficking Data Collaborative (CTDC) dataset. The present study focused on cisgender women and girls who were registered with the CTDC as SDSTs. Exploratory structural equation modeling (ESEM) was used to analyze SDSTs' reported MOCs in the CTDC dataset, and explore the single-factor and inter-factor loadings onto the objectification and fragmentation stages of the theoretical cycle. The findings supported the validity of the overlapping objectification and fragmentation stages. The present study employed a novel approach, ESEM, to explore theory testing around an understudied population. The quantitative findings also offer opportunities for additional research to enrich, clarify, or

challenge understandings of power and control dynamics in domestic sex trafficking. There remains a need for more consistent and explicit theoretical integration in research, regardless of methodology.

58. Relationship Between Nursing Home Quality Rating and Pain in Dementia

Sorah Levy

Oral Session G (Room 115)

Levy, S., Resnick, B., Holmes, S.

Pain is highly prevalent among nursing home (NH) residents with dementia. Estimates suggest 35-80% of NH residents with dementia experience pain. Pain had been identified as a quality indicator used to measure NH performance. The Center for Medicare and Medicaid Services (CMS) Five-Star Quality Rating System is intended to inform the public of NH quality metrics. There should, therefore, be evidence that facilities with higher star ratings provide better pain management resulting in lower odds of having residents showing signs of pain. This cross-sectional secondary data analysis used baseline data from an implementation study testing the impact of an intervention to manage behavioral symptoms in NH residents with dementia. The sample included 553 residents with dementia living in 55 NHs. Generalized linear mixed models (GLMM) were used to test the relationship between CMS five-star rating and pain controlling for comorbidities, cognition, and profit status. On average, NHs in the sample had a five-star rating of 3.5 (SD= 1.3) and pain was observed in 22.6% (n=125) of the sample. Five-star rating was significantly associated with pain (p=0.023) such that the odds of experiencing pain decreases by 34.8% for each star increase in five-star rating, indicating that higher five- star ratings are associated with a lower likelihood of pain among residents with dementia. Findings from this study demonstrate that quality of care indicated by CMS star rating is associated with lower pain. It may be particularly important to focus on pain management in NHs with low star ratings.

59. Cell-type Specific Transcription Factor Activity Underlies Immune Checkpoint Inhibitor Resistance in Head and Neck Squamous Cell Carcinoma

Ian Mills

Oral Session G (Room 115)

Mills, I., Gaykalova, D.A.

Only 15-20% of head and neck squamous cell carcinoma (HNSCC) patients respond to immune checkpoint inhibitor therapy (ICI). To further investigate intra-tumoral characteristics between patients who respond vs don't respond to ICI, single cell RNA sequencing (scRNAseq) was analyzed to create gene regulatory networks and cell-type specific transcription factor activity. Raw data were obtained from a previously peer-reviewed study and a sub-cohort of seven patient samples with annotated clinical ICI response was created. The cohort contained 3 ICI responders and 4 non-responders. Transcription factor activity was calculated through fitting scRNAseq gene expression data and gene-transcription factor interaction weights to a univariate linear model. A total of 63,051 individual cells were analyzed, averaging 1500 expressed genes per cell. Distinct cell types including cancer cells, epithelial cells, macrophages, T cells, and NK cells were identified using established marker gene sets. Differential transcription factor activity showed distinct cell-type specific

transcriptional differences between ICI responders and non-responders. In cancer cells, nonresponding tumors were found to have higher MYC activity. In T cells, non-responding tumors had higher type-I interferon activity through the cumulative activity of a STAT1-STAT2-IRF9 ISGF3 transcription factor complex. The highest expressed type-I interferon stimulated genes were further examined to understand their function in ICI resistance. These results show that transcription factor activity is a valuable tool in understanding characteristics of responsiveness to ICI. Further analysis of scRNAseq data can provide cell type specific targets to increase ICI efficacy and improve patient outcomes with this therapy.

60. Unexpected Low Bone Mass Induced by Global Deletion of Keratin 18 But Not Keratin 19 in Mice

Philippa Murray

Oral Session G (Room 115)

Murray, P.J., Buck, H.V., LeBlanc, K.W., Leser, J.M., Pathy, S.M., Bloch, R.J., Stains, J.P.

Work from our lab has investigated the role of the cytoskeleton in osteoblasts and osteocytes. Our prior work has shown a role for a subset of post-translationally modified tubulin in the osteocyte response to mechanical stimuli and a role for the type IV intermediate filament protein, synemin, in bone mass acquisition. Here, we demonstrate a role for Keratin18 in bone physiology. Keratin18 (gene name Krt18) and Keratin19 (gene name Krt19) are both type I intermediate filaments. Heteropolymers of type I (acidic) and type II (basic) intermediate filaments form important cytoskeletal structures. Interestingly, Keratin18 and Keratin19 are often found to compensate for one another as they have the capacity to heteropolymerize with the same type II intermediate filament, Keratin8. Here, we characterize the impact of the global deletion of Keratin18 in 13-weeks-old male and female mice in bone and the global deletion of Keratin19 in 12-weeks-old male mice in bone. Notably, we observed osteopenia in Krt18 but not Krt19 global knockout mice. Using micro computed tomography, we observed significant ($p<0.05$) osteopenia in Krt18-/- mice (>22% decrease in trabecular BV/TV in males and females). In contrast, we found no significant osteopenia in Krt19-/- mice. Moving forward, we sought to further characterize the skeletal effects of the absence of Krt18 in bone. Dynamic histomorphometry revealed no significant decrease in trabecular BFR, disqualifying a role for Keratin18 in osteoblast function. Therefore, we hypothesize that this phenotype may be due to an increase in osteoclast resorptive activity. This will be the subject of future work.

61. Determinants of Health Literacy Among Cancer Family Caregivers: A Scoping Review

Moses Akwobugi

Poster Session H (Room 349)

Akwobugi, M., Oduro B.E., Holmes, S.

Background: Cancer caregivers play a vital role in supporting patients living with cancer to navigate complex treatment decisions, yet their support is often limited by low health literacy. Moreover, the determinants of their health literacy remain poorly understood. Objective: To identify and synthesize empirical literature on the determinants of cancer caregivers' health literacy. Method: Guided by the Joanna Briggs Institute methodological recommendation and Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews, we conducted a scoping

review. We searched PubMed, CINAHL, EMBASE, and Google Scholar databases. We used the Social Ecological Model to organize the key findings. Results: Our preliminary findings revealed key determinants of health literacy among cancer caregivers across multiple levels. At the individual level, caregivers who were young, educated, female, had prior cancer caregiving experience, and had effective communication skills exhibited higher health literacy. Interpersonal determinants included family support, care involvement, and seeking a second opinion about care decisions. Community-level determinants included access to the internet, living in urban areas, and cultural beliefs. Institutional-level determinants included access to cancer materials and the method of cancer information delivery by providers. Conclusion: Our findings highlight the multifaceted nature of determinants of cancer caregivers' health literacy and the need for a multi-level educational intervention to support them.

62. Longitudinal Assessment of Physical Function and Health in Older Veterans Participating in the Gerofit Program

Ben Friedman

Poster Session H (Room 349)

Friedman, B., Giffuni, J., Drumheller, J., Kelly, M., Rekant, J., Addison, O.

Aging is associated with declines in physical function and health, which can significantly reduce quality of life. Older adults with mobility impairments face greater risk for falls and increased healthcare utilization and costs. Veterans have above average BMI and increased comorbidities compared to non-veterans, making them particularly vulnerable to poor health outcomes. While consistent exercise participation can improve functional mobility and strength, research beyond 5 years is limited. PURPOSE: This study analyzed longitudinal changes in physical function over a 10-year period in veterans participating in Baltimore Gerofit, an unstructured, supervised exercise program for Veterans over 65. We anticipated that regular participation in Gerofit would mitigate age-related declines in physical function. METHODS: 15 Veterans (69.2±3.39 years old at baseline) with physician clearance to exercise were included. Paired sample t-tests or Wilcoxon signed rank tests were used to compare baseline and 10-year outcomes. RESULTS: Veterans maintained physical function in measures of lower extremity (LE) strength (30s chair stand, $p=0.07$), speed, agility, and balance (8-foot up and go, $p=0.31$), and LE function and balance (Short Physical Performance Battery, $p=0.68$). Gait speed was reduced ($p<0.01$) but remained above age-predicted declines and normative values. Submaximal cardiovascular endurance declined (6MWT, $p<0.05$) but did not differ significantly from norms ($p=0.80$). CONCLUSIONS: The program mitigated typical age-related declines in physical function over a decade. Gerofit demonstrates the effectiveness and scalability of unstructured exercise programs in promoting health and physical function in high-risk aging populations.

63. Assessing Pharmacists' Readiness for Age-Friendly Care: A Needs Assessment Survey

Yu-Hua Fu

Poster Session H (Room 349)

Fu, Y., Wu, J., Zarowitz, B., Worz, C., Thomas, A.L., Poore, L., Valeriann, C.R., Zajac, D.P., Brandt, N., Cooke, C.E.

The Age-Friendly Health Systems (AFHS) initiative, focusing on the set of 4Ms—"Medication," "Mentation," "Mobility," and "What Matters"— aims to provide high quality care to older adults. A collaborative, interprofessional approach is essential, and pharmacists are well-positioned to champion the 4Ms. However, little is known about pharmacists' awareness and comfort with the 4Ms. A needs assessment survey was conducted to evaluate familiarity with the 4Ms and confidence in assessing and acting on the 4Ms concepts. Data were collected from April 13 to July 15, 2024. The survey had a view rate of 11.3% (398/3,522), with a participation rate of 58.3% (232/398). Of 232 respondents, 51.7% practiced in post-acute and long-term care settings. While 62.1% were aware of the AFHS initiative, only 20% reported facility-level involvement. Overall, only 17.7% of respondents were comfortable assessing the set of 4Ms. Comfort in assessing each of the 4Ms varied: "Medication" (73.3%), "What Matters" (71.1%), "Mobility" (28.9%) and "Mentation" (27.2%). Although 95% of respondents routinely assessed high-risk medications, only 70% were confident in optimizing or deprescribing them. Notably, a sizable percentage had never assessed "Mobility" (67%) or "Mentation" (47% for depression; 53% for dementia). These findings highlight gaps in pharmacists' readiness to fully implement the AFHS framework. Targeted educational efforts are needed to strengthen proficiency in "Mobility" and "Mentation" assessments, enhance confidence in medication optimization, and promote integration of the 4Ms as a cohesive approach to person-centered care.

64. Herbal Prophylactic in Your Tea: An Endgame for Bacterial Sepsis and Malaria

Grace Charles Mazinga

Poster Session H (Room 349)

Mazinga G,

Peach and clove extract contains bio-compounds with antimicrobial, antiinflammatory and antioxidative effects. These compounds are evidenced to participate in pathways that are involved in the pathogenesis and immunological response to bacterial sepsis and malaria. This is suggestive of a potential therapeutic application against one of the most leading causes of death. Prevention will be as easy as drinking tea!

65. Novel Antimicrobial and Remineralizing Resin-Based Clear Aligner Attachment Orthodontic Materials

Heba Alqarni

Poster Session H (Room 349)

Alqarni, H., Ba-Armah, I., Almutairi, N., Alenizy, M., Jirun, S., Weir, M. D., Xu, H. H. K.

Clear aligner orthodontic treatment provides a more hygienic and esthetic alternative to fixed appliances. Attachments are crucial in clear aligner therapy, but prolonged use is associated with plaque accommodation and white spot lesions. This research aimed to develop a novel resin-based antibacterial and remineralizing clear aligner attachment material to reduce white spot lesions during treatment while maintaining good mechanical and physical properties. The resin-based clear aligner attachment material was formulated by adding triethylene glycoldivinylbenzyl ether (TEG-DVBE) and urethane dimethacrylate (UDMA), denoted as (UV), along with 3% of the antibacterial monomer dimethylaminododecyl methacrylate (DMADDM), nano-amorphous calcium phosphate (NACP) and glass fillers at

different mass fractions (45%,50%,55%). Transbond and Vitremer were selected as commercial controls. Flexural strength, elastic modulus, degree of conversion and microhardness were evaluated. The experimental groups with 45%,50% and 55% glass fillers exhibited flexural strength from (109.2±8.6)MPa to (96.4±8.2)MPa, exceeding the ISO standard for resin-based materials. The elastic modulus for the group containing 20% NACP+45% glass was (8.75±0.42)GPa, significantly higher than the other experimental groups ($p<0.05$). The degree of conversion for all experimental groups with different glass mass fractions (45%,50%,55%) ranged from (53.4±2.3)% to (68.3±0.9)%, significantly higher than the commercial control (37.1±4.1)% ($p<0.05$). Hardness was higher for the 20% NACP+45% glass group at (2.4±0.2) GPa and the 10% NACP+55% glass group at (2.4±0.1) GPa than the other groups ($p<0.05$). All experimental groups with 3% DMADDM showed 6-log CFU reduction and 90% reduction of metabolic activity and lactic acid production.

66. Racial Identity, Racial Discrimination, and Psychological Distress among Non-White Immigrant Young Adults Living in the United States

Ardith Allison

Poster Session H (Room 349)

Allison, A.A.

Racial discrimination remains pervasive in the U.S., shaping interactions, policies, and institutions and creating inequitable opportunities for many minoritized racial groups including immigrant populations. For immigrants, racial discrimination often complicates their transition to the U.S., resulting in unique challenges. Several studies have indicated racial discrimination's adverse consequences on this population's physiological wellbeing. Furthermore, concepts such as race, ethnicity, or a combination of both have been found to buffer this association. However, the bulk of this research has focused broadly on adults. Thus, little is known specifically of the effect of racial discrimination on non-White immigrants between the age of 18-29, and the exclusive influence of racial identity on this relationship, making it difficult to understand how such experiences have affected their mental health. To understand the unique influence of race, this study integrated the ecological systems, minority stress, and stress-coping models to examine whether two dimensions of racial identity—race centrality and private regard—moderated the association between racial discrimination and psychological distress. Using hierarchical multiple regression analyses, the data indicated that racial discrimination was significantly and positively associated with participants' level of psychological distress. Also, private regard had a buffering effect on this association. The study's findings expanded on the existing knowledge of the outcome of racial discrimination on immigrants' experiences within the U.S. Implications for research and practice for new policies and programs were discussed.

67. Roles for HMGB1 and RAGE in EV-D68 Infection

Ashley Benton

Poster Session H (Room 349)

Benton, A., Jassey, A., Jackson, W.T.

Enterovirus-D68 (EV-D68) is a non-enveloped, positive-sense single-stranded RNA virus.

Although EV-D68 infections usually cause mild cold-like symptoms in rare cases the virus can cause Acute Flaccid Myelitis (AFM) in children, a paralysis disease that has no known cure or therapeutics. Like many RNA viruses, EV-D68 utilizes the cellular autophagy pathway to promote its own replication. HMGB1 (High-mobility group B1) is a multifunctional DNA binding nuclear protein with established roles in autophagy regulation. Because of this, we posited a role for HMGB1 in EV-D68 production. We observed that when HMGB1 is knocked down in cells, those cells infected with EV-D68 show a significant decrease in both intra- and extracellular viral titers, suggesting that HMGB1 is beneficial to viral replication. Its overexpression however, is associated with cancer. HMGB1 can bind to at least two known cell surface receptors: TLR4 (Toll-like receptor 4); and RAGE (Receptor for Advanced Glycation End products) both promising targets for cancer therapeutics. While we have been unable to show a specific role in virus replication for TLR4 binding by HMGB1, the RAGE inhibitor FPS-ZM1 caused a large decrease in intracellular titers and viral RNA replication. We have evidence that multiple steps in EV-D68 production are inhibited in the absence of functional RAGE signaling. Our data suggest multiple roles for HMGB1 and its surface receptor RAGE in EV-D68 replication.

68. Exploring Discrimination in Healthcare Utilization among Emerging Adults from Black, Indigenous, and other Communities of Color

Tharyn Giovanni

Poster Session H (Room 349)

Giovanni, T. N.

Emerging adults from Black, Indigenous, and other communities of color (BIPOC) report discrimination at higher rates which can adversely affect emotional well-being, exacerbate medical issues, and contribute to inequities in healthcare access and utilization. Despite the common misconception that emerging adults are universally healthy, young BIPOC adults face unmet health needs due to the compounding effects of systemic racism and discrimination. This study examines the relationship between discrimination and healthcare service utilization among BIPOC emergent adults ages 18-25. Five hundred fourteen BIPOC individuals responded to an online survey. Findings suggest that BIPOC individuals reporting high levels of discrimination were more likely to use emergency room services (OR = 1.04 SE = .02, $p = .02$) and had higher odds of engaging in mental health treatment (OR = 1.11 SE = .02, $p < .001$). There was no significant association between discrimination and primary care utilization ($p = .69$). Future research and implications are discussed.

69. Parental Moral Distress: A New Way of Thinking about Distress in Parents of Children with Serious Illness

Lydia Fassett

Poster Session H (Room 349)

Fassett, L. H., and Mooney-Doyle, K.

This poster describes how moral distress, the feeling of negative self-directed emotions that arise when a person is prevented from doing what they believe to be correct or the morally correct action is not clear, manifests itself in parents of children with serious pediatric illnesses (CSPI). To do this, we conducted a preliminary analysis of individual, cross-

sectional interviews with seventeen parents of CSPI admitted to a large, tertiary children's hospital in the Mid-Atlantic region of the U. S. in 2014. The children ranged in age from infants to adolescents. Interviews were audio recorded, professionally transcribed, and subjected to conventional content analysis. Rigor was maintained through peer review meetings, methodological expert review, thick description, an audit trail, and reflexivity journal. Preliminary findings suggest that these parents experience moral distress in the intrapersonal, interpersonal, and spiritual/existential dimensions. In the intrapersonal dimension, parents described feeling moral distress when they felt prevented from doing what was best for their families or could not do what they felt a parent should do. In the interpersonal area, parents described conflicts with the care team or problems meeting the conflicting needs of family and friends. Finally, in the spiritual/existential dimension, parents described distress from their attempts to understand the meaning of their experience as well as their relationships with the Divine. Describing the concept and experience of moral distress in parents can help professionals understand the complexity of family life in serious pediatric illness and help develop supportive practices and interventions.

70. What individual, interpersonal, and community-level factors contribute to adolescent involvement in gun violence? Literature Review

Darrel Freeman

Poster Session H (Room 349)

Freeman, D.C.

Background: Adolescent gun violence has become a critical public health crisis in the United States, with far-reaching consequences for individuals, families, and communities. In 2020 alone, nearly 20,000 deaths were attributed to interpersonal gun violence, including over 4,000 adolescents who were killed or injured by firearms. The long-term emotional, psychological, and social impacts are severe, adding to an estimated $671 billion in annual economic costs. Objective: This literature review aims to examine the individual, interpersonal, and community-level factors contributing to adolescent gun violence in the U.S., using the Socio-Ecological Model as a guiding framework. Methods: A structured literature search was conducted across major scientific databases using key terms such as "gun violence", "adolescents" and "United States". The inclusion criteria required studies to be U.S.-based, focus on youth ages 12–17, and be peer-reviewed empirical research published in English. The initial search yielded 462 articles, and after reviewing titles and abstracts, 307 were excluded. Of the 155 full-text articles assessed, 45 met all inclusion criteria and were selected for detailed review. Data extracted included study focus, year, location, population, outcomes, and design. Results: Key contributors to adolescent gun violence were identified, including substance use, exposure to violent or conflict-driven content on social media, and access to unregulated "ghost guns" These factors were consistently linked to elevated risks of firearm-related incidents. Conclusion: Addressing adolescent gun violence requires comprehensive, evidence-based strategies targeting behavioral, social, and systemic determinants to effectively reduce harm and protect youth.

71. Hepatic Micropatterned Co-Culture Models for the Evaluation of DILI

Sara Geriesh

Poster Session H (Room 349)

Geriesh, S., Li, L. , Heyward, S., Gaffney, J. , Cottier, K., Chen, M. , Sadrieh, N. , and Wang H.

Background: Drug-induced liver injury (DILI) is a major cause of drug attrition, leading to acute liver failure and death. However, early preclinical prediction remains challenging due to the limitations of traditional 2D cell cultures and species-specific differences in animal models. Novel microphysiological systems offer improved drug safety assessment. This study optimizes the hepatic micropatterned co-culture (MPCC) model, HEPATOPAC®, and employs the HEPATOMUNE® model to evaluate hepatotoxic drugs and their non-toxic analogs. Methods: HEPATOPAC and HEPATOMUNE are engineered using microfabrication techniques to create collagen "islands" for hepatocyte seeding, with fibroblasts serving as stromal cells. HEPATOMUNE also incorporates Kupffer cells to assess immune-mediated toxicity. We evaluated the hepatotoxicity of three DILI drug pairs—trovafloxacin/moxifloxacin, ibufenac/ibuprofen, and ximelagatran/dabigatran—by measuring cell viability, urea synthesis, and inflammatory cytokine release. Transcriptome profiling via RNA-seq is ongoing. Results: Trovafloxacin, but not moxifloxacin, dose-dependently reduced hepatocyte viability in both models, with LPS sensitizing toxicity in HEPATOMUNE. Trovafloxacin also induced IL-8 release, highlighting its proinflammatory effects. Ibufenac and ibuprofen exhibited similar cytotoxicity (IC50: 1.6-2.0 mM), exceeding reported Cmax ($\sim$100 μM), without affecting Kupffer cell cytokine release. Ibufenac's IC50 in HepG2 cells (3.1 mM) suggests metabolism enhances its toxicity. Ximelagatran and dabigatran showed negligible cytotoxicity, though DILI from ximelagatran is linked to specific MHC alleles, suggesting donor selection may improve model sensitivity. Conclusions: HEPATOPAC and HEPATOMUNE serve as promising in vitro platforms for DILI assessment, with HEPATOMUNE demonstrating sensitivity to inflammatory DILI drugs like trovafloxacin and LPS. These models could help refine FDA guidelines and advance non-animal testing in drug development.

72. Virtual Reality Induced Fear of Falling Responses During Reactive Balance

Katherine Dudek

Poster Session I (Room 349)

Dudek, K. E., Hua, A., Westlake, K.

A heightened fear of falling has been linked to a greater risk of actual falls, making it essential to explore how anxiety-related factors influence balance recovery following unexpected disturbances. Reactive balance control typically involves swift, coordinated movements of both the arms and legs. When individuals experience threat-related anxiety, this can alter balance responses—often leading to increased co-contraction of opposing leg muscles, more pronounced arm movements, and earlier, stronger muscle activation in both upper and lower limbs. Despite these known effects, the specific impact of anxiety on coordination between arm and leg muscles during reactive balance remains unclear. In this study, ten participants were immersed in a virtual environment that simulated either a stable ground-level scenario or a high-elevation scenario. They were then subjected to several slip-like perturbations. Anxiety levels, assessed

using the Subjective Units of Distress Scale (SUDS), were significantly higher in the height condition compared to ground level (46.6±18.8 vs. 31.1±16.6, p=0.004), indicating successful induction of anxiety. Notably, threat-related anxiety influenced intermuscular coherence (IMC) between shoulder and leg muscles. Under the elevated condition, gamma-band IMC between the deltoid muscles and the rectus femoris (RF) of the stance leg rose by 91% (p=0.01), while coherence between the deltoids and the tibialis anterior (TA) on the same side increased by 72% (p=0.04). These results help facilitate understanding of the neural mechanisms contributing to upper- and lower-limb coordination among older adults with fear of falling and balance deficits.

73. Kinetic Adaptations of The Intact Limb of Bone Anchored Unilateral Transfemoral Amputees Using Microprocessor Knees Across Different Terrains

Chioma Ezeajughi

Poster Session I (Room 349)

Ezeajughi, C.M., Desai, G.A., Fakhar, M., Shim, J.K.

Advancements in prosthesis, such as microprocessor knees (MPKs) and bone-anchored prosthesis (BAP), have improved the walking abilities of unilateral above-knee amputees. For instance, BAP users with MPKs demonstrated improved hip extension and knee flexion moments when walking on hard floors. However, the effects of varying terrains on the intact limb kinetics of BAP users using MPKs remain unknown. PURPOSE. To investigate the impact of walking on grass and carpet compared to hard floors on the intact limb kinetics of BAP users using MPKs. HYPOTHESIS. The intact joint moments and powers will be higher on hard floors compared to grass and carpet due to the rigidity of the hard floor, which could result in higher external or ground reaction forces (GRF). METHOD. Five BAP users (mean age: 53 ± 7.03 yrs, height: 1.73 ± 0.14 m, body mass: 66.5 ± 22.9 kg) were recruited. Participants walked at self-selected speeds (~1 m/s) on grass, carpet, and hard floors along a 15m level walkway. GRF (Kistler; 1000 Hz) and motion capture data (Vicon; 200 Hz) were recorded. Inverse dynamics (Visual 3D) was used to calculate joint moments and powers. A non-parametric one-way ANOVA with Mann-Whitney U test was used for statistics. RESULTS & DISCUSSION. Significant terrain differences were observed. The mean of hard floors showed the highest hip and knee moments and knee power, while grass produced higher hip power and ankle moments. Ankle power showed no significant differences across terrains. These findings suggest that terrain influences intact limb loading, which could impact joint health.

74. Exploring How Nursing Adjunct Faculty Develop Self-Efficacy in Teaching Leadership: A Case Study

Suzanna Fitzpatrick

Poster Session I (Room 349)

Fitzpatrick, Suzanna, S

This qualitative case study explores how nursing adjunct faculty develop self-efficacy in teaching leadership at West University. Despite strong clinical expertise, nursing adjunct faculty often face significant challenges in developing teaching competence due to limited pedagogical preparation, minimal orientation, unclear role expectations, insufficient mentoring, and limited access to professional

development opportunities compared to full-time faculty. Grounded in Bandura's social cognitive theory, which emphasizes the triadic interaction between behavior, personal factors, and environment, this study examines the unique experiences of nursing adjunct faculty who have taught leadership courses to DNP students between 2020 and 2024. The research employs purposeful sampling of 10-15 nursing adjunct faculty, collecting data through in-depth interviews and focus groups. Analysis will be conducted using Dedoose software with multiple coding cycles, ensuring trustworthiness through member checking, peer debriefing, pattern matching, rich descriptions, consistent procedures, and reflexivity. This study addresses a significant gap in the literature regarding how nursing adjunct faculty develop self-efficacy in teaching leadership, with important implications for addressing the nursing faculty shortage. Findings will contribute empirical data on adjunct faculty self-efficacy development, extend social cognitive theory in the nursing education context, and inform the design of more effective professional development programs and support systems for nursing adjunct faculty.

75. Investigating the Mechanism of Action and Evaluating ZZW115 as a Novel Compound for Acute Myeloid Leukemia (AML) Treatment

Ye Jun Kim

Poster Session I (Room 349)

Kim, Y., Eberly, C.L., Smith, M., Kim, M., Hatchet, T., Civin, C.I.

Acute myeloid leukemia (AML) remains a challenging hematological malignancy with only a 30% 5-year survival rate and high rates of relapse. This emphasizes the urgent need for novel antileukemic drugs with improved efficacy and decreased toxicity. The NUPR1 inhibitor, ZZW115, exhibited activity against cancer cell lines of many different lineages, including acute lymphoblastic and myeloid leukemias, suggesting its potential as a novel antileukemic compound. We have found that ZZW115 inhibited the proliferation/survival, metabolic activity, clonogenicity, and induced cell death of AML cell lines in vitro at low uM concentrations. At equal and higher concentrations, ZZW115 spared the proliferation/survival and generation of erythroid and granulocytic/monocytic colonies by normal primary human CD34+ hematopoietic stem-progenitor cells (HSPCs). Surprisingly, ZZW115 exhibited activity against AML cell lines expressing minimal amounts of NUPR1, and NUPR1 knockout (KO) and overexpressing (OE) AML cell lines did not have altered sensitivity to ZZW115. This suggested that ZZW115's antileukemic mechanism of action (MOA) may be independent of NUPR1 expression in AML. Ongoing RNAseq analyses of ZZW115-treated AML cell lines will identify additional candidate genes potentially involved in its antileukemic MOA. Future genetic gain-of-function and loss-of-function studies will assess the necessity/sufficiency of candidate molecules for ZZW115-mediated AML cell death. Defining its antileukemic MOA may unveil additional targets for AML drug discovery and identify current AML drugs that may form highly synergistic combination regimens with ZZW115. Ultimately, ZZW115's favorable therapeutic window between AML cell lines and their normal cells-of-origin demonstrates its potential as a novel drug candidate for AML therapeutic development.

76. A Real-World Analysis of Patient Cost Burden from COPD and its Treatment Regimens

Hyung Seok John Kim

Poster Session I (Room 349)

Kim, J., Miller, B., Luttmann, M., Poudel, N., Oh, J., Slejko, J.F.

While the system-level burden of chronic obstructive pulmonary disease (COPD) has been well characterized, more limited data are available surrounding its economic impact on patients. We identified newly diagnosed COPD patients aged ≥ 35 years using 2016-2022 data from a 25% random sample of IQVIA PharMetrics® Plus for Academics. Patients were grouped into six maintenance therapy regimens using the earliest 90-day episode of use following diagnosis. All-cause and COPD-specific OOP costs were calculated over the first year following diagnosis and following treatment initiation. Costs were adjusted to mid-year 2024 USD using the medical component of the Consumer Price Index. Of 11,138 newly diagnosed COPD patients, 2,848 initiated long-term therapy. Patients paid on average $620 for COPD-related expenses in the year following diagnosis, which made up 17% of total annual spendings. Across all service settings, the emergency department had the highest proportion of COPD-specific costs, which accounted for 56% of all ED-related expenses. There were significant differences in OOP costs across therapy regimens. LABA+ICS was the most frequently utilized regimen with the highest all-cause OOP costs ($4,308) and statistically significantly higher outpatient costs than other categories ($1,744, $p<0.01$). For COPD-specific OOP costs, LABA+ICS remained among one of the costliest treatment strategies alongside triple therapy at $821 and $875. Although current guidelines do not recommend the use of LABA+ICS, it was the most utilized and among the costliest regimens from the patient's perspective. Aligning treatment decisions with updated guidelines may improve outcomes while also resulting in better cost offsets for patients.

77. Factors Affecting Shared Decision-Making in Maternity Care

Crystal Trent Paultre

Poster Session I (Room 349)

Trent Paultre, C., Breman, R.

Background: In 2022, over 800 maternal deaths occurred in the US. More than 80% of maternal deaths are preventable, and persistent racial disparities exist. Shared decision-making, which is a process of communication in which clinicians and patients work together to make informed healthcare decisions, is thought to be part of the solution to poor maternal health outcomes. The CHOICEs-22 measure is a tool for measuring shared decision-making in maternity care. Purpose: The objectives of this analysis are to: (a) examine how socioeconomic factors such as health insurance, income, and education impact shared decision-making in maternity care; and (b) explore if race moderates the relationship between socioeconomic factors and shared decision-making. Methods: Using data from a cross-sectional online survey completed by participants across the United States, we used the general linear model to test associations between income, education, health insurance, and shared decision-making using ten covariates relevant to demographics, pregnancy, and birth. Results: Lower education level was associated with slightly higher shared decision-making scores. Income and insurance

were not associated with shared decision-making scores. There was no statistically significant relationship between socioeconomic variables and shared decision-making scores when accounting for race. Doula support, childbirth class attendance, and midwifery care were significantly associated with shared decision-making. Conclusion: Socioeconomic influences are an important factor in maternal health, and holistic interventions such as doula support, childbirth education classes, and midwifery care can improve shared decision-making.

78. Development of an attenuated S. flexneri 3a Shigella-ETEC Vaccine Strain Expressing ETEC Colonization Factor CS1

Viktoria Van Nederveen

Poster Session I (Room 349)

Van Nederveen, V.A., Wu, T., Grassel, C.L., Broussard, M., Brethour, B., and Barry, E. M.

Both Shigella and enterotoxigenic E. coli (ETEC) are major causes of diarrhea in children under five years of age in low- and middle-income countries. A vaccine that provided protection against both pathogens would have high value in target populations. Since multiple serotypes of Shigella exist as well as multiple ETEC colonization factor antigens, a broadly protective vaccine will need to be multivalent with a selection of the most common serotypes and antigens. Our long-term strategy for a combined vaccine is to genetically engineer attenuated strains of the most prevalent Shigella strains, that each express critical ETEC antigens. This project focuses on developing and characterizing one important component of this vaccine, attenuated S. flexneri 3a expressing ETEC colonization factor CS1. The operon encoding CS1, driven by a constitutive promoter, was inserted in the chromosome of attenuated S. flexneri 3a. Expression of CS1 was validated using Western blots and agglutination assays with anti-CS1 serum in CVD 1213::CS1. Functional cell binding assays using human intestinal cells were used to assess adhesion properties. In separate assays, the invasion and replication of CVD 1213::CS1 was compared to the wild-type (WT) S. flexneri 3a strain. The vaccine strain expressing CS1 invaded intestinal cells at equivalent levels to the WT strain but was attenuated for intracellular replication. These assays will eventually be used to evaluate protection of vaccine-induced antibodies against a geographically diverse set of recent S. flexneri and ETEC clinical isolates. We predict antibodies from vaccinated animals will block invasion and adherence of clinical isolates.

79. Prevalence of Pseudomonas aeruginosa Lipid A Acyl Chain Variation and its Implications in TLR4/MD-2 Signaling

Ian O'Keefe

Poster Session I (Room 349)

O'Keefe, I.P., Hofstaedter,C.E., Met, C.M., Wu, L., Vanderwoude, J., Shin, S., Diggle, S.P., Riquelme, S.A., Rasko, D.A., Doi, Y., Harro, J.M., Ernst, R.K.

Pseudomonas aeruginosa (Pa) is a gram-negative bacterium that causes chronic lung infections in people with Cystic Fibrosis (CF). To establish chronic pulmonary infection, Pa undergoes numerous adaptations to host-specific airway pressures. One such adaptation is structural modifications to its lipid A, the membrane-embedded anchor of lipopolysaccharide. Lipid A is a potent agonist of the toll-like receptor (TLR)4/myeloid differentiation factor (MD)-2 complex, and the structure of lipid A affects the strength of

TLR4/MD-2 signaling and the resulting proinflammatory response. Prior work has identified Pa strains with genetic mutations in lipid A acyl chain modifying enzymes that arise during chronic CF lung infection. However, the phenotypic prevalence and innate immune signaling of these lipid A structures is not well understood in CF isolates. Here, we we have performed MALDI-TOF mass spectrometry to characterize the lipid A structural variation in a cohort of 90 CF isolate Pa strains collected longitudinally from 10 people with CF. Several of these isolates exhibit lipid A structures characterized by a lack of lipid A hydroxylation mediated by the enzymes LpxO1 and LpxO2, as well as lipid A 3OH deacylation mediated by the PagL enzyme. To determine differences in TLR4/MD-2 signaling based on lipid A acyl chain variation, we purified LPS from CF-isolate Pa and assessed its immunostimulatory properties in vitro using NF-kB reporter cells. Uncovering the structural prevalence and immune signaling properties of these CF-specific lipid A structures will lead to a better understanding of the effects of lipid A variation on host morbidity and mortality.

80. Role of STRADA in cortical interneuron migration

Ria Parikh

Poster Session I (Room 349)

Parikh, R.K., Hijazi, A, Sbornova, I., Nguyen, T., Crino, P.B., Parker, W.E.

Polyhydramnios, Megalencephaly, and Symptomatic Epilepsy (PMSE) syndrome, is a rare neurodevelopmental disorder characterized by an autosomal recessive deletion of exons 9-13 of the LYK5/STRADA gene, encoding the STRADA protein. STRADA is a psuedokinase that recruits liver kinase B1 (LKB1) from the nucleus to the cytoplasm and allows it to phosphorylate AMPK, ultimately leading in the inhibition of mTOR, the mechanistic target of Rapamycin. Our group observed paucity in GAD-67 expression in the cortex of a PMSE patient brain compared to control, leading to a hypothesis that STADA loss impairs the migration of GABAergic interneurons to cortex during development. Here, we are testing this hypothesis using a germline knockout mouse and immunohistochemistry to label interneuron progenitors and subtypes in the somatosensory cortex to evaluate the role of STRADA in the migration and lamination of cortical interneurons. This work will would allow us to broaden our understanding of the consequences of STRADA loss, and aid in the development of treatments for PMSE and other neurodevelopmental disorders.

81. Branched PEGylation as a Strategy to Overcome the Mucus Barrier to Aerosolized Nanomedicine

Alexa Stern

Poster Session I (Room 349)

Stern, A., Duncan, G.

Delivery of aerosolized therapeutics to the lungs is severely limited by the mucus barrier. Nanoparticles often get trapped in the mucus mesh and cleared from the airways before they can render therapeutic benefit. To address this, nanoparticles can be coated with polyethylene glycol (PEG) to enhance their penetration through the mucus barrier. While linear PEG is conventional, we have recently investigated how PEG structure and branching impacts nanoparticle mobility through the extracellular matrix. We now turn our focus to the effect of PEG branching on aerosolized nanoparticle

delivery. For these studies, we cultured bronchial epithelial cells (BCis) at air liquid interface (ALI) and after fully differentiating, we collected mucus and analyzed nanoparticle mobility using particle tracking. We found that 10 kDa branched PEG coatings enable more efficient nanoparticle mobility in airway mucus as compared to linear PEG types. Building upon these findings, we are investigating how PEG type impacts aerosolized nanoparticle uptake in an in vitro airway model. For these ongoing studies, we are using a VITROCELL in vitro exposure system to aerosolize nanoparticles coated with PEG of varied structure for delivery in fully differentiated ALI cultures. Future studies will evaluate in vivo biodistribution of branched PEGylated nanoparticles delivered locally to the lung.

82. Resin Coating with Antibacterial and Remineralization Properties to Combat Root-Caries

Nader Almutairi

Poster Session J (Room 349)

Almutairi, N., Alhussein, A., Alenizy, M., Ba-Armah, I., Alqarni, H., Oates, T.W., Masri, R., Hack, G.D., Sun, J., Weir, M.D., Xu, H.H.K.

Tooth root caries account for 10.1% of all dental caries in the USA. This study developed a multifunctional resin coating with calcium (Ca) and phosphate (P) ion release and antibacterial properties to combat root caries. The effects of nano-sized amorphous calcium phosphate (NACP) and dimethylaminohexadecyl methacrylate (DMAHDM) on mechanical, physical, and antibacterial properties against Streptococcus mutans, and cytotoxicity on dental pulp stem cells and gingival fibroblasts were evaluated. A coating resin combining urethane dimethacrylate (UDMA), triethylene glycol divinylbenzyl ether (TEGDVBE), DMAHDM, and NACP was synthesized and compared with Seal&Protect and Vanish XT. Experimental groups (UV + 5% DMAHDM + 10%, 15%, and 20% NACP) showed flexural strength (70.9 ± 8.0 to 81.1 ± 6.0) MPa, significantly higher than Seal&Protect (48.2 ± 7.2) MPa ($p < 0.05$) and comparable to Vanish XT (70.2 ± 13.6) MPa, ($p > 0.05$). Elastic modulus (2.2 to 3.3) GPa was lower than Vanish XT (9.4 ± 1.1) GPa ($p < 0.05$). Experimental groups showed an 8 log CFU reduction, 96% reduction in metabolic activity and 87% in lactic acid production, and increased Ca (1.25 ± 0.03) mmol/L and P (0.8 ± 0.001) mmol/L release over 35 days. Cytotoxicity for experimental groups against dental pulp stem cells and human gingival fibroblast was low and matched those of commercial controls already used in clinic. The resin demonstrated potent antibacterial properties, high ion release, low cytotoxicity, and maintained physical and mechanical integrity, offering potential to prevent root caries formation and progression.

83. Understanding Terpenes: Evaluating Consumer Knowledge in Cannabis Flower Inhalation Method

Laportia Sherrill

Poster Session J (Room 349)

Sherrill, L., Gray, S.

The blooming cannabis industry has led to consumers increasingly seeking cannabis for recreational and medicinal use. This causes for the understanding of cannabis' chemical components to be essential. This study targeted adult cannabis flower inhalation consumers across the Midwest to the East Coast of the USA, assessing their knowledge of terpenes—aromatic compounds that significantly

influence the therapeutic effects of cannabis. A questionnaire revealed that over 75% of participants lacked a fundamental understanding of terpenes and their impact on cannabis experiences. Terpenes play a crucial role in determining the therapeutic effects of individual strains. Our findings indicate that 65% of consumers reported purchasing products that did not meet their desired effects. Importantly, 85% of respondents expressed a strong interest in personalized terpene assessments, recognizing that understanding their unique terpene profiles could enhance their selection and purchasing experience. By implementing standardized terpene diagnostic assessments, consumers could identify their personalized terpene palette. Notably, 90.9% of respondents expressed a desire to learn more about terpenes, with most indicating interest in consultations. Data suggests that consumers who understand their terpene preferences experience a 50% increase in achieving desired effects from their cannabis products. Additionally, 70% of participants stated that clearer labeling and educational resources on terpenes would greatly influence their purchasing decisions. In conclusion, this study emphasizes the necessity for increased terpene education and the implementation of standardized personalized diagnostic assessments for cannabis consumers. Closing these knowledge gaps is vital for empowering consumers, optimizing their cannabis experiences; ultimately benefiting consumer health and overall well-being.

84. Electromyographic Changes in Lower-Limb Tendinopathies: A Systematic Review

Stephen Eaton

Poster Session J (Room 349)

Eaton, S., Gray, V., Zarro, M.

Background: Lower limb tendinopathies are a group of conditions that cause considerable burdens to both highly active and sedentary individuals, including pain, impaired function, and reduced activity participation. Electromyography (EMG) is a tool that has been used in previous studies to elucidate changes in the neuromuscular system that accompany tendinopathy, but to date no review of the literature has been performed. The goal of this systematic review is to synthesize the available evidence for changes in EMG activity in subjects with tendinopathies of the lower limb. Methods: A systematic search of CINAHL, Scopus, PubMed, and Embase was performed to include studies that had at least one EMG outcome and compared patients with tendinopathy to a control group. Studies were excluded if they had confounders such as surgery, neuromuscular disease, or chronic medical conditions. Results: A total of 20 cross-sectional studies were included, 16 in achilles tendinopathy (AT), 2 in gluteal tendinopathy (GT), 1 in flexor hallucis longus tendinopathy (FHLT), and 2 in patellar tendinopathy (PT). Outcomes were heterogeneous and highly task and muscle dependent. No consistent pattern was found across all lower limb tendinopathies, with each exhibiting distinct changes ranging from overall underactivity or overactivity to increased or decreased variability. Conclusion: AT is associated with increased and delayed soleus activation, decreased and delayed gluteal muscle activation, and task-specific changes in tibialis anterior activation. GT is associated with increased gluteal muscle activation and reduced EMG variability. There is a lack of robust evidence to draw strong conclusions in FHLT or PT.

85. Effects of Stroke on Turning Movement: Systematic Review

Mohand Altemani

Poster Session J (Room 349)

Altemani, M.A., Lateef, S., Fu, Y., Gray, V.L.

Background: Turning movements have a crucial role in our daily activity, constituting about 40% of the steps we take. Unfortunately, stroke survivors frequently experience difficulties with turning due to various motor, balance, and cognitive impairments. Objective: This systematic review aimed to identify the predominant impairments associated with turning after a stroke and to highlight existing research gaps in turning performance. Methods: We conducted a systematic review using the PRISMA guidelines, searching four databases (PubMed, CINAHL, Scopus, and Embase) for relevant literature. A total of 30 studies met the inclusion criteria: observational studies involving adult chronic stroke survivors (≥18 years) with hemiparesis that assessed turning performance using clinical evaluations or instrumented methods. Exclusion criteria: no comparative group, studies with mixed populations, and intervention studies. Results: Key findings show that individuals post-stroke exhibit significant turning impairments. In comparison to healthy controls, individuals post-stroke take longer to complete a turn and require more steps. They also displayed reduced postural stability during turning and impaired trunk and segmental coordination. However, across the stroke population, there was no clear preference for turning to the paretic side versus the non-paretic side. In addition, many individuals demonstrated reduced automaticity of movement and reported an increased fear of falling throughout a turn. Conclusion: Turning is not a minor component of gait and is a critical aspect of post-stroke mobility and should be a focus in rehabilitation to improve functional independence and enhance participation in the community.

86. Investigating the Role of Allergic Asthma in Viral Respiratory Infections in Mice

Grace Garrett

Poster Session J (Room 349)

Garrett, G.B., Ardanuy, J., Sun, W., Keegan, A.D., Frieman, M.B.

In most viral respiratory infections (e.g. influenza, rhinovirus), asthma is a risk factor for developing serious complications. Surprisingly, asthmatic patients are not over-represented in severe COVID-19 cases, and asthma may even protect individuals from severe COVID-19. We aim to understand the mechanism by which allergic asthma results in drastically different outcomes during respiratory infection with different viruses. We have established a house dust mite induced allergic asthma model in Balb/c mice. These asthmatic mice, along with control non-asthmatic mice, were challenged separately with SARS-CoV-2 and influenza A virus (IAV). In the SARS-CoV-2 challenge, the asthmatic mice had reduced weight loss and mortality, while in the IAV challenge, the asthmatic mice had increased weight loss and mortality, as compared to control mice. There was no significant difference in viral lung titer in the IAV challenge, but significant reduction in titer in the SARS-CoV-2-infected asthmatic mice. To begin to understand the mechanism behind this difference, we quantified mucin levels in the lungs via IHC and lung eosinophil levels via flow cytometry. In the SARS-CoV-2 experiment, we found that the levels of MUC5AC and MUC5B in the lungs were increased in the asthmatic mice before and after infection compared to controls. We also found

that lung eosinophils were increased in the asthmatic mice before and after infection compared to controls. Our future experiments will utilize knockout mouse models in order to determine which factors within the allergic asthma milieu are responsible for the differential outcomes in mice upon SARS-CoV-2 versus IAV infection.

87. CasMINI toolkit for cell-type specific and light-inducible epigenome editing applications

Mikah Green

Poster Session J (Room 349)

Green, M., Hajirnis, Ganapathy, S., N., Choi, E., Chandra, R., Lobo, M.

CRISPR epigenome editing, using CRISPRa or CRISPRi allows for more physiologically relevant manipulation of gene expression. Recent advances have paved the way for using a Cas12f derived system (dCasMINI) instead of Cas9. The main advantage of dCasMINI is that dCasMINI is less than half the size of dCas9 allowing for packaging in adeno-associated viruses. For CRISPRi KRAB is fused to dCasMINI, and for CRISPRa VP64 is fused to dCasMINI. These constructs are paired with a gRNA construct targeting hub genes. These hub genes were found to be upregulated or downregulated in significant gene network modules of mouse brain neuron subtypes following forced abstinence from fentanyl. We have validated dCasMINI expression in neuronal cells at the mRNA and protein level for the first time. We have also shown that both the dCasMINI-KRAB & dCasMINI-VP64 constructs paired with gRNA can successfully downregulate or upregulate targeted gene expression levels. We also developed a light-inducible Opto-dCasMINI system for temporal-specific control of gene expression. For this, dCasMINI is fused to CIBN and KRAB or VP64 are fused to Cry2. Prior to light stimulation, the gRNA construct recruits dCasMINI-CIBN to the target-gene locus. Upon light stimulation CIBN & Cry2 fuse, recruiting transcriptional regulator (VP64 or KRAB) to the target gene. We have successfully manipulated expression of target genes in-vitro using these tools. The potential to use these tools to alter transcription of specific genes in a cell type-specific manner in the brain will allow routine use of AAV CRISPR epigenome editing tools in-vivo.

88. Hormone-Based Maturation Enhances Pharmacological Responses of IPSC-derived Cardiomyocytes

Emma Gudmundsson

Poster Session J (Room 349)

Gudmundsson E., Vieira D., Hussey J., Lee A., Owoyemi J., Fadiran O., DiSilvestre D., Dick I.

Induced pluripotent stem cell derived cardiomyocytes (iPSC-CMs) are a robust and widely used tool for studying heart function and disease. However, iPSC-CMs exhibit an immature electrophysiological profile when compared to adult human cardiomyocytes. Additionally, they have a reduced response to certain drugs, including calcium channel blockers. Previous research has shown that treating cells with the hormones triiodothyronine (T3) and dexamethasone (Dex) (TD) during the second half of differentiation increases the maturity of iPSC-CMs. This study examined how the use of TD affects the electrophysiological properties and drug response of iPSC-CMs. We found that using TD lengthens the action potential, indicating increased cell maturation. Additionally, TD treatment improves iPSC-CMs

response to the calcium channel blockers verapamil and nifedipine. Overall, TD treatment promotes more mature electrophysiological and pharmacological properties, making them a more reliable and relevant model for drug testing and disease modeling.

89. Exploring the role of protocadherin-15 in the murine retina

Mary Hackbarth

Poster Session J (Room 349)

Hackbarth, M.E., Riazuddin S., Ahmed, Z.M.

Usher syndrome type 1 (USH1) is a rare neurosensory disorder characterized by prelingual hearing loss, vestibular deficits, and retinitis pigmentosa. Biallelic pathogenic variants in PCDH15, encoding the atypical cadherin protocadherin-15, are responsible for USH type 1F. Within the retina, protocadherin-15's role is not well characterized, and there are no treatment options available to halt or reverse the associated progressive vision loss. Previously, our lab has demonstrated that the PCDH15R245X mouse model exhibits light sensation issues and impaired visual cycle enzymes levels, indicating functional deficits in multiple retinal compartments. In this study, we seek to inspect the functional role of protocadherin-15 in a cell-type specific manner within the mouse retina. Utilizing the cre-lox conditional knockout technique, we generated three mouse strains, with Pcdh15 disruption driven by promoters specific to retinal pigment epithelium (Pcdh15-RPE), rod photoreceptors (Pcdh15-PR), or ubiquitous knockout (Pcdh15-CMV). These mutant strains are being evaluated for visual function measured via electroretinography and optokinetic response to light stimuli. Optical coherence tomography, immunohistology, and biochemical analysis are underway to examine the structural integrity of the retina and expression of key visual proteins. Preliminary data from Pcdh15-RPE animals indicate no significant visual deficits, which suggest either functional redundancy or no essential role for protocadherin-15 in the RPE. Taken together with findings from PCDH15R245X mice, these results indicate that protocadherin-15 likely regulates visual cycle components through its expression in photoreceptors. Ongoing work will help elucidate the effects of Pcdh15 loss in the intricate interactions between photoreceptors and RPE necessary for retinal homeostasis and function.

90. The Impact of Peer Mentorship on the Academic Experience of Graduate Health Professions Education (HPE) Students

Josline Ali-Napo Dibonge

Poster Session J (Room 349)

Ali-Napo Dibonge, J. B.

Existing literature has identified a variety of challenges within health professions training including burnout, anxiety and complexity of acquiring clinical competencies. In response to these challenges, mentorship has been studied as a feasible and cost-effective method to improve the academic experiences of students in various health professions, however, there is little evidence on peer mentorship and the impact it has on student's perceived clinical competence within the scope of their unique discipline. This literature review aims to explore the impact of peer mentorship on graduate level health professions students' academic experience. A total of 15 published articles were included for this review. The studies selected reflect a discussion of outcomes related to

formal and informal peer mentoring. The analysis yielded support for peer mentorship as a tool to improve academic achievement and clinical competence, provide emotional and social support and enhance professional development. All the studies included in this literature review provide evidence that participation in a peer mentorship relationship was associated with positive outcomes for students in both academic and clinical settings. The major themes that emerged include mentorship as a tool to support academic achievement and the development of domain specific competencies, promote mental health and socialization needs and assist in transition from student to skillful and competent professional. Given the consistency of positive outcomes, it would be a practical implication for educators to incorporate peer mentorship as a cost-effective component of health professions education programs and curriculum to enhance the learning experience for both mentors and mentees.

91. Perceived Discrimination, Social Media, Financial Socialization, and Substance Use: Impacts on BIPOC Emerging Adults' Well-Being

Hilary Phillips

Poster Session J (Room 349)

Phillips, H.

Emerging adulthood (ages 18–25) is a critical phase characterized by financial instability, heightened mental health challenges, and increased exposure to systemic inequities. This study examines how financial socialization, everyday discrimination, social media use, and substance use collectively influence financial well-being and psychological distress among BIPOC (Black, Indigenous, and People of Color) emerging adults. Using survey data from 514 participants, we assess the role of parental financial socialization, perceived discrimination, social media engagement, and substance use in shaping financial resilience and mental health outcomes. Key findings indicate that higher levels of parental financial socialization correlate with lower financial well-being, suggesting complex financial transmission dynamics. Additionally, discrimination is strongly associated with substance use, highlighting the potential coping mechanisms employed by marginalized groups. Regression models demonstrate that discrimination and substance use predict higher psychological distress, whereas experiential financial learning acts as a protective factor, reducing distress levels. Social media use did not significantly predict psychological distress, though engagement patterns varied across demographic groups. The financial model explains 15% of the variance in financial well-being. In comparison, the psychological distress model accounts for 25.9% of variance, reinforcing the critical role of systemic inequalities in shaping financial and mental health outcomes. Findings underscore the need for culturally tailored financial education and intervention strategies to mitigate financial insecurity and psychological distress among BIPOC youth. Addressing discrimination through economic empowerment initiatives may enhance resilience and foster improved financial well-being within these communities.

92. The Role of Angiopoietin-Like 4 in Head and Neck Squamous Cell Carcinoma Resistance to Cisplatin

Emmanuel Asiedu

Oral Session K (Elm Ballroom)

Asiedu, E., Kumar, A., Luciano, D., Lo, K., Sharma, D., Ma, T., Rassool, F., Sodhi, A., Montaner, S.

Drug chemoresistance is the major reason for treatment failure in cancer patients. In many neoplasias, including those with robust initial responses, cancer cells eventually acquire the capacity to evade drug cytotoxicity, compromising patient survival. In head and neck squamous cell carcinoma (HNSCC), cisplatin-based chemotherapy remains the gold standard for advanced stage tumors but often faces the drawback of resistance. We have previously shown that angiopoietin-like 4 (ANGPTL4) is a molecular biomarker of both oral dysplasia and HNSCC. We also found that ANGPTL4, through interaction with NRP1, activates migratory and proliferative autocrine and paracrine signals that contribute to HNSCC development. This study investigated the role of ANGPTL4 in HNSCC resistance to cisplatin and elucidated the molecular mechanism underlying the observed effect. Using HNSCC patient tumor derived organoids (PTDOs), (3D) in vitro tumor spheroids and (2D) cell cultures of HNSCC cell lines, CAL27, HN13 and HN4, here we provide evidence of the role of this pluripotent protein in the development of platinum-based chemoresistance in HNSCC, through the promotion of DNA damage response (DDR) and homologous recombination (HR). ANGPTL4 enhanced these mechanisms by promoting the phosphorylation of RAD51 recombinase in Tyr54 through an NRP1/ABL1-dependent mechanism. Indeed, pharmacologic inhibition of NRP1 or ABL1 reversed ANGPTL4-mediated DDR and HR, and increased HNSCC cell death in combination with cisplatin, in vitro and in vivo. Our results suggest that the ANGPTL4/NRP1/ABL1 is a critical pathway in cisplatin-induced DDR and HR and point to this signaling route as a novel therapeutic alternative target for advanced stage HNSCC.

93. Short-term Pharmacodynamic Effects of Canagliflozin in Healthy Amish Volunteers

Salma Bargal

Oral Session K (Elm Ballroom)

Bargal, S. A., Montasser, M. E., Streeten, E. A., Whitlatch, H. B., O'Connell, J. R., Yazdi, Z. S., Taylor, S. I., Beitelshees, A. L.

BACKGROUND: Canagliflozin is a sodium-glucose cotransporter-2 inhibitor (SGLT2-I), a class of antidiabetic medications that has been recently considered first choice for many patients with type 2 diabetes and comorbidities due to their cardioprotective and renoprotective effects. Nevertheless, SGLT2-Is also have serious potential side effects, including bone loss/fractures (canagliflozin), urosepsis, and ketoacidosis. Here, we report preliminary pharmacodynamic findings of the Genetics of Response to Canagliflozin (GRC) study. METHODS: We completed a short-term intervention in healthy Old Order Amish volunteers. Participants were administered canagliflozin 300 mg/day for 5 days, completed 24-hour urine collection, and had blood drawn at baseline, day 3, and day 6. Primary endpoint: glucosuria. Secondary endpoints: additional biomarkers for efficacy and safety related to bone, cardiovascular disease, and ketosis. RESULTS: 403 participants completed the study. Canagliflozin induced average glucosuria of 34±10 ggluc/gcr (ranged from 12.4-86.2, ~7-fold variation) with heritability of 31% (p=1.68e-02). The baseline characteristic most strongly associated with glucosuria was eGFR (effect size=2.93e-01, p=3.03e-11). Upon dividing eGFR into tertiles, four-to-seven-fold

variability in glucosuria remained within each tertile. Canagliflozin induced clinically significant changes in bone mineral biomarkers that confirmed known interrelationships, which negatively impact bone health: phosphate increase(day3:+5.0%, p=1.39e-20), which triggers fibroblast growth factor-23 increase(day3:+20.3%, p=4.51e-15), which in turn decreases 1,25-dihydroxyvitamin D(day3: -25.0%, p=2.29e-78), which increases parathyroid hormone(day3:+23.0%, p=8.67e-30). Other confirmatory results: decrease in serum uric acid(day6: -33.2%, p=1.72e-201) and increase in beta-hydroxybutyrate(day3:+71.8%, p=2.57e-22). CONCLUSION: GRC study offers opportunity to identify genetic predictors of safety and efficacy biomarkers for SGLT2-I response that could help guide future diabetes treatment decisions.

94. Polymer Nanoparticle-Induced Modulation of Macrophage Metabolism for Obesity Treatment

Andrea Cottingham

Oral Session K (Elm Ballroom)

Cottingham, A.L., Mohaghegh, N., Dharmaraj, S., Shaw, J.R., Andrade, V., Xu, F., Shu, Y., Najafabadi, A.H., Pearson, R.M.

Obesity is a growing global health concern, driven by chronic low-grade inflammation and metabolic dysregulation. Macrophages regulate adipose tissue metabolism, shifting between pro-inflammatory (M1) and anti-inflammatory (M2) states. In obesity, M1 macrophages drive chronic inflammation, impair insulin signaling, and disrupt adipocyte function, promoting metabolic dysfunction. Conversely, M2 macrophages support tissue repair and induce adipose beiging, enhancing energy expenditure and improving metabolic health. Here we developed an itaconate-based polymer nanoparticle therapy to reprogram macrophage metabolism, shifting them from an M1 to M2 state. The polymer was synthesized with variations in chain length and molecular weight, and its effects were tested in steady state macrophages (M0), M1, and M2 macrophages, using CD206 expression as a biomarker for phenotypic switching. Nanoparticle uptake and concentration studies furthered NP optimization for downstream studies. To assess the therapeutic potential of our treatment, a high-fat diet-induced obesity model was employed. We found that our nanoparticle reduced systemic inflammation, upregulated beige fat-associated genes, and improved metabolic outcomes, accompanying weigh loss. This nanoparticle-based approach offers a novel strategy for targeting obesity-related inflammation and restoring metabolic balance through macrophage modulation.

95. Cargo-less Itaconate-Based Nanoparticles for Immunometabolic Modulation in Allergic Airway Inflammation

Shruti Dharmaraj

Oral Session K (Elm Ballroom)

Dharmaraj, S, Cottingham, A.L., Chapoval, S., Keegan, A., Pearson, R.

Allergic diseases affect over 50 million annually in the U.S., with standard treatments being non-curative. Allergy-related pathology is characterized by the production of Th2 cytokines, including IL-4, IL-5, and IL-13, which drive IgE synthesis, and eosinophil activation. Allergen-specific immunotherapies represent an antigen (Ag)-specific approach to modulate Th2 dysregulation in allergy, but chronic administration of soluble Ag risks anaphylaxis. Activation of Ag presenting cells by foreign Ags

induces metabolic shifts disrupting the tricarboxylic acid (TCA) cycle. Specifically, Irg1, a gene encoding for cis-aconitate decarboxylase, is upregulated and catalyzes production of the immunomodulatory metabolite itaconate. Nanoparticles (NPs) can deliver bioactive substances, enabling local retention, and controlled release properties but effective delivery may require higher doses and frequent administration formulation issues. To address this, our lab developed biodegradable, cargo-less itaconate-based NPs for sustained release to target metabolic dysregulation in allergy. Previously, these formulations demonstrated an ability to induce an anti-inflammatory, M2- like phenotype in bone marrow derived macrophages stimulated with lipopolysaccharide. Intratracheal delivery abrogated Th2 cytokines and total IgE in a therapeutic OVA-induced allergic airway inflammation model. Further analysis of cells in the alveolar spaces, indicated a marked reduction in macrophage and eosinophil infiltration. Furthermore, CD11b+Ly6G+Ly6Clo cells were significantly increased in the lung after NP treatment, which was not observed for 4-octyl itaconate, a cell permeable surrogate of itaconate. These results demonstrate metabolite-based NPs ability to modulate Th2 disease by targeting dysregulated metabolism in allergy.

96. KaML for pKa prediction

Mingzhe Shen

Oral Session K (Elm Ballroom)

Shen M., Dayhoff G.W., Kortzak D., Shen J.

Accurate prediction of protein ionization states is critical for understanding biological functions and facilitating drug discovery; however, it remains challenging for both physics-based methods and machine learning (ML) models. Here, we present KaML, a state-of-the-art end-to-end ML pipeline for predictions of protein pKa values from sequence OR structure. The pipeline makes use of neural networks that exploit evolutionary information and gradient-boosted decision trees for structure-based predictions. Model training was enabled through a newly curated experimental pKa database (PKAD-3), which expanded significantly upon its predecessor PKAD-2. The KaML evolutionary models establish the new state of the art, with root-mean-square errors (RMSE) of Asp, Glu, His, and Lys approaching the range of experimental errors while Cys RMSE is about 1.1 pH units, which is substantially lower than the previous state of the art. We anticipate KaML tools to facilitate a wide range of applications, from drug design and protein engineering to molecular simulations.

97. Latino Pediatric Caregiver Experiences: A Scoping Review

Erika Ventura Castellon

Oral Session K (Elm Ballroom)

Ventura Castellon, E., Estrada Ibarra, E., Maldonado Herrera, C., Betz, G., Lerret, S., Mooney-Doyle, K.

Background: Over 1800 children receive transplants annually in the United States. Latino children account for approximately 24% of the pediatric solid organ transplant (PSOT) recipient population. Latino caregivers have a shared responsibility with the transplant team to provide medical and general everyday care to their child in the post-transplant phase. Caregivers play an integral role in the care of their child with a transplant. Caregivers are susceptible to experiencing higher levels of

parenting stress and psychological stress. Given this information, caregiver focused research in this population should be explored. Purpose: This review sought to identify literature surrounding Latino caregiver experiences in pediatric solid organ transplants. Methods:This review was conducted using the Arskey and O'Malley Framework. Four databases were reviewed for studies published. The inclusion criteria include Latino/a/x caregivers or parents of children who received a solid organ transplant (heart, lung, liver, intestinal, small or large bowel, kidney, or multi transplant) and caregiver outcomes documented in empirical publications: qualitative, quantitative, or mixed methods. Results: Preliminary results based on a total of 273 articles that were screened and 5 full text assessed for eligibility thus far. Discussion/Conclusion: The preliminary scoping review findings indicate that Latino caregiver or parent-specific experiences in PSOT literature are lacking. To promote the well-being of PSOT recipients and their families, efforts should also be directed at understanding their caregivers' experiences and needs in their transplant journey.

98. Optimizing Reactive Balance Training through Practice Schedule in Persons with Parkinson's Disease and Age-match Controls

Ruth Akinlosotu

Oral Session L (Room 203)

Akinlosotu R.Y., & Westlake K.P.

Two out of three persons with Parkinson's disease (PD) experience falls each year. Many of these patients are recurrent fallers due to impaired reactive balance impairments. Balance perturbation training where fall-inducing disturbances are applied unpredictably can improve reactive balance in older adults. However, persons with PD exhibit set-shifting impairments that can hinder motor skill acquisition, retention, and generalization under unpredictable practice conditions. Consequently, motor learning strategies that are effective for those without PD may not yield the same results in this population. We investigated the effects of practice schedules on the motor learning of protective stepping stability in persons with PD and age-matched controls. Methods: We randomly assigned 20 persons with PD and 20 age-matched controls to a blocked and random practice group to receive a session of fall-inducing perturbations in a blocked or random fashion while participants wore a safety harness. Additional random perturbations were administered to both groups 24 to 48 hours after the first practice session. We recorded their postural responses using motion capture systems that allowed us to quantify their responses in three dimensions and compared performance between practice groups at baseline, posttest, retention, and generalization tests. Results: Persons with PD retained protective stepping stability through blocked but not random practice after 24 to 48 hours of practice ($t=3.642$, $p=0.001$). With additional random practice, improvement persisted up to 48 to one week after practice. Conclusion: Varying the predictability of balance challenges in balance rehabilitation protocols for persons with PD may yield long-lasting improvements.

99. Spatial Transcriptomic Characterization of Proliferative Leukoplakia

Shahd Alajaji

Oral Session L (Room 203)

Alajaji, S. A.*, Wu, W.*, Yousef, N., Molloy, E. K., Nguyen, J., Sultan, A. S.

Proliferative leukoplakia (PL) is an aggressive form of oral leukoplakia characterized by high rate of malignant transformation to oral squamous cell carcinoma (OSCC) or verrucous carcinoma. It almost exclusively occurs in geriatric women (4:1 ratio to men, median age 67 years, age range up to 93 reported in the literature). The limited predictive value of histopathologic evaluation and lack of traditional environmental risk factors highlight the need to investigate the molecular landscape of PL. Herein, we use spatial transcriptomics to characterize our longitudinal cohort of paired PL cases that transformed to OSCC and those that were stable. A total of 8 oral biopsies from 5 different patients were collected. scRNA sequencing and spatial transcriptomics was performed using Visium HD (10x Genomics). Unsupervised gene clustering resulted in delineated layers of gene clusters in the oral epithelium of our PL samples. We were able to characterize significant genes at different oral epithelial layers. We also noticed sharp interruption of gene clustering at areas with host immune reaction indicating neoantigen pathogenesis. The top differentially expressed genes (DEG) between crevicular epithelium (internal control) and PL are S100A genes. Analysis at malignant transformation zone resulted in 6 DEGs (PI3, SPRR1B, S100A8, S100A9, KRT14, and KRT16). Moreover, FLG gene was consistently expressed at the top layers of stable PL cases and significantly decreased after malignant transformation indicating a tumor suppressor function and potential target therapy. Our findings offer valuable insights into the pathogenesis of PL and potential biomarkers for predicting malignant transformation and guiding therapeutic strategies.

100. Social Isolation and Depression in Community-Dwelling Older Adults

Lori Anderson

Oral Session L (Room 203)

Anderson, L.R., Chen-Edinboro, L.P., Orwig, D.L., Wagner, F.A.

Introduction: Studies show that 25% of older adults experience social isolation and approximately 28% experience depression, and both are linked to increased risk of chronic health conditions and poor health outcomes. This study examines the association between social isolation and depression in a nationally representative sample of community-dwelling older adults. Methods: Using the 2011 National Health and Aging Trends Study (NHATS), logistic regression models assessed the cross-sectional association between social isolation and depression, accounting for common sociodemographic factors and health conditions. Social isolation was measured using a previously validated measure in NHATS; depression was measured using the PHQ-2. Results: The analytic sample for this study included 6,802 participants aged 65 and older. Fully adjusted models showed mild social isolation having 24% greater odds of depression [OR=1.24 (95%CI: 1.07,1.43), p< 0.01] compared to those without social isolation. For severe social isolation, bivariate analysis showed borderline significance of 37% greater odds of depression compared to those without social isolation [OR=1.37 (95%CI: 0.99,1.89), p=0.054], and became insignificant when controlling for sociodemographic and health factors. Conclusion: Mild social isolation was associated with depression in community-dwelling older adults; severe social isolation was not. Longitudinal studies are warranted to confirm this difference between mild and severe

social isolation and their association with depression in older adults. These results remain important as an increasing number of older adults in the United States experience social isolation. These findings may help inform clinical and policy efforts to improve depressive symptoms by helping to reduce social isolation in older adults.

101. The Role of Estradiol Biosynthesis Enzyme, Aromatase, in the Aged Mouse Brain

Abagail Postle

Oral Session L (Room 203)

Postle, AF, Davis, D, Clark, SM, Georgiou, P, Gould, TD

Estrogens are traditionally considered protective factors in cognitive function, which is attributed to potentiation of excitatory synaptic transmission, increase in dendritic spine density, and anti-inflammatory properties. However, normal age-associated decline in serum estrogens in both males and females is not consistently associated with cognitive decline suggesting that serum estrogens may not be important for cognitive function. Instead, regulation of de novo biosynthesis of estrogens in the brain via the rate-limiting enzyme, aromatase, may play an important, protective role in cognition. To characterize the age-associated changes in aromatase, 3- and 23-month-old male mice underwent orchiectomy or sham surgery and recovered for nine weeks before tissue collection. Brains were processed with fluorescent in-situ hybridization, RNAscope. Images were acquired from dorsal and ventral hippocampus, ventromedial hypothalamus, basolateral amygdala, and medial amygdala. We identified an age-associated increase of aromatase in both NeuN and GFAP expressing cells in each of the brain regions studied independent of peripheral hormone status. To understand the significance of this age-associated increase in aromatase we performed electrophysiological field potential recordings of the Shaffer-collateral to CA1 synapse in the hippocampus of 3-, 6-, and 26-month-old mice and have shown no effect of aromatase inhibition on basal transmission or synaptic plasticity. These experiments will determine if de novo estrogen biosynthesis in the brain has potential therapeutic application for improving cognitive performance and mitigating cognitive decline in older adults.

102. Tau protein drives microtubule changes in aging skeletal muscle

Kaylie Pinto

Oral Session L (Room 203)

Pinto, K., Ursitti, J., Shi, G., Ward, C.

Tubulin post-translational modifications (PTMs) regulate microtubule (MT) structure and function. Our works in skeletal muscle found that MTs enriched in detyrosinated a-tubulin (deTyr-tubulin) regulate cytoskeletal mechanics, mechanotransduction, and the maintenance of the myofibrillar structure. Our further works in Duchenne muscular dystrophy (DMD) identified the proliferation of deTyr-tubulin-enriched MTs as a consequence of dystrophic pathology that increases the muscle fiber passive mechanics, mechanotransduction, and myofibrillar alterations that impair muscle function. Our new evidence finds similar MT changes in aging muscle. This parallel result has led us to define dystrophy-independent mechanisms that are involved in the loss of muscle function. The microtubule-associated protein, Tau, is responsible for stabilizing and bundling MTs and has been extensively studied

in the context of neurodegenerative disease. We find tau progressively increases in aging muscle fibers along with levels of deTyr-tubulin. Both are enriched at areas of disrupted myofibrillar structure, highlighting a potential role in the generation of these disordered regions. We further show that short-term overexpression of tau-GFP in the flexor digitorum brevis (FDB) of young mice phenocopies the observations made in aged muscle. GFP controls have no deleterious impact. We propose that tau accumulation is a consequence of aging that predisposes the proliferation of deTyr-enriched MTs that alter skeletal muscle structure and function.

103. Determining the Critical Window of Expression of Rfx1/3 and Their Underlying Molecular Mechanisms in Cochlear Hair Cell Development and Maintenance

Ningjin Wu

Oral Session L (Room 203)

Wu N., Gwilliam K., Amanipour R., Song W., Milon B., Elkon R., Hertzano R.

Our lab previously demonstrated that conditional deletion of Rfx1 and Rfx3 (Rfx1/3;Gfi1-Cre) in cochlear hair cells at embryonic day 16.5 causes profound hearing loss and rapid outer hair cell (OHC) degeneration, highlighting the essential role of Rfx1/3 during development. However, the critical window of Rfx1/3 expression and the molecular mechanisms by which they regulate hair cell maintenance remain unclear. To define the spatiotemporal expression of Rfx1/3, RNAscope™ was performed on cochlear tissue from embryonic and postnatal C57BL/6 mice. To assess their stage-specific function, we generated Rfx1/3 conditional knockout (cKO) models: Rfx1/3;Myo15-Cre, with postnatal day 0 deletion, and Rfx1/3;Prestin-CreERT2, with tamoxifen-induced deletion at P4 or P8. Auditory brainstem response (ABR) and distortion product otoacoustic emissions (DPOAEs) were used to evaluate hearing, followed by histological analysis. scRNA-sequencing on P7 Rfx1/3;Myo15-Cre cochlear sensory epithelia was performed to identify downstream targets. Rfx1/3 were expressed in hair cells throughout embryonic and early postnatal development. Rfx1/3;Myo15-Cre mutants showed elevated ABR and DPOAE thresholds by P16, with OHC loss starting at P12 in a basal-to-apical gradient. Rfx1/3;Prestin-CreERT2 mutants injected at P4 showed high-frequency hearing loss and OHC degeneration, whereas P8-injected mutants exhibited no significant deficits. Gene Ontology and KEGG analyses revealed pathways potentially regulated by Rfx1/3 in cochlear hair cells. These findings indicate that Rfx1/3 are essential for OHC development and maintenance, with a critical expression window before P8. Ongoing studies aim to determine their role in hair bundle formation and identify key survival-related targets downstream of RFX1/3.

104. The impact of chronic stress on RhoA expression in NAc D1-SPN region and projection-specific populations

Payel Das

Oral Session M (Room 223)

Das P., Khatri S.K.C., Campbell R.R., Franco D., Lobo M.K.

One of the predominant risk factors of Major Depressive Disorder is chronic stress (CS). In mice, in response to CS (chronic social defeat stress: CSDS; chronic witness defeat stress: CWDS), stress-susceptible mice show enhanced

negative affective behavior in behavioral tests. CS affects the nucleus accumbens (NAc) that has two subtypes of spiny projection neurons (SPNs): D1- and D2-SPNs, enriched with dopamine receptors 1 and 2, respectively. The D1-SPNs in different sub-regions of NAc play specific roles: activation of D1-SPNs in the NAc dorsal and ventral shells enhances reward and drives aversion, respectively. However, whether these subregion-specific or different projection (NAc->VTA/VP) -specific D1-SPNs have differential responses to CS is unclear. To gain insight into this, we are examining Ras homolog family member A (RhoA) expression in D1-SPN populations to VTA/ VP across NAc subregions after CSDS in males and CWDS in females. Previously, our lab has shown that CSDS induces RhoA in NAc-D1-SPNs, resulting in their dendritic atrophy and stress susceptibility. C57 mice that received retrograde Cre into the VTA/ VP mice underwent CS. After stress exposure, stress susceptibility and resiliency were detected by performing a three-chamber social interaction test. RNAscope on NAc slices showed that VTA projecting NAc-D1-SPNs in both dorsal and ventral shells of stressed groups have increased RhoA mRNA expression compared to the non-stressed controls. The susceptible group has a significantly higher RhoA mRNA expression than the control and resilient groups. The analysis in VP D1-SPNs is in progress.

105. Impact of antioxidant addition on drug dissolution: implications for NDSRI mitigation biowaivers

Rutu Valapil

Oral Session M (Room 223)

Valapil, R. R. , Polli, E. J.

Background: Nitrosamine impurities have garnered recent attention due to their presence in pharmaceuticals and their mutagenic risks. Recent studies and regulatory guidance emphasize on controlling nitrosamine impurities by the addition of antioxidants to tablets and capsules. Recent FDA guidance supports this, however, practical experience with this new guidance update remains limited. Objective: The study investigates the impact of added antioxidants on dissolution of diclofenac potassium tablets. Diclofenac potassium is BCS class II and has a secondary amine in its structure, making it susceptible to nitrosation. Six antioxidants were tested for their effect on in vitro dissolution. Methods: Two tablet formulation families of 50mg diclofenac potassium were fabricated with and without antioxidant. Tablets were subjected to some quality tests, including in vitro dissolution in Simulated Intestinal Fluid (USP SIF) and in sodium bicarbonate buffer. Dissolution profiles were compared using the similarity factor f_2. Results: All tablets using ascorbic acid, L-cysteine, or sodium bicarbonate did not impact dissolution in USF SIF and sodium bicarbonate buffer, per a liberal interpretation of f2 calculation in the 1997 FDA dissolution guidance, except formulation B tablets with antioxidant sodium bicarbonate in sodium bicarbonate buffer. Meanwhile, all tablets using caffeic acid, fumaric acid, or sodium ascorbate slowed dissolution in USF SIF and sodium bicarbonate buffer, except formulation B tablets with antioxidant sodium ascorbate. Conclusion: The addition of several antioxidants listed in the FDA control of nitrosamine impurities guidance did not affect in vitro dissolution of diclofenac potassium tablets, supporting potential biowaivers of such tablets.

106. LLGL2 protein participate in the brain development and cognitive function, likely through regulation of glutamate neurotransmission

Amna Zaib

Oral Session M (Room 223)

Aurang Zaib, A., Yaping, J., Taylor, R., Ahmed, Z.M., Riazuddin, S.

LLGL2 (MIM: 618483) encodes a polarity protein complex component 2 (Lethal giant larvae 2) that establishes basolateral polarity, asymmetric cell division, and cell migration. We identified six individuals from four unrelated families harboring splicing and three missense variants in the LLGL2 segregating with neurodevelopmental disorder(NDD), intellectual disability(ID), and microcephaly. Ex-vivo, overexpression of constructs harboring NDD-associated variants impacted the subcellular localization of encoded LLGL2 and cytoskeletal architecture. To get a deeper insight into cellular pathologies, we introduced a c.1456G>A;(p.Glu486Lys) LLGL2 variant HEK293T cells using the CRISPR-Cas9 system. High-resolution Imaging of Knockin cells revealed reduced expression of LLGL2 at plasma membrane, deficits in centrosome assembly, multipolar mitotic spindles, altered centrosome number and diameter, increased frequency of multinucleated cells, abnormal cytokinesis, increased DNA damage, and reduced proliferation potential. Flow cytometric analysis further validated significant alterations in all the cell cycle phases. Bulk mRNA sequencing showed significant dysregulation of the glutaminergic pathway and ERK1/2 regulator effect networks in Knockin cells, which are known to control excitatory neurotransmission and several physiological functions of the brain, including mood, behavior, and cognitive abilities. To further confirm the critical role of LLGL2 in brain development and function, we generated zebrafish morphants. Similar to human patients, we observed significant developmental deficits and reduced movement patterns in the llgl2 morphants. These deficits were significantly rescued with the co-injection of human wild-type LLGL2 mRNA but not the NDD-associated variants harboring mRNAs, further validating their pathogenic nature. In conclusion, our studies demonstrate a critical role of LLGL2 in neurodevelopment and cognitive function.

107. Functional characterization of capsule expression and epithelial cell invasion among Shigella serotypes

Brock Brethour

Oral Session M (Room 223)

Brethour, B. W., Wu, T., Barry E. M.

Shigella is the most prevalent cause of moderate-to-severe diarrhea in children between 1-5 years of age in low- and middle-income countries (LMIC). S. flexneri and S. sonnei are the most common species isolated in LMICs at approximately 68% and 25% respectively. One of the features that differ between these two species is the expression of a Group 4 Capsule (G4C) in S. sonnei. Previous literature demonstrated that a fourteen base pair deletion in etk, a gene necessary for capsule expression, prevents S. flexneri 2a strain 2457T from expressing a capsule; however, the presence or absence of a G4C has yet to be widely investigated across a broad collection of Shigella strains and serotypes. We hypothesize that there are additional S. flexneri serotypes that express a capsule, which impacts the ability to invade epithelial cells, a key feature of

Shigella pathogenesis. A comparison of the G4C genetic cluster among multiple different serotypes and strains was performed to better understand presence or absence of G4C both between as well as within serotypes. Mutations in etk were engineered in strains with an intact locus to determine the impact capsule has on epithelial cell invasion. The mutants that lack a capsule invaded HT29 epithelial cells at a significantly higher rate compared to WT. These observations support a more widespread expression of G4C on Shigella strains than previously recognized with important implications for pathogenic properties and for the development of efficacious vaccines.

108. Cathepsin B causes trogocytosis-mediated CAR T cell dysfunction

Kenneth Dietze

Oral Session M (Room 223)

Dietze, K.A., Nguyen, K., Pathni, A., Fazekas, F., Gebru, E., Atanackovic, D., Upadhyaya, A., Luetkens, T.

Chimeric antigen receptor (CAR) T cell therapy has shown remarkable efficacy in cancer treatment. Still, most patients receiving CAR T cells relapse within 5 years of treatment. CAR-mediated trogocytosis (CMT) is a potential tumor escape mechanism in which cell surface proteins transfer from tumor cells to CAR T cells. CMT results in the emergence of antigen-negative tumor cells, which can evade future CAR detection, and antigen-positive CAR T cells, which has been suggested to cause CAR T cell fratricide and exhaustion. Whether CMT indeed causes CAR T cell dysfunction and the molecular mechanisms conferring CMT remain unknown. Using a selective degrader of trogocytosed antigen in CAR T cells, we show that the presence of trogocytosed antigen on the CAR T cell surface directly causes CAR T cell fratricide and exhaustion. By performing a small molecule screening using a custom high throughput CMT-screening assay, we found that the cysteine protease cathepsin B is essential for CMT and that inhibition of cathepsin B is sufficient to prevent CAR T cell fratricide and exhaustion. Our data demonstrate that it is feasible to separate CMT from cytotoxic activity and that CAR T cell persistence, a key factor associated with clinical CAR T cell efficacy, is directly linked to cathepsin B activity in CAR T cells.

109. Novel basal ganglia pathways for regulating motor variability

Sophie Elvig

Oral Session M (Room 223)

Elvig, S.K., Oladunni, O., Wolff, S.B.E.

From dancing ballet to tying our shoelaces, complex motor skills are essential for our everyday lives. Over the course of learning these skills there is a transition from variable behavior to precise and stereotyped movements. This change in motor variability must be flexible, but also tightly regulated as variability is necessary to explore the motor space to find rewarded solutions, but also impairs peak performance. The mechanisms by which variability is regulated and implemented in the mammalian brain remain unclear. The basal ganglia have been implicated, and a transition from dorsomedial striatum (DMS; variable behavior), to dorsolateral striatum (DLS; stereotyped behavior), correlates with the decrease in variability during learning. Here, we suggest a novel mechanism which contributes to regulating the DMS-DLS transition and thereby variability during skill learning and execution. The subthalamic nucleus (STN)

sends largely unexplored feedback projections to striatum: directly to DLS and indirectly to DMS via the anterior thalamic nuclei (ATN). STN receives broad cortical and subcortical input, allowing an integration of striatal signals with internal and external state information. Thus, STN is well positioned to modulate the DMS-DLS transition and dynamically regulate motor variability. Chronic silencing of the STN-DLS projection impairs, while silencing of the STN-ATN or ATN-DMS projections promotes stereotypy during skill learning. STN-ATN silencing in experts has no effect, while STN-DLS silencing disrupts stereotyped performance. Our results suggest novel roles for STN in regulating motor variability, likely by modulating DMS-DLS interplay, as well as highlighting the unappreciated complexity in the basal ganglia motor circuitry.

110. Ca2+/Calmodulin Dependent & Independent Regulation of Obscurin Kinase 1

Rex Gonzales

Oral Session N (Room 115)

Gonzales, R. R., Takagi Y., Wright, N., Kontrogianni-Konstantopoulos, A.

The heart is a functional syncytium composed of cells that must beat in unison to ensure effective blood circulation. This coordinated contraction requires the rapid transmission of electro-mechanical information from cardiomyocyte to cardiomyocyte. The Intercalated Disc (ICD) – a specialized microdomain of the cardiac sarcolemma, couples adjacent cardiomyocytes and is known to be dysregulated in disease. N-cadherin, the sole classical cadherin molecule at the ICD, serves as both a receptor and ligand for communicating mechanochemical signals between cells. Obscurins are cytoskeletal proteins with regulatory roles in myofibrillogenesis and cellular adhesion. As signaling molecules, Obscurins act as linkers between the sarcomere and the subcellular domains of muscle cells including the sarcoplasmic reticulum and the ICD. Obscurin-B (~870 kDa),the largest known isoform, has two enzymatically active kinases. In particular, our group has demonstrated that Kin1 promotes cardiomyocyte adhesion and chemical coupling via phosphorylation of N-cadherin, at Serine 788. Despite Kin1's crucial role in cardiomyocyte communication, the regulatory mechanisms that modulate its function remain undefined. In vitro binding & activity assays support Kin1's regulation by calmodulin (CaM). Interestingly, in-silico modeling suggests that mechanical force can induce unwinding of Kin1's regulatory domain independent of CaM binding. This unwinding promotes a conformational change to a semi-stable intermediate state that may be capable of substrate binding and/or enzymatic activity. To address this hypothesis, the mechanical properties of Kin1 are being assessed using single molecule magnetic tweezer force spectroscopy. This approach facilitates measurement of key folding & unfolding parameters of Kin1 in the physiological force regime.

111. KATP channel–dependent electrical signaling links capillary pericytes to arterioles during neurovascular coupling

Dominic Isaacs

Oral Session N (Room 115)

Isaacs, D., Xiang, L., Hariharan, A., Longden, T.

The brain has evolved mechanisms to dynamically modify blood flow, enabling the

timely delivery of energy substrates in response to local metabolic demands. Several such neurovascular coupling (NVC) mechanisms have been identified, but the vascular signal transduction and transmission mechanisms that enable dilation of penetrating arterioles (PAs) remote from sites of increased neuronal activity are unclear. Given the exponential relationship between vessel diameter and blood flow, tight control of arteriole membrane potential and diameter is a crucial aspect of NVC. Recent evidence suggests that capillaries play a major role in sensing neural activity and transmitting signals to modify the diameter of upstream vessels. Thin-strand pericyte cell bodies and processes cover around 90% of the capillary bed, and here we show that these cells play a central role in sensing neural activity and generating and relaying electrical signals to arterioles. We identify a KATP channel–dependent neurovascular signaling pathway that is explained by the recruitment of thin-strand pericytes and we deploy vascular optogenetics to show that currents generated in individual thin-strand pericytes are sent over long distances to upstream arterioles to cause dilations in vivo. Genetic disruption of vascular KATP channels reduces the arteriole diameter response to neural activity and laser ablation of thin-strand pericytes eliminates the KATP-dependent component of NVC. Together, our findings indicate that thin-strand pericytes sense neural activity and transform this into KATP channel–dependent electrometabolic signals that inform upstream arterioles of local energy needs, promoting spatiotemporally precise energy distribution.

112. Microtentacle-Mediated Heterotypic Clustering of Tumor Cells and Neutrophils in Breast Cancer Metastasis

Julia Ju

Oral Session N (Room 115)

Ju, J.A., Thompson, K.N., Annis, D.A., Mull, M.L., Gilchrist, D.E., Moriarty, A., Noto, M.J., Vitolo, M.I., Martin, S.S.

Circulating tumor cells (CTCs) travel through the vasculature to seed secondary sites and serve as direct precursors of metastatic outgrowth for many solid tumors. Heterotypic cell clusters form between CTCs and white blood cells (WBCs) and recent studies report that a majority of these WBCs are neutrophils in patient and mouse models. Even though CTC clusters encompass a small fraction of total CTC events, they have a 25-50x higher metastatic potential and are associated with decreased overall survival compared to single CTCs. Our lab discovered that CTCs produce tubulin-based microtentacles (McTNs), which promote reattachment, retention in distant sites during metastasis and formation of tumor cell clusters. Neutrophil-CTC clusters help CTCs survive the harsh vascular environment to promote successful metastasis, however, the mechanism of this interaction is not fully understood. Utilizing TetherChip technology to recapitulate the nonadherent environments of metastasis, we found that primary and differentiated neutrophils produce McTNs composed of detyrosinated and acetylated α-tubulin and vimentin. Differentiation into neutrophils induced homotypic cluster formation, migration, and reattachment to fibronectin, which were suppressed with the tubulin-depolymerizing agent, Vinorelbine. Finally, co-culturing neutrophils and tumor cells formed heterotypic clusters that enhanced migration and Vinorelbine treatment reduced these phenotypes. CTC-neutrophil clusters have higher metastatic efficiency, and by demonstrating that neutrophils form McTNs, we reveal a new possible mechanism for how

neutrophils interact with tumor cells. These findings further support the idea that developing cluster-disrupting therapies could provide a new targeted strategy to reduce the metastatic potential of cancer cells and yield more successful clinical outcomes.

113. Paradoxical Role of CD8+ T Cells and Lung Cancer Derived IFN-γ in Downregulating the Anti-Tumor Immune Response

Christina Kratzmeier

Oral Session N (Room 115)

Kratzmeier, C., Taheri, M., Mei, Z., Lim, I., Khalil, M., Leyder, E., Li, D., Banerjee, A., Krupnick, A.S.

Being a barrier mucosal organ, the lung provides a unique immunoregulatory environment. We hypothesized that immunoregulation of lung cancer differs from that of other malignancies. Contrary to the accepted dogma, we found that the presence of CD8+ T cells accelerated the growth of genetically engineered, carcinogen induced, and transplantable lung tumor models, while ameliorating the growth of non-lung tumor models. Specifically, we found that CD8+ T cells promote homing of CD4+Foxp3+ T regulatory cells to the tumor bed by increasing levels of CCR5 chemokines, CCL3/4/5. Further cytokine analysis of the tumor beds revealed a significant increase of Th-1 polarizing cytokines, IFN-γ and TNF-α, in LLC lung cancer-bearing but not B16 melanoma-bearing mice in the presence of CD8+ T cells. Importantly for translational applications, high levels of IFN-γ are also seen at mRNA and protein levels in human lung cancer patients. Neutralization of these Th1 cytokines resulted in accelerated tumor growth in B16-bearing mice but counterintuitively decreased tumor growth in LLC-bearing mice. Surprisingly, we identified lung tumor cells themselves as prominent producers of IFN-γ, and knockout of IFN-γ from LLC cells significantly reduced their growth in vivo. Our data suggests that immunoregulation of lung cancer is unique and may require novel immunomodulating strategies for future treatments.

114. The Impact of Product Formulation on the Pharmacokinetics and Pharmacodynamics of Cannabis Edibles

Emma Salazar

Oral Session N (Room 115)

Salazar, E., Kumar, L., Zamarripa, A., Weerts, E., Wolinsky, D., Klawitter, J., Christians, U., Vandrey, R., Spindle, T.

The purpose of this study is to learn more about the short-term effects of oral cannabis products, which are also called edibles. We are interested in studying how different formulations of cannabis edibles affect your ability to perform certain tasks such as balancing, short-term memory, and attention. This research also is being done to understand if these different formulations change how THC moves through your body. THC is the main component in cannabis that makes people feel high. This research is becoming more important because there is a growing interest in the use of cannabis edibles for health conditions or recreational use, and these products are now available in a variety of formulations. The results of this study will help us better understand whether the effects someone feels from using cannabis edibles or if the amount of THC they get into their system differs based on the formulation they use.

115. The TNF Receptor Superfamily Member Fn14 Extends Survival and Modulates Innate and Adaptive Immune Responses in High-grade Gliomas

Pranjali Kanvinde

Oral Session N (Room 115)

Kanvinde, P. P., Malla, A. P., Seas, A. A., McFarland, E., Sharifai, N., Bar, E. E., Winkles, J. W., Woodworth, G. W.

The TNF receptor superfamily member, fibroblast growth factor-inducible 14 (Fn14), promotes glioma cell survival and invasion and is associated with poor patient outcomes. Fn14 overexpression in gliomas enhances brain invasion, increases recruitment of tumor-associated macrophages/microglia (TAMMs) and corelates with reduced survival in both human patients and murine models. Fn14 expression has been detected in non-tumor cells within the glioma tumor microenvironment (TME), but the functional impact of these cells remains unclear. Here, we sought to determine the impact of tumor- vs host-derived Fn14 on malignant progression, survival and immune microenvironment using Fn14-intact and -knockout (-KO) cells and immunocompetent mice. We found that both tumor and host-derived Fn14 contribute to tumor progression. Dual deletion of Fn14 significantly prolongs survival and reduces levels of infiltration of TAMMs and exhausted T-cells in the TME. Thus, our study identifies Fn14 as an important factor contributing to tumor progression, survival and immunosuppression in gliomas.

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